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PROF. DILDAR KONUKOGLU
Address: Maslak Mah. AOS 55. Sok. No: 2, 42 Maslak A
Phone: Blok Daire: 231 Sarıyer, İstanbul-Turkey
Fax: +90 212 241 26 53
e-mail: +90 212 241 26 54
web: www.kbud.org.tr
info@kbud.org.tr

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Phone: +90 216 550 61 11
Fax: +90 212 550 61 12
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PL-01

The Preference of Serum or Plasma Samples for Biochemical Analyses: Advantages and Disadvantages

Goncagül Haklar

Department of Biochemistry, School of Medicine, Marmara University, Marmara University Pendik E&R Hospital Biochemistry Laboratory, İstanbul

Quality can be attained after obtaining a specimen fit for analysis and reporting accurate and reliable results in the shortest possible time. Analytical and/or biological interferences play a pivotal role in decreasing quality throughout the total testing process. An ideal sample should be ready to use, stable, and pure (acellular). Besides, it should reflect the in vivo state, not lead to any interference, and not effected from preanalytic factors. Several anticoagulants are used in clinical biochemistry for different purposes. Many factor effect our decision making on sample type. Turnaround time can have a direct effect on patient outcome. Recommended clotting times for serum collection tubes generally range from 30-60 minutes. Use of plasma allows laboratories to process and test specimens quickly, while avoiding latent fibrin formation due to incomplete clotting. Sample volume and sample quality are also important factors. On the other hand serum is almost "cell free". Most assays are compatible with both serum and plasma. But for certain assays, differences in results necessitate a change in reference ranges. Serum samples are nearly cell-free, have good storage stability for most analytes, and useful in wide range of assays. Plasma samples have also several advantages: Shorter TAT, more representative of in vivo state, available plasma yield 15-20% higher than serum, no interference due to delayed clotting, and decreased risk for hemolyis and thrombocytolysis. On the other hand disadvantages for serum usage are risk of pseudohyperkalemia in patients with thrombocytosis, longer TAT, and instrument or test interference from fibrin, esp. with anticoagulation therapy. Likewise, disadvantages for plasma samples are risk of the formation of small clots, difficulty in producing platelet free plasma, presence of fibrinogen, and influence of anticoagulant on assay. In conclusion, serum and heparin plasma both have benefits and limitations in clinical chemistry and the selection of serum or heparin plasma may be dependent on the specific setting.

PL-02

Effect of Blood Collection Technique in the Prevention of Hemolysis

Evin Ademoğlu

Department of Medical Biochemistry, Istanbul University, Istanbul Faculty of Medicine, Istanbul

In clinical laboratories hemolysis is responsible approximately 60% of unsuitable samples and it is a foremost cause of preanalytical errors that lead to erroneous test results, sample re-collection, prolonged turnaround time and waste of resources. 97-98% of hemolyzed samples are related to in vitro factors such as phlebotomist, blood collection technique and devices and, handling and centrifugation of blood samples. The rest of hemolyzed samples occur in vivo due to biological factors such as hemoglobinopathies, severe infections, transfusion reaction, and thus virtually unavoidable. In accordance with the degree of hemolysis, it causes both false positive results by additive effect and spectral interference and, false negative results by chemical interference and dilution effect in many tests such as K^+, LDH, AST, GGT, ALT, creatinine, CK, glucose, uric acid, cholesterol. In addition, it affects coagulation tests through thromboplastic compounds released from blood cells. The traditional methods like blood collection by syringe account a remarkable cause of in vitro hemolysis. Blood collection by syringe cause hemolysis due to excessive pressure and turbulence that created by rapid withdrawal of plunger during blood collection and/or high pressure to the plunger while transferring the blood to a tube. Since, syringe may reduce the physical stress on the blood cells by controlling the pressure during venipuncture, it is still in use as an alternative in patients with fragile veins such as pediatric and oncologic cases. At variance with available commercial systems, S-Monovette® (Sarstedt AG&Co., Germany) offers an alternative blood collection system both with vacuum and aspiration options. Depending on the patient's veins and the preference of phlebotomist, S-Monovette® can either used as a standard evacuated tube or a syringe with no need of blood transfer from the syringe.

In vitro hemolysis cannot be totally prevented but, it can be minimized by standardization and tight control of preanalytic stages. The selection of blood collection devices and technique take an important part in achieving this goal. In all conditions where a difficult venipuncture and/or vacuum force of the tube may increase the probability of hemolysis, care should be taken to select the most appropriate blood collection device and technique.

PL-03

Preanalytical Phase in Ethanol Assays

Turan Turhan

Department of Clinical Biochemistry, Ankara Numune Training and Research Hospital, Ankara

As with all other biochemical assays, problems stemming from preanalytical errors in ethanol assays can misguide decision-making on diagnosis and treatment of patients, as well as judicial processes. Therefore, preanalytical phase in ethanol assays is of utmost importance, and ethanol analysis is one of the most bothersome tests for the laboratory specialist. Awareness of the variables in preanalytical phase of ethanol assays is important to minimize these problems.

The difference between ethanol concentrations in blood and in other sample types such as exhaled air, saliva or urine may be clinically irrelevant, but important in forensic terms. Breathalyzers, which are being used routinely in the legal practice to measure ethanol concentrations in exhaled breath, are low-cost devices yielding accurate, precise and legally acceptable results.

As mandated in Item 12 of Regulations on Clinical Laboratories, titled 'Operating Principles of Clinical Laboratories', which was published on Official Gazette dated 09/10/2013 and issued 28790, stating 'Operating principles of clinical laboratories conducting analysis of illicit and abused drugs and substances and of laboratories present in alcohol and drug dependence treatment centers are established by the Ministry'; directives regarding the working principles of clinical laboratories conducting ethanol analysis in blood samples were established and published on 11/07/2017 with issue number 95966346.

PL-05

Biological Variation and Test Quality

Fatma Taneli

Department of Clinical Chemistry, Manisa Celal Bayar University Faculty of Medicine, Manisa

Laboratory medicine is a science that provides information about the health status of the patient based on analysis on the biological fluids. However, the concentrations of the analytes in the biological fluids are not stable due to the constantly changing human nature and this is briefly defined as biological variation. Understanding of biological variation is important for accurate evaluation of laboratory results.

Classification of sources of biological variability:

1. It covers changes throughout human life: covers the neonatal period, childhood, adolescence, menopause, old age and age related reference intervals.
2. Includes cyclical changes in the rhythmic part of the subjects over time. It includes daily (cortisol, growth hormone), monthly (LH, FSH, progesterone), seasonal (vitamin D). In order to make clinical interpretation, it is necessary to know the reference values appropriate to these cycles and to perform serial analyzes during different periods of this return for clinical interpretation for some tests.
3. Includes random value changes at decision points

Variabilities may arise from preanalytical phase (preparation of patient, preparation of sample containers, sampling, laboratory transfer, preparation before analysis), analytical phase and postanalytical phase (final control, delivery of results).

Individual variation CVI is defined as random fluctuations around the equilibrium point of each individual.

Variation between individuals: CVG Individuals's equilibrium points can be different from each other, and the variation resulting from this difference is defined as inter-individual variation.

Biological variation calculation algorithm; It can be summarized as choosing few reference individuals, applying exclusion criteria, storing samples for batch analysis, canceling out the outliers values, calculation of CVA, CVP,CVI by ANOVA analysis.

Each laboratory does not have to assess its own biologic variation calculations, they can apply guidelines and literature data.

In order to have different results in serial measurements, the numerical difference of the results should be larger than the total variation. This value is called the critical difference (CD) or reference change value (RDD).

RDD=2½* Z* (CVA2+CVI2) ½

The RDD value is the same for all laboratories since the formula used to achieve the desired quality values of the laboratories depends on CVI in particular. This means that for changes in health status, the majority of analytes will show a better approach than the population-based reference intervals of the RDD concept because of the high individuality (the in-person biological variation is lower than the inter-individual biological variation)

Individuality index: Population-based reference values are named index of individuality (II) and are determined by the ratio of intra-individual biological variation to inter-individual biological variation. The individuality index (II) is calculated by the formula CVI/CVG.

Interpretation of the individuality index: The individuality index is a parameter giving information about the suitability of the test results to be compared with the reference interval. As the index result is smaller, individuality is increased. If II < 0.6, individuality is high and the results of the person cover only a small part of the reference interval. For this reason, it is appropriate that the results are assessed according to one's own previous results. If II> 1.4 the patient results covers the majority of the reference interval and it is appropriate to evaluate the results according to the reference values. As a result, it is sufficient to compare the result of a single test with the population-based reference intervals for analytes whose individuality index is above 1.

Biological variation data can be used in; analytical quality evaluation, setting quality criteria, the usefulness of population based reference ranges for tests, notification of the clinical meaningful changes in the test results to the doctor in medical laboratories.

PL-06

Interferences in Biochemical Measurements

Sabahattin Muhtaroğlu

Department of Medical Biochemistry, Erciyes Üniversity Faculty of Medicine, Kayseri

In the clinical laboratory, errors that occur in the preanalytical phase of testing may account for up to 75% of total laboratory errors; 26% of these may have detrimental effects on patient care, which contribute to unnecessary investigations or inappropriate treatment, increase in lengths of hospital stay, as well as dissatisfaction with healthcare services. Hemolysis, icterus and lipemia (HIL) are the most frequent endogenous interference that can influence results of various laboratory methods by several mechanisms. The most often reason of hemolysis is the result of improper specimen collection and handling.The most common preanalytical cause of lipemic samples is inadequate time of blood sampling after the meal or parenteral administration of synthetic lipid emulsions. The major exogenous sources of interference are drugs and their metabolites. Components from blood collection tubes, such as stoppers, lubricants, surfactants, and separator gels, can leach into specimens and/or adsorb analytes from a specimen; special tube additives may also alter analyte stability. Because of these interactions with blood specimens, blood collection devices are a potential source of pre-analytical error in laboratory testing. Recently, sophisticated chemical analyzers have automatically detected the HIL status and have reported HIL index values. The HIL alert index (also known as the threshold level) is defined as the lowest concentration of HIL that interferes with chemical analyses, yielding a bias >10%.

PL-07

Preanalytical Phase and Hemostasis Tests

Mesude Yılmaz Falay

Department of Clinical Biochemistry, Ankara Numune Training and Research Hospital, Ankara

Hemostasis is the homeostasis between the blood cells, the vein wall and the plasma proteins. Excessive bleeding is prevented when tissue integrity is impaired, blood is left in the blood vessel under physiological conditions, and adequate and quality wound healing is achieved with hemostasis. Hemostasis stages include primary hemostasis (weak plugging), secondary hemostasis (intact plugging), and fibrinolysis (wound healing). In daily practice, the tests we use most often are the secondary hemostasis tests PT, APTT, TT and Fibrinogen. The second-line hemostasis tests we performed in the in vitro environment do not show the complete in vivo environment. For this reason, the preanalytical universe must be well standardized and the limitations of the hemostasis test must be well known by the laboratory expert. Pre-analytical factors in hemostasis tests can lead to false positive or false negative results, leading to diagnostic errors. Blood sample should be taken with blue capped tubes containing sodium citrate (105-109 mM or 129 mM, 3.2% or 3.8%). PT and aPTT

results are longer and INR is higher in 3.8% sitrat-containing tubes. The ideal anticoagulant / blood ratio is 1/10. The blood volume should not be less than 90% of the total tube volume. Poor filling of the tubes leads to erosion at the time of clotting due to sample dilution and excessive citrate calcium binding. Venous stasis during blood intake should not last longer than 1 minute, increase in fibrinogen and other factors, shortening of aPTT and PT may occur in the case of stasis. After blood ingestion, the tube should be inverted 3-6 times to prevent interference with the sample and anticoagulant and clotting. Heavy exercise should be avoided 24 hours before blood is given. Laboratory information should be provided about heparin, vitamin K antagonists, anti-coagulant drugs such as DOACs, or patients using antiplatelet drugs. Samples should be run within 1-4 hours. The sodium citrate maintains the sample pH between 7.30-7.45. Plasma samples that are not to be studied immediately can be stored at -8 ° C. The pH value of the sample is kept at -8 °C. Previously frozen specimens should be thawed for 5 to 10 minutes in a 37 °C water bath. For platelet function tests, the patient must have been on an empty stomach and should have been smoking cigarettes. If drugs that affect platelet function are used (aspirin, NSAID), these drugs should be discontinued 10-14 days before the test. The pneumatic system should not be used in the sample transport, the samples should be run within 4 hours, not placed on ice or in the refrigerator.

PL-08

Preanalytical Error Sources in Urine Specimens

Cevat Yazıcı

Department of Medical Biochemistry, Erciyes University, Faculty of Medicine, Kayseri

Urine may be a waste product, but it contains an enormous amount of information. Well-standardized procedures for collection, transport, sample preparation and analysis should become the basis of an effective diagnostic strategy for urinalysis. As reproducibility of urinalysis has been greatly improved due to recent technological progress, preanalytical requirements of urinalysis have gained importance and have become stricter. Since the patients themselves often sample urine specimens, urinalysis is very susceptible to preanalytical issues. In order to increase the reliability of the test results and to reduce the cost, the precautionary measure and prevention is very important in the preanalytical phase. The laboratory must monitor and evaluate the overall quality of the preanalytic systems and correct identified problems for each specialty and subspecialty of testing performed. The laboratory must establish and follow written policies and procedures for an ongoing mechanism to monitor assess, and when indicated, correct problems identified in the preanalytic systems. The preanalytic systems assessment must include a review of the effectiveness of corrective actions taken to resolve problems, revision of policies and procedures necessary to prevent recurrence of problems, and discussion of preanalytic systems assessment reviews with appropriate staff. The laboratory must document all preanalytic systems assessment activities. An effective diagnostic strategy from urine should be based on standard procedures for collection, transport and analysis. The time of specimen collection must be recorded both on the examination request and on the subsequent report to aid in the correct interpretation of findings.

PL-09

Importance of Communication for Preanalytical Processes

Uzay Görmüş DéGrigo

Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Solna, Sweden

It is well-known that although the total amount of errors may change for each laboratory, 60-75% of the total laboratory errors are of preanalytical origin worldwide. The most common preanalytical errors can be summarized as follows:

- Inappropriate sampling
- Sample or test loss
- Incorrect barcode or name on the sample
- Sampling during intravascular drug or fluid applications
- Incorrect tube usage
- Inadequate blood/anticoagulant ratio
- Improper handling and storage conditions

In terms of patient-centered evaluations, error classification is expanded; in this manner, pre-preanalytic phase covers the test request decisions in combined to the clinical evaluations of patients, while preanalytic phase contains the subsequent processes beginning with obtaining the sample till the measurement of the parameters. As preliminary errors mostly involve the procedures prior to the laboratory, such as patient preparation, sample collection, and specimen collection, the efforts spent to reduce laboratory errors will not be enough without communicating with all related staff. Since health area is directly related to human life, it is very important for all departments to communicate well with each other. Moreover, in various publications, it was emphasized that laboratory experts should increase communication with clinicians not only for the preanalytic stage, but also during prepreanalytic and postpostanalytic stages. Only a few weeks ago, at the beginning of this year (2018), the Ministry of Health published the 'Rational Laboratory Usage Consultation Procedure' and the workflow schedule were established to emphasize the importance of the communication between laboratory and almost every unit in the healthcare area, but it is essential to determine the communication principles and programs of each laboratory independent of the procedures and schedules, to reduce mistakes and to obtain more reliable results. For this purpose, it is necessary to establish a patient-oriented communication plan in which all relevant units are included, taking into consideration the general communication rules of each laboratory. Today, even when international quality standards are established, the importance of sharing information and evaluating the use of shared information is emphasized. As 60-80% of the clinical decisions were made by the help of various laboratory results, the communication of laboratory experts, clinicians and healthcare professionals is crucial for faster and more accurate decisions.

PL-10

Pre-Pre-Analytical Phase: Inappropriate Test Requests and Quality Indicators

Dildar Konukoğlu

Department of Medical Biochemistry, Istanbul University Cerrahpasa, Cerrahpaşa Medical Faculty, Istanbul

There are three general reasons accounted for most laboratory test ordering: Diagnosis, monitoring therapy and screening for asymptomatic disease. The process between performing the test request and using the results for the benefit of the patient is called the ''Total Test Process''. According this term total test process has been divided into five phases: pre-pre-analytic, pre-analytic, analytic, postanalytic, and post-post-analytic. Pre-pre-analytic steps contain initial procedures not performed in the clinical laboratory and outside the control of laboratory personnel (i.e. patient identification, the time of test order, appropriateness of the test, sample collection and sample transportation. The post-postanalytic steps are final procedures performed outside the laboratory, ie. receiving, interpreting, and using laboratory information for patient management. It has been suggested that pre-pre-anaytic and post-post analytic phases are more error-prone than the other phases. In particular, studies performed on the pre-pre-analytical phase show that failure to order appropriate diagnostic tests are related to the missed and delayed diagnosis. Laboratory related causes of diagnostic error are classified as;

- Inappropriate test ordered
- Appropriate test not ordered
- Appropriate test result not used properly
- Appropriate test result delayed/missed
- Appropriate test result wrong/inaccurate

Studies of laboratory test ordering have shown that unnecessary utilization of diagnostic tests in teaching hospitals is common. The unnecessary repetition of tests is the most common type of laboratory test overutilization. Unnecessary tests increase the laboratory workload and costs. Although some of the overuse of diagnostic tests is due to physicians' practice of defensive medicine, it is also clear that most physicians do not know how much tests cost. Other factors, such as patient expectations, insufficient understanding of the limitations (operating characteristics) of tests, inability to retrieve the results of a test already performed, learned behaviors, and economic incentives, may also influence ordering behavior. It is also important that the test is used according to the diagnostic power of the test as well as selecting the correct test for both clinicians and laboratorians. The characteristics of diagnostic test accuracy are sensitivity, specificity, predictive values, likelihood ratios, the area under the Receiver Operator Characteristics (ROC) curve, Youden's index and diagnostic odds ratio.

Arange of quality indicators has established by The International Federation of Clinical Chemistry and Laboratory Medicine WG on Laboratory Errors and Patient Safety. Quality indicators for inappropriate test requests are associated with Appropriateness of Test request and Request form Order entry as following.

1. Number of requests with clinical question (outpatients)/total number of requests (outpatients)
2. Number of appropriate requests, with respect to clinical question (outpatients)/number of requests reporting clinical question (outpatients)
3. Number of unintelligible outpatient requests/total number of outpatient requests
4. Number of outpatient requests with errors in physician ' s identification/total number of outpatients requests
5. Number of outpatients requests with errors concerning test input (missing)/total number of outpatient requests
6. Number of outpatient requests with errors concerning input of tests (added)/total number of outpatients requests
7. Number of outpatients requests with errors concerning test input (misinterpreted)/total number of outpatients requests
8. Number of inpatients requests with errors concerning test input (missing)/total number of inpatients requests
9. Number of inpatients requests with errors concerning input of tests (added)/total number of inpatients requests
10. Number of inpatients requests with errors concerning test input (misinterpreted)/total number of inpatients requests

In conclusion, clinicians and laboratorians should all be concerned about the effects of that laboratory test and whether the performance of it was useful for the patient or for the public's health. Also, the use of diagnostic test algorithms can be improve test selection.

PL-11

The Importance of Preanalitical Phase in Immune Tests

Özlem Gülbahar

Department of Medical Biochemistry, Gazi University, Medical Faculty, Ankara

Immunoassay methods are widely used in clinical laboratories and many tests are analyzed with them. Immun-nephelometric and immuno-turbidimetry methods, radioactive labeled methods (RIA/IRMA) and non-isotope-labeled methods (chemiluminescent, electrochemiluminescent, fluorescent, enzyme etc.) are various methods used in immunoassays. All immune methods depend on antigen-antibody binding principle. Immunoassays are highly affected by any situation affecting antigen-antibody binding than preanalytical factors such as hemolysis, icter and lipemia affecting clinical chemistry tests. For example, some medications are important preanalytical factors that can lead to false positive or false negative (lesser) results. Additionaly, it should be considered that the metabolites of the drug may mimic the analytes in the measurement of immunosuppressive drug levels, and may cause false positivity via cross-reaction. Also, various serum antibodies may cause false positive or negative results. These may be specific (HAMA etc.) or nonspecific (RF etc.) antibodies. Thus, preanalitic factors should be evaluated as soon as the incompatibility are found between immunoassay test results and the clinical situation of the patient (medications, presence of an additional disease which may lead to the formation of interferent antibodies etc.). In case of antibody-based interference suspection, demonstration by further examination is necessary. As a result, antibody interference should be kept in mind during interpreting the results.

PL-12

Autoverification and Preanalytic Errors

Yavuz Gülen

Department of Medical Biochemistry, Erenkoy Physiotheraphy Hospital, İstanbul

In recent years, various autoverification applications have been developed and implemented in order to safely reduce the increasing workload due to increasing work volume and variety of tests in clinical laboratories.

According to CAP (College of American Pathologists), Auto verification is an application submitting the test results that occur on devices to LIS and comparing test results with labarotory-defined acceptance parameters. If the results fall within this defined parameters The Results are released to patient reporting formats without any additional laboratory staff intervention. Any data that fall outside the defined parameters is reviewed

by laboratory staff prior to reporting [1]. The aim of this application is to provide accurate, fast, reliable and objectively verified results.

We applied an autoverification application based on delta check and previous results of patients at Beykoz State Hospital between 23 March 2012-5 january 2014 time interval for 125680 patients report. It included various algorithms combining verification range,delta check, dates, previous results. Total Autoverification rate was % 70 for all reports having Biochemistry, Hormone, Coagulation test results. Most of unautoverified results were nonerroneous and were mannually verified. The rest of results had various preanalitic, analitic and postanalitic errors. Most of erroneous results were preanalitic errors including interference (hemolysis,lipemia,icterus), contamination (gel, EDTA, i.v fluid), mislabeled specimen and some analitic errors due to reagent deterioration, cross reaction to some analytes and postanalitic errors due to script error.

A study involving 49 facilities was conducted by CAP in 2014. An important finding in this study was that the use of higher number different delta check analytes detected significantly more problems [2]. Using a larger number of different analytes for delta checks appears to have more value than using only a few. Basicaly delta check using applications have more advantage than others.

PL-13

Management of Preanalytical Processes in Metabolism Tests

Asuman Gedikbaşı

Department of Biochemistry, Dr. Sadi Konuk Education and Research Hospital, İstanbul

The Metabolic Laboratory provides a national service for the screening, diagnosis and monitoring of patients with suspected and known inborn errors of metabolism through a highly skilled tecnical and clinical team. The laboratory offers investigations into amino acids in urine and plasma, urine organic acids, acylcarnitines in dried blood spots for metabolic disorders. There is a range of analytical chemistry instruments applied in the metabolomics analyse: techniques for separation of metabolites (gas chromatography, liquid chromatography and capillary electrophoresis), detection techniques that allow the analysis of metabolites (mass spectroscopy and nuclear magnetic resonance spectroscopy) and the use of various software-data banks for the identification of metabolites. Metabolism tests are associated with a wide range of preanalytic variables that might affect test performance and test results because of the diverse specimen types and conditions, patient preparation status, and highly complex test procedures. Obtaining necessary clinical, medication, nutritional status, and other patient information that is critical for effective test result interpretation also can be challenging.

In this presentation; the preanalytical phase in metabolism tests was handled in two directions by giving examples from own experiences. The first is patient-related process that must be questioned in clinical interpretation such as; nutritional status, drug use, and maternal interference factors, especially in neonatal screening tests. The second is the sample related process which include correct sampling, processing and storage at the appropriate conditions. Firstly; preanalytic process control in neonatal screening tests with Tandem Mass Spectrometry (TMS); the feeding and treatment status of the baby and the interferences of the dry blood sample taken on the filter paper will be discussed through real cases. Later, the preanalytical process of serum and plasma samples in quantitative amino acid analyzes by liquid chromatography mass spectroscopy (LC-MS/MS), and preanalytical process of organic acid analysis in spot urine sample by gas chromatography-mass spectrometry (GC/MS) will be presented by own experience.

PL-14

Preanalytic Process Control in Dialysis Patients

Sema Uslu

Department of Medical Biochemistry, Eskişehir Osmangazi University, Faculty of Medicine, Eskişehir

Chronic renal failure is defined as chronic and progressive deterioration of all functions of the kidneys. When the glomerular filtration rate decreases to 5-10 ml/min, patients who enter into end-stage renal failure need dialysis treatment from this period. Properly scheduled and appropriate dialysis therapy is life-saving for many patients.

Biochemical laboratories make a significant contribution to the treatment of dialysis, but the complications they are exposed to during the course of treatment, like the changes in exercise and lifestyle, and many dietary factors can affect the results of biochemical analysis negatively. It is not desirable to see negative reflections on the treatment protocols of patients when these adverse events are added to unwanted errors in the intake and transport of biological samples such as blood and urine.

In addition to the removal of toxic substances and metabolites accumulated in the body by dialysis, some essential molecules may also be lost. Replacement therapy for these molecules can interfere with biochemical analysis techniques. Certain guideline tests, such as serum or urine creatinine, glomerular filtration rate, albumin, can be seriously affected by all the summarized preanalytical factors.

Dialogue between the clinician and the laboratory specialist on the preanalytical control of dialysis patients can be controlled by the clinician accurately and thoroughly describing the patient's information and laboratory experts by the clinician evaluating the probabilities and reasons for refusing hemolysis, bilateral, lipemic or heparinized blood samples.

One way of this control includes a procedure in the laboratory test guides that defines the sampling and transport phases of the dialysis patients in order to break the wrong habits of some healthcare personnel and minimize the sources of preanalytical errors.

In today's conditions, patient awareness cannot be ignored, which is why guidelines for the education of patients and their families can provide a wide range of information to minimize the patient-related part of the source of preanalytical errors. Thus, patients will be able to follow themselves and become an important leg of control.

PL-15

Preanalytical Phase and Point of Care Testing

Banu İşbilen Başok

Department Medical Biochemistry, University of Health Sciences Tepecik Training and Research Hospital Izmir

Point of Care Testing (POCT) defines as ‘a test can be done with a kit, device, or equipment that is hand-carried or transiently brought to the patient near side by a nurse, physician, medical laboratory technician or medical laboratory technician' according to the Medical Laboratory Regulation. POCT includes laboratory tests that analyzed by non-laboratory personnel in any field outside the laboratory. For this reason, errors that may occur in preanalytical, analytical and postanalytical phases as in the tests performed in medical laboratories apply in POCT. Commonly used POCT are: glucose, blood gas analysis/electrolytes, ACT test for heparin monitoring, urine strips, pregnancy test, stool occult blood, cardiac markers, drug/toxicological analyzes.

Today, one out of every four tests is done at the patient's near side and there is a 12% increase in the use of POCT every year. The most important reason for the increase is the advantages provided by POCT. The most im

portant advantages are the shortening of turn around time, the elimination of mistakes in sample transport and handling, the reduction of blood loss due to sampling (especially important in the pediatric patients), ease of use for the patient/healthcare worker/clinician and patient comfort. POCT also has some significant disadvantages. The most important are: standardization problems, errors caused by large number of users, the inadequate management of the data, lack of education/experience, inadequate follow-up of device maintenance, calibration and control, sampling errors and high cost.

POCT is more vulnerable to errors in the preanalytical process. This is because the testing performed by the lack of training and incompetence non-laboratory personnel affects the reliability of test results. Furthermore, due to the ease of operation, there is a false perception that there is no risk or harm to the patient, even if the test procedure is not fully followed. The primary limiting factor in ensuring concordance between POCT and laboratory results, as emphasized in the literature, is the preanalytical process. Common errors in POCT in preanalytical processes include: incorrect identification, errors in sampling time, incorrect selection of the sampling site, inadequate patient conditions, inadequate/erroneous sample preparation, inadequate/erroneous sampling, poor sample mixing, and erroneous transport and storage. The reasons for these errors and the precautions to be taken to avoid them will be discussed in detail. One of the most common used POCT, blood gas analyzes that are vulnerable some specific preanalytical errors will also discussed in the presentation. Thus, it is aimed to raise the awareness of laboratory professionals about errors in preanalytical processes in POCT. By arranging the quality of the preanalytical process with a multidisciplinary approach in the clinician-laboratory collaboration, significant improvements can be achieved in the results of POCT.

Oral Presentations

OP-01

Matrix Effect in Chemotherapy Patients

Hatice Bozkurt Yavuz

Department of Medical Biochemistry, Karadeniz Technical University Faculty of Medicine, Trabzon

Complete blood count is one of the most studied tests in clinical laboratories. The number of leukocytes and subgroups have a great importance in evaluating the immune system and in the diagnosis and follow-up of infectious diseases. In some patients, automated whole blood count analysers can not measure leukocyte subgroups, and most of these patients are chemotherapy recipients. The inability to measure of leukocyte subgroups in patients receiving chemotherapy suggests the reasons such as presence of atypical cells in the samples or the matrix changes caused by drugs. Isotonic sodium chloride solution (NSS) replacement technique is defined as the replacement of the plasma with NSS and recommended in cold agglutinin cases which erythocyte indices can not be measured at 37ºC. Matrix effect is evaluated by using NSS replacement technique in samples which leukocyte subgroups that can not be measured. Twenty-nine chemotherapy patients whom leukocyte subgroups could not be measured by the Beckman Coulter LH-780 complete blood count autoanalyzer were evaluated. Peripheral smear was sent from these patient samples, then the NSS replacement technique was applied and the samples were analysed in the same autoanalyser. Leukocyte results measured before and after NSS replacement and leukocyte subgroups counted by peripheral smear and measured after NSS replacement were also compared. There was no statistically significant difference between post-NSS replacement leucocyte subgroup parameters and peripheral smear results, and leucocyte counts before and after NSS replacement. There was a statistically significant difference between platelet counts before and after NSS replacement. Samples that leukocyte subgroups can not be measured by a complete blood count autoanalyzer, this may be due to the matrix effect. We found that when samples which leukocyte subgroups can not be measured, can be accurately measured by means of NSS replacement technique. In such cases, we think that before reporting the results it is appropriate to repeat the measuring of leukocyte and its subgroups instead of repeating all the complete blood count parameters because of the changes in thrombocyte count. We think that larger studies should be done in order to investigate the matrix effect in samples that are not measured in other full blood count autoanalyzers.

OP-02

Effects of Centrifugation, Freezing, Thawing and Recentrifugation on Specific Coagulation Parameters

Pınar Vatansever, Ali Yaman, Önder Şirikçi, Goncagül Haklar

Department of Biochemistry, School of Medicine, Marmara University, Marmara University Pendik ER Hospital Biochemistry Laboratory, İstanbul

Objectives: Specific coagulation markers are generally aliquoted, stored and batch analyzed for economic efficiency. Preanalytical factors should be carefully considered for these samples. In our study, we aimed to look for the effect of centrifugation, freezing, thawing conditions on specific coagulation markers.

Materials and Methods: Blood samples were drawn from 30 non-smoking healthy donors into citrated tubes (Becton Dickenson, NJ, USA). None of the donors had a known coagulation defect or were treated with drugs that might affect coagulation function. Samples were centrifuged at 1500xg for 15 minutes, once or twice and aliquoted. Some of the plasma samples were analyzed fresh or frozen at –20°C for 24 h. To observe the effects of thawing and re-centrifugation, frozen samples were thawed in a 37°C thermostat controlled water bath in a duration of 5 and 15 minutes and analyzed, whereas some were re-centrifuged before analysis. Relative bias percentages from the baseline (as measured by immediate analysis after centrifuging either once or twice, according to manufacturer's suggestions) were calculated for each condition and compared with total change limit for analytical biases and reference change values for clinical biases.

Results: We observed that freezing significantly affected the results for FV activity for each tested condition and those samples should be analyzed fresh. For FVIII measurements, although single centrifugation is recommended before freezing, we have observed that only an additional centrifugation after thawing for 5 min (–4%) or double centrifugation without extending the thawing duration more than 5 min (–7.5%) had acceptable biases. Factor IX, X, protein C, protein S and thrombin generation tests were stable (<±10%). Double centrifugation seemed appropriate for factor II assay although single cenrifugation was suggested by manufacturer. Also for APCR, double centrifugation must be preferred. Finally, lupus anticoagulant test were found to be stable for each condition.

Conclusions: In our study we demonstrated that the different storage and thawing conditions might affect coagulation testing. Therefore, the laboratory should test preanalytic variables accordingly.

OP-03

Root Cause Analysis in Preanalytical Errors

Çiğdem Sönmez

Minister of Health, Ankara Provincial Health Director at Central Laboratory, Ankara

Objectives: Laboratory errors are generally evaluated by preanalytical, analytical and postanalytical stages. Although clinical laboratories focus on the errors in the analytical phase for years, 46-68% of the errors observed in laboratories are seen in the preanalytical phase. İdentification of the cause provides a reduction in the observed error rates.We aimed to improve the process by examining the root causes of preanalytical error rates of our laboratory.

Material and Methods: During 2015-2017, the number of accepted tubes, rejection type and rejection rates were examined. Our laboratory, which accepts samples from 26 hospitals, evaluated rejection rates and their causes on a monthly basis. From the laboratory information system (LIS) different reporting formats were used to examine the proportions of preanalytical errors on the basis of cause, hospital and parameter.

Results: During 2015-2017, 1.150.156, 1.456.427 and 1.616.866 samples were accepted. The average rejection rates for each year were 1.72%, 1.49% and 1.0%, respectively. Rejection rates reduced over the years. When we evaluate the rejection reasons for 36 month, insufficent sample was the reason except for the first, second and the eighth month. For the first two months the rejection reason was inappropriate sample cup while the hemolysis was the reason of the 8th month. By the preparation of the test catalog and sending to the clients, inappropriate sample cup rejection reason didn't seen again. When we evaluate the hemolysis rejection rates by the hospitals, it was seen only in one hospital and after traning the phelobotomist/nurses this rejection type didn't seen again. For the rejection reason, insufficent sample remained unchanged during the 33 months while the observed hospital and the test name were var

ied. In the first period, insufficent sample was specific for zinc test, then followed by ELISA tests. When we evalute the rejection type and rates by test based and hospital-based, ELİSA test names and the hospital names were not spesific for any type. After detection of the root causes of the errors the process was improved with corrective and preventive action.

Conclusions: In our laboratory rejection rates were decreased by performing root cause analysis of preanalytical errors. In the process improvement, the laboratory should evaluate and monitor the rejection types, rates and source in details in order to find the root causes and should do corrective and preventive activities.

OP-04

Reducing Preanalytical Errors in a Public Health Laboratory: Laboratory and Primary Healthcare Staff Collaboration

Esin Avcı[1], Rukiye Nar[2], Mehmet Türk[3]

[1]Department of Clinical Biochemistry Uşak Public Health Laboratory, Clinical Biochemistry Laboratory, Uşak

[2] Department of Medical Biochemistry, Kırşehir Ahi Evran University, Kırşehir

[3]Eskişehir Public Health Laboratory, Clinical Biochemistry Laboratory, Eskişehir

Objectives: Most laboratory errors occur in the pre-analytical phase of the total testing process. The aim of the study was to evaluate whether effective communication and education were effective to reduce preanalytical errors (PEs) in public health laboratory practice.

Material and Methods: The sample rejections were screened retrospectively in the Laboratory Information System (LIS) for the years 2013 and 2014. Haemolysed sample, missed sample, coagulated sample, inadequate sample and inappropriate test order were selected as indicators of quality. The causes of rejection for each type of tube were grouped for two years under the heading of quality indicators. We conducted a meeting was held with only Primary Physicians on the pre-analytic phase and the questionnaire named "Primary Physicians Feed-back Form" including 10 questions. Eight of the 10 questions in this questionnaire were multiple-choice questions, while 2 were open-ended questions, where the physicians expressed their opinions. Preanalytical training was administered to primary physician staff (including primary physician and nurses). Visual training aids were used for appropriate collecting of samples, sample drawing and barcoding techniques, with demonstrations on sample collecting by making use of power point presentations. Appropriate centrifugation conditions and key points were highlighted by the educators.

Results: According to data obtained retrospectively from screening the Laboratory Data System; the number of tubes reaching our laboratory in 2013 was 267140, reaching 275.580 in 2014. A decrease was observed in orders for urine and sedimentation, with an increase in orders for biochemistry, hormone, serology and ELISA tests. The evaluation of quality indicators was done for each tube type for these two years, and rates of rejection, error in a thousand and statistical significance according to years are presented in detail. Primary physicians' answers to feed-back form were showed as a pie graphic.

Conclusions: In this study we showed that training the staff about preanalytical phase and an effective communication between primary physician and laboratory have decreased the frequency of tube rejection dramatically. We believe that decreasing errors will require continuous training and a network of communication.

OP-05

Evaluation of Analytical Performance with Six Sigma Methodolgy

Esra Laloğlu

Department of Biochemistry, Palandöken State Hospital, Erzurum

Objectives: The present study aimed to evaluate the analytical phase using six sigma as a quality indicator in Biochemistry Laboratory of Erzurum Palandoken State Hospital.

Material and Methods: Sigma values of Na, creatinine, glucose, total protein, K, LDH, total cholesterol, Cl, AST and ALT biochemistry tests were determined using bias, variation coefficient and total allowable error (TEa) within six months period (July-November 2017). Bias and variation coefficient were calculated external quality control and internal quality control data, respectively. TEa ratios were obtained from Clinical Laboratory Improvement Amendents (CLIA 88).

Results: According to TEa ratio of CLIA, in at least one internal quality control sample, sigma values were determined to be smaller than three for Cl. While creatinine, glucose, total protein, K, total cholesterol had sigma value between three and six, ıt was calculated greater than six for LDH, AST and ALT.

Conclusions: Laboratory performance is expected to be three sigma and over. The determination of different quality control rule for each test according to sigma values may be improve performance. OPSpecs graphs can be used to determine appropriate quality control rules.

OP-06

Evaluation of Measurement Uncertanity for Serum Hormone Parameters with the External Quality Method (KBUDEK)

Saadet Çelik

Department of Medical Biochemistry, Bilecik Public Health Laboratory, Bilecik

Objectives: External quality control is a system based on a comparative assessment of the analytical performance of laboratories performed by independent organizations. With the recent standardization of analytical methods and the use of certified reference materials, measurement variability between laboratories is steadily declining nowadays. Our aim was to calculate the uncertainty of serum vitamin D, TSH, FT3, FT4, vitamin B12 and folate measurement via internal and KBUDEK external quality control data of serum Vitamin D, TSH, FT3, FT4, vitamin B12 and folate tests.

Material and Methods: The internal quality results and external quality (KBUDEK) control results of serum Vitamin D, TSH, FT3, FT4, vitamin B12 and folate tests that are obtained between10.01.2017-01.01. 2018 were used in our study. In the calculation of measurement uncertainty, six step "uncertainty calculation model", that is defined in Nordest guide was followed.

Results: For Vitamin D, TSH, FT3, FT4, vitamin B12 and folate tests, the extended measurement uncertainty was calculated as ±%17.44, ±%15.87, ±%5.66, ±%12.96, ±%13.83, ±%22.98 in the 95% confidence interval.

Conclusions: According to the last three months' data, the measurement uncertainty of serum Vitamin D, TSH, FT3, FT4, vitamin B12 and folate were calculated to be as ±%17.44, ±%15.87, ±%5.66, ±%12.96, ±%13.83, ±%22.98, respectivley. Adding measurement uncertainty to the categorized Vitamin D, TSH, FT3, FT4, vitamin B12 and folate results helps us to obtain more accurate and reliable results. As a result, if the laboratories analyze measurement uncertainty calculations at regular intervals; this may improve the confidence of laboratory results by preventing improper treatment by increasing the power of clinical interpretation.

OP-07

Multidisciplinary Harmonization Study of a Preanalytic Quality Indicator Example in Urine Samples

Belkız Öngen İpek, Elçin Akduman Alaşehir, Mustafa Erinç Sitar

Department of Medical Biochemistry, Medical Microbiology, Maltepe University, Faculty of Medicine, İstanbul

Objectives: Usage of contamination rates as a quality indicator is a promising criterion in urine samples. A multidisciplinary approach is needed to use this quality indicator. Evaluation of urine strip and sediment according to the presence of contamination effect the rates of accurate test result, guidance of the clinician correctly, patient follow-up and requesting new sample. This feature also fulfils the rule of objectivity in quality indicators. It also plays an important role in the monitoring and effectiveness of regulatory and preventive activities.

Material and Methods: Urine culture samples which were resulted as contaminated and synchronous full urinalysis test results were scanned retrospectively between July 2017 and December 2017. The patients were evaluated according to their age, sex, and being inpatient or outpatient. Strip and microscopy findings were evaluated from the results of full urine analysis.

Results: 1537 urine culture test results were analyzed in 6 months for the study. Those which were considered as contamination were evaluated together with their total urine analysis at the same time. It was found that 82% were female, 18% were male, 58% were older than 65 years, 24% were between 18-65 years, 11% were <1-year-old of these patients. The test was requested 67% and 33% respectively from outpatient and inpatient. Leukocyte esterase and nitrite were found positive %33 and %16 respectively in urine strips. When urine microscopy was evaluated, 52% had abundant bacteria and 56% had more than 5 leukocytes in each area. It was found that 63.3% of the patient have no signs in microscopy or strip in <1-year-old group.

Conclusions: In our study, it was found that contamination rates were higher especially over 65 years and female sex. It is important to explain the method of sampling and to be more careful when approving the test results of full urine analysis in this population. Considerations during sample collection and the selection of materials are of great importance for clinical follow-up in younger than 1-year-old population.

OP-08

The Significance of Measurement Uncertainty in Thyroid Function Tests

Mehmet Kalaycı[1], Hakan Ayyıldız[1], Musa Yılmaz[2]

[1]Department of Medical Biochemistry, S.B.Ü. Elazığ Training and Research Hospital, Elazığ

[2]Department of Medical Biochemistry, Yozgat City Hospital, Yozgat

Objectives: Measurement uncertainty is a significant parameter that can identify the range of the result by combining the measured analyte and the factors, which can affect analysis performance. Measurement uncertainty is used to keep quality-control rules and the performance of a test at acceptable criteria. The aim of the study is to determine the measurement uncertainty of TSH, free T3 and free T4 hormones by using test performance data of our laboratory and to acknowledge physicians about measurement uncertainty.

Material and Methods: Measurement Uncertainty in thyroid function tests was calculated according to ISO/DTS 21748 Guidance, the European Accreditation Guideline described in Nordest Guideline and the European Technical Report.

Results: Measurement Uncertainty in thyroid function tests was measured as TSH±7.61%, free T3±8.6%, free T4±7.4% respectively at 95% confidence interval. These results, calculated in our laboratory were found to be lower than the allowable total error values determined by the international institutions (CLIA, RILIBAK, Fraser Rules).

Conclusions: We consider that the study will guide laboratory specialists in the issue of measurement uncertainty in order to realise the suggestion that "Medical laboratories should calculate measurement uncertainty for quantitative results." Furthermore, reporting measurement uncertainty along with test results will acknowledge physicians of measurement quality and provide them with awareness regarding this issue.

OP-09

Emergency Laboratory Preanalytic Process Arrangements According to the Ministry of Health Emergency Service General: Pilot Hospital Application

Yüksel Gülen Çiçek, Asuman Gedikbaşı

Department of Medical Biochemistry Laboratory, Health Sciences University, Bakırköy Dr Sadi Konuk Training and Research Hospital, İstanbul

Objectives: Yellow and green area inspection and short meetings were scheduled to last not more than two hours in the Emergency Service General dated 31.01.2018 issued by the Ministry of Health. Bakırköy Dr. Sadi Konuk Education and Research Hospital was designated as pilot hospital. The aim of this study was to investigate the effects of preanalytical arrangements for shortening the turnaround time of emergency laboratory. Our study was conducted with Emergency Service.

Material and Methods: The preanalytical process, the most important phase affecting the quality of the laboratory service, has been dealt with in two parts: outside the laboratory (the process from the physician's request to the entrance of the sample to the laboratory) and inside the laboratory (processing of the sample and preparing the sample for analysis). Accordingly, in order to make the preanalytical process simpler, many arrangements were made in the area of emergency medical examination. A new blood collection unit was configured, a pneumatic system was added, patient information screens were set up. Lithium heparinized tube was used to shorten the waiting time for centrifugation. The total photometric speed of the single autoanalyzer used in the emergency laboratory was provided in two devices (back up) to prevent delays. Following the regulations, laboratory turnaround times of December 2017 and January 2018 were compared for emergency laboratory, from the datas of laboratory information system.

Results: Statistically significant shortening was observed between emergency laboratory outcomes in all the tests for December 2017 and January 2018. The percentage of tests completed within one hour was 65% in December 2017 and 92% in January 2018.

Conclusions: Shortening the turn around time, reducing the length of stay in the hospital and, in this regard, the clutter in the emergency departments; increased both employee and patient satisfaction. Laboratory services play a central role in inpatient treatment facilities. This study has provided awareness of hospital management and clinicians and it has been observed that the management of this process together has strategic consequences.

OP-10

Three Different Approaches to the Lipemia Interference

Nesibe Esra Yaşar, Ayşegül Özgenç, Erkam Coşkun, İbrahim Murat Bolayırlı, Dildar Konukoğlu

Department of Medical Biochemistry, İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, İstanbul

Objectives: Lipemia interference is one of the endogenous interference sources and has a significant effect on measurement accuracy. The presence of lipemia in patient samples can be determined in three ways; visually, by determination of triglyceride concentration or lipemia index. The aim of this study is to evaluate the methods that can be used to relieve lipemia interference.

Material and Methods: Routine biochemical parameters and lipid index (LI) were determined in the lipemic patients sample. Lipemic sample was aliqued into three portions and three different methods were done to remove the lipemia interference; dilution (1:10), the precipitation with polyethylene glycol (PEG) and the high-speed centrifugation. After these procedures biochemical analysis were reperformed in the treated samples (Roche Cobas c702).

Results: In pretreatment lipemic sample, total cholesterol, LDL, HDL, triglyceride and LI levels were found to be as 913 mg/dL, 63 mg/dL, 43 mg/dL, 233 mg/dL and 2176, respectively. While creatinine and bilirubin could not be determined, total protein, sodium, calcium and chloride were found to be extremely low. The triglyceride concentrations after procedures of dilution, PEG precipitation and high-speed centrifugation were 8490, 202, 1128 mg/dL, respectively. LI were determined to be 560 after dilution, 34 after precipitation with PEG, and 96 after high speed centrifugation. Creatinine, bilirubin and LDL could not be determined in diluted samples. After precipitation with PEG, albumin and LDL could not be determined and extremely low HDL and CRP were obtained. All biochemical test parameters were determined to be in reportable levels after high speed centrifugation.

Conclusions: In order to avoid lipidemia interference, there are various approaches such as removal of lipids (such as ultracentrifugation, high-speed centrifugation, extraction with organic solvents and precipitation with polyanionic compounds etc.) and dilution. In this study, high-speed centrifugation and PEG methods were found to be very successful in removing lipids from the serum. Nevertheless, laboratory findings were not be reliable. PEG removes lipids from the serum; it can also affect protein analysis by causing protein precipitation. Dilution method seems to be more reliable in evaluating triglyceride level than other methods. This study shows that in the presence of excessive lipemia, the accuracy of biochemical test results was to affected, even though lipemia interference was eliminated.

OP-11

Macro CK as a Preanalytic Factor

Alperen Aksoy, Emre Yalçınkaya, Eray Kıraç, Afife Şerifoğlu, Nevin Genç Kahraman, Rabia Korkmaz, Fatih Yeşildal, Hayriye Erman, Ferruh Kemal İşman

Departmen of Clinical Biochemistry Laboratory, İstanbul Medeniyet University Göztepe Research and Training Hospital, Istanbul

Objectives: Creatine kinase (CK) is an enzyme associated with ATP regeneration in contractile and transport systems with a molecular weight of approximately 82.000 kD. There are various studies that have shown rare CK isoenzymes showing different electrophoretic properties than the three major isoenzyme fractions identified as CK-MM, CK-MB, CK-BB. These atypical forms are usually consist of two types and are called macro CK and mitochondrial CK (CK-Mi). Macro-CK contains CK-BB, which mostly forms complex with immunoglobulin. In many cases, this immunoglobulin is IgG, while the complex with IgA has also been identified. Macro-CK is also used to express the complex formed by lipoproteins with CK-MM. Macro CK has a frequency of 0.8-1.6%. Until now, no macro-CK related disease has been found and it is usually associated with age and sex and it is more common in women over 50 years of age. In this study, a 36-year-old male patient with prolonged CK elevation hospitalized in the internal medicine service was investigated for macro-CK.

Material and Methods: Serum of the patient suspected of having macro-CK was mixed with 1: 1 ratio of polyethylene glycol (PEG). This mixture was centrifuged at 2500 g for 10 min. The obtained supernatant was re-analyzed for CK.

Results: The CK results of the patient during november were 12.819 U/L, 24.185 U/L, 24.209 U/L, 25.458 U/L, 63.340 U/L, 84.775 U/L, 112.285 U/L, 112.932 U/L respectively. After precipitation with PEG, the CK value of the patient was measured as 22 U/L.

Conclusions: The fact that the CK value of the patient had fallen in to the reference value after intervention with the PEG confirmed the presence of macro-CK in the patients sample. Macro CK was found to be a preanalytical factor that could significantly affect the CK result of the patient.

OP-12

Effect of Sample Type, Centrifugation and Storage Conditions on TSH, FT_3 and FT_4

Eray Kıraç, Afife Şerifoğlu, Emre Yalçınkaya, Nevin Genç Kahraman, Alperen Aksoy, Rabia Korkmaz, Hayriye Erman, Ferruh Kemal İşman, Mustafa Baki Çekmen

Department of Clinical Biochemistry Laboratory, Istanbul Medeniyet University Göztepe Research and Training Hospital, Istanbul

Objectives: Thyroid disease is one of the most common health problem. TSH (Thyroid Stimulating Hormone) FT3 (FreeT3) FT4 (FreeT4) tests are indispensable for diagnose and treatment. Since these tests are analyzed by transferring the specimen to the central laboratory at our institution, they are analyzed after significant waiting periods.

Material and Methods: Blood samples were taken from 4 healthy volunteers using 4 tubes of BD Vacutainer SST II serum and 2 tubes of BD Vacutainer K2EDTA 10 ml tubes. The blood specimens were divided into two groups and centrifuged at room temperature and at 4 °C (1300xg 10 min) for each group and analysed immidiately at 0 Hour. The separated plasma and sera were aliquoted and stored at room temperature (25 °C) and refrigerator temperature (4-8 °C). Hidden samples were measured at 4. hour, 24. hour. TSH, FT3, FT4 measurements were performed using the chemiluminescence immunoassay method on Abbott Architect i1000. The results were evaluated using the Microsoft Excel 2016 software.

Results: Average percent change for the 4th hour and 24^{th} hour results were calculated by considering the 0. hour result as the reference value. The differences obtained were within the permissible ranges according to Ricos desirable total allowable error limits criteria.

Conclusions: TSH, FT3, FT4 test results did not change using plasma or serum as a sample or using refrigerated or uncooled centrifuge. Results of TSH, FT3, FT4 obtained after the storage of the samples at room temperature and in the refrigirated conditions proved that the transfer conditions did not effect the clinical decision. It was concluded that it would be beneficial to add individuals outside the reference intervals and extend the measurement durations for future studies.

OP-13

Preanalytical Erorrs and Preventive Methods

Yavar Hajısoy, Leyla Mammadova, Elnara Afandiyev

Azerbaijan Medical University, Training Surgical Clinic, Central Laboratory, Baku

Objectives: Laboratory services are the basis of the modern health sector. Effective laboratory service is the combination of precision, accuracy, and speed of reports delivered to the patient. The elaboration of patient samples in clinical laboratories is a very complex process, and needed multidisciplinary approach. In laboratory practice this period is divided into preanalitic, analytical and postanalitic stages. Any mistake in any of these processes may cause serious errors in test results. The standardization of the preanalytical stage is more difficult than others, and most of the sources of errors are reflected in many publications at this stage. The preanalytical phase is an important component of laboratory medicine. Preanalytical errors constitute more than 70% of all errors occured in clinical laboratories. Most of the pre-analytical errors occur during patient preparation, sample collection, sample transportation and preparation and sample storage.The aim of this study was, investigation the role of preanalytical errors in the samples sent to biochemistry and microbiological laboratories and training procedures to prevention from these errors.

Material and Methods: All samples taken from our laboratory in 2017 have been retrospectively investigated. Rejected samples were classified to categories of preanalitic errors (contaminated, clotted, hemolysis etc) and study groups. The types of errors are calculated based on the sample count and the total error. Blood and urine specimens were also studied in terms of age and sex. The results of the preanalysis stage were compared with previous findings after training programs.

Results: Preanalytical errors were observed in 0.89% of all samples. The most common cause of error was contamination (28.05%), hemolysis (21.80%) and clotted (14.23%) samples. In bacteriology department the contamination was higher in urine cultivation samples (82.8%), than blood culture samples (17.2%). In samples taken for urinary cultivation, contamination was higher in women (68%), than in men (32%). Compared to age group, more contamination was observed in women over the age of 50 (44%) and in males under 18 (43%). Distribution of preanalytical errors in years revealed, that errors in preanalytical phase in non-training year (2016) were 1.7% and decreased to 0.89% in 2017, when regular trainings were held.

Conclusions: In order to reduce preanalytial errors in laboratories, laboratory should provide continuous training programs to phlebotomy and laboratory personal. As well, the instruction of guidelines for urine sampling must be in samples receiver rooms.

OP-14

The Digoxin Levels and Its Stability in the New Generation Lithium Heparinized Tubes (BD Barricor™ LH Plasma Tube)

Fatma Demet Arslan[1], İnanç Karakoyun[1], Banu İşbilen Başok[1], Hatice Solmaz[2], Merve Zeytinli Aksit[1], Anıl Baysoy[1], Can Duman[1]

[1]Departments of Medical Biochemistry and [2]Cardiology Clinic, University of Health Sciences, Tepecik Training and Research Hospital, Izmir

Objectives: Digoxin is a drug in which the blood levels need to be monitored due to the narrow range of therapeutic doses and the risk of toxicity. Blood collection tubes containing gel barrier have different effects on therapeutic drug levels. Thus we aimed to evaluate the effect of tube with new generation barrier (BD BarricorTMLH Plasma tube) (Barricor) on digoxin levels and drug stability.

Material and Methods: Samples from 30 volunteers who received digoxin therapy were collected in five different tubes: no additive and gel-free glass tube (Z tube) (reference tube); clot-activator tube containing gel (SST and Vacusera); barrier-free lithium heparinized tube (LiH); and newly produced lithium heparinized tube with a barrier (Barricor). Digoxin levels in each tubes were analyzed immediately after centrifugation and after storage for 48 hours at $^{+}$4°C. The differences of digoxin levels between four blood tubes and the reference tube, and between 0th h and 48th of each tubes were evaluated statistically and clinically.

Results: There was no the statistically difference between the 0th and 48th h results in other tubes, except for LiH and the difference in LiH was also not clinically significant. Digoxin levels in other tubes were not found statistically different according to the reference tube, but not in Barricor tube. Digoxin level in Barricor tube was clinically higher than the reference tube. Although there was strongly correlation between digoxin results of Barricor and Z tubes, a proportional error was determined.

Conclusions: The digoxin levels were higher in Barricor tube than other tubes, and the difference in digoxin levels of Barricor tube in process of time was not significant. The reason of this may be a better separation between cell and supernatant performed by the Barricor tube. It was considered that the effect of the new generation barrier on digoxin levels was minimal compared to other tubes. As a result, it is believed that the reliability and accuracy of digoxin results may increase by the identification of new therapeutic range for Barricor tube. It was considered that Barricor tube makes a difference because it has both a new generation barrier and lithium heparin as anticoagulant.

OP-15

Examination of the Effect of the "Reflex Test" application on tPSA Test Request

Kübranur Ünal

Department of Biochemistry, Ankara Polatlı Public Hospital, Ankara

Objectives: The free PSA test is used to calculate free-to-total PSA ratio for prostate cancer screening. It is used differential diagnosis between benign and malign at prostate diseases. The international guidelines recommend that performing f PSA value in the patients with 4-10 ng/mL PSA values which called "gray zone". In our study, we aimed to investigate the effect of the tPSA reflex test application which we initiated in our hospital.

Material and Methods: The request of free PSA test in the patients with t PSA<4 ng/ml and t PSA>10 ng/ml was considered unnecessary test. The data were analyzed six months before and six months after the reflex test application.

Results: After the application of the reflex test, unnecessary test for all clinics decreased from 64% to 20%. Before the application of the reflex test, the free PSA has been requested in 64% of patients with t PSA<4 ng/ml and t PSA>10 ng/ml. Also in this period, the request of free PSA be found 14% in the patients with 4-10 ng/mL PSA values.

Conclusions: After the application of the reflex test, unnecessary test requests decreased apidly and seriously in our hospital. This study showed that reflex test have positive effects on cost effectiveness by reduction of unnecessary test requests.

OP-16

Sample Rejection Rates and Causes of Urine Drug Abuse Testing

Hüseyin Kurku

Department of Medical Biochemistry, Health Sciences University, Konya Training and Research Hospital, Konya

Objectives: The primary purpose of drug abuse testing in urine is to identify the use of illegal or banned medications or substances in various cases in accordance with the laws. The aim of this study is to evaluate the sample rejection rates in the urine samples brought to the laboratory of Alcohol and Substance Addiction Treatment and Training Centre (AMATEM) for drug abuse testing.

Material and Methods: In this retrospective study, the data of the urine samples brought to Konya Training and Research Hospital, AMATEM laboratory between October 2013 and December 2017 were taken from the laboratory information system and analysed. The sample rejection rates, reasons for rejection, and units from which the rejected samples were brought were identified.

Results: It was calculated that 51.302 (M=96.22%, F=3.78%) urine samples were brought to our laboratory during this period for drug abuse testing and a total of 798 (1.56%) samples were rejected. According to the frequency order, the reasons for rejection were found to be the deterioration of urinary integrity (91.73%) (732), insufficient sample (7.52%) (60), and other reasons (7.50‰) (6). Rejection rates were calculated as 1.34% (454) for the samples coming from AMATEM, 1.96% (289) for the samples brought from the probation unit, and 2.13% (55) for the samples of other units.

Conclusions: The samples rejected in drug abuse testing laboratories are very important from medical, legal, and social aspects. Rejection rates and rejection causes should be compared to those of other similar laboratories and problems and solution suggestions should be discussed. The number of trainings on sampling and sample transfer should be increased. The step where fraud is most commonly seen in urine drug abuse testing is sampling.Unsupervised urine sampling is open to interference and fraud can be easily seen during sampling. Samples should be taken under supervision in order to provide legal and administrative evidence. It is observed that urinary integrity may be deteriorated even in sampling under supervision. New sample types and/or supervision methods that attach importance to the individual's privacy and health risks, can be easily applied by healthcare personnel, take our society's general moral principles into consideration, are more humane and would guarantee sample safety should be developed. New tests that are suitable for routine use (reliable, easy to apply, affordable, etc.) for the samples that do not allow fraud (such as hair and nail samples) should be developed for drug abuse testing.

OP-17

Does Ointment Really Makes Glyceroluria?

Soner Erdin[1], Asuman Gedikbaşı[1], Tufan Karaçam[2]

[1]Department of Medical Biochemistry, İstanbul Sadi Konuk Training and Research Hospital, İstanbul

[2]Department of Chemistry, İstanbul University, Faculty of Engineering, İstanbul

Objectives: Glycerol excretion in the urine is primarily observed in the absence of glycerol kinase deficiency and fructose 1,6-bisphosphatase, two metabolic diseases with hypoglycaemia. The use of perineal lotions or suppositories is thought to cause glycerin-induced contamination and lead to the detection of secondary glycerol as a preanalytical defect in urine organic acid analysis (1). However, as far as we know, this information obtained from experience has not been adequately tested. In this study, we wanted to investigate whether the ointment used in infants actually leads to glyceroluria.

Material and Methods: Residual urine samples of two patients whose glycerol was not detected in urine organic acid analysis were taken. Each patient sample was divided into 3 pieces and 3 different brands of ointments obtained from the market were mixed with about 3 mg for each. The creams were numbered 1, 2 (containing glycerol and its derivatives) and 3 (containing no glycerol and its derivatives). Vortexed urine was taken back to organic acid analysis. The organic acids extracted with ethylacetate and derivatized with N-methyl-N-trisylyl-trifluoroacetamide for urine organic acid analysis. The prepared extract was analyzed by Thermo Fischer Trace GC Ultra GC/MS. Glycerol>0 mmol/mol creatinine was evaluated as positive in the urine.

Results: Of the 6 samples analyzed, only one (urine sample containing ointment 2) was found to have glycerol (5.2 mmol/mol creatinine). No glycerol was detected in other urine specimens.

Conclusions: The use of perineal lotions or suppositories is thought to cause glycerin-induced contamination and lead to the detection of secondary glycerol as a preanalytical defect in urine organic acid analysis. In our study, glycerol was detected in one urine specimen containing only ointment 2 from 4 urine specimens mixed with lotions containing glycerol and its derivatives. Although higher levels of glycerol are generally expected to be associated with metabolic diseases, even low-level positives from contamination can lead to confusion during interpretation and diagnosis in laboratories.

OP-18

Preanalytic Drug Interference on Chromatographically Measured 25-Hydroxyvitamin D_3 Test: Tamoxifen Example

Özgür Baykan

Balıkesir Atatürk State Hospital, Central Laboratory, Balıkesir

Objectives: The preanalytical phase of the total testing process is very difficult to control. Many factors can be effective in this process, such as the drugs used by the patients which are among the factors that are dependent on the patient. Inconsistent results may be reported if the medications used by the patient is not taken into account during the test request. Commonly known drug-test interactions in routine assays are often taken into consideration by the clinicians. Interferences that are not known yet should be identified and added to the literature by the manufacturers or laboratory experts. In our study, we aimed to determine and eliminate the interference that we have noticed to be caused by Tamoxifen (selective estrogen receptor modulator) on 25-hydroxyvitamin D3 test measured by HPLC method.

Material and Methods: In our laboratory, 25-hydroxyvitamin D3 levels are measured using ODS Hypersil (150x4.6, 3u) column and UV detector at 265 nm wavelength in a HPLC system (Ultimate 3000, Thermo Scientific). Patient chromatograms showed interfering peaks with 25-hydroxyvitamin D3 peaks at similar retention times.These peaks were belong to the patients treated for breast cancer. Colloborating with the physicians of the patients, it was determined that those patients were using a drug called Tamoxifen. In order to confirm this situation tamoxifen is spiked to tamoxifen-free plasmain in-vitro conditions. It was documented that the seen peak was observed again.

Results: When drug was added to the plasma without tamoxifen, the problem was observed to continue.In order to avoidthe interference, column oven temperature was decreased and the peaks were separated from each other.

Conclusions: Drugs used can cause changes in body fluid components, resulting in tissue and organ damage. The presence of substances that are physically and chemically similar to the analyte that we are trying to measure may cause erroneous results in the analytical process.For tamoxifen, the maximum absorbance reported in the literature is 240-260 nm. Problems arising from column separation capacity, mobile phase content, column oven temperature or pre-extraction stage are among the factors that affect the analytical performance of the HPLC method. In addition, we should not forget that drugs used by patients are among preanalytical factors and new drug interferences may appear each day.

Poster Presentations

PP-01

Effect of Cold Agglutinins on CBC Parameters

Büşra Ecer, Esra Paydaş Hataysal, Abdullah Sivrikaya, Sedat Abuşoğlu,Hüsamettin Vatansev, Ali Ünlü

Department of Biochemistry, Selçuk University Faculty of Medicine, Konya

Objectives: Many preanalitic factors cause false results in the complete blood count. One of them is cold aglutinin.Autoimmune hemolytic anemia (OIHA) is a disease characterized by the formation of antibodies against the patient's own erythrocytes, the breakdown of erythrocytes and anemia. There are generally two types of autoimmune hemolytic anemia. If hemolysis is seen in 37ºC, it is called autoimmune hemolytic anemia with warm antibody.If the hemolysis is seen under the body temperature, cold autoimmune hemolytic anemia is called. This study is a case report of falce CBC results associated with cold agglutinins.

Material and Methods: A 57-year-old male patient has pulmoner neoplasm who admitted to Selçuk University Medical School Hospital on 25.01.2018. The patient had normal platelet and leukocyte counts; but the hemoglobin (Hb:11.8 g/dl) and hematocrit (HCT:19.6) results were incompatible. Other preanalitic factors which can mismatch between hemoglobin and hematocrit values were evaluated. Complete blood count was performed with Beckman Coulter LH780.

Results: During our routine laboratory studies we found inconsistencies in the CBC results from the EDTA tube from the patient. Hb:12.1 g/dl, Hct:%19.6, WBC:13.5 K/ul, PLT:307 K/ul. The patient had a diagnosis of pulmonary neoplasm. Hemolysis could be observed in the patient's tube. In this case, we suspected cold agglutination.Then we incubated the patient's tube for 2 hours at 37ºC. We observed that aglutination was reversible after incubation. Finally, hemolysis was not seen on the tube, and Hg:11.7 g/dl and hct: %35.2 values normalized.

Conclusions: As a result, there are too many preanalytic factors that will affect hemogram results.One of them is cold aglutinin. Cold agglutinins can interfere with Hct, MCV, MCH and MCHC results.

PP-02

Rejected Hemostasis Test Results of 2017, Ankara Numune Training and Research Hospital Emergency Laboratory

Arzu Sakallı, Çiğdem Yücel, Turan Turhan

Department of Medical Biochemistry, Ankara Numune Training and Research Hospital, Ankara

Objectives: Coagulation tests are among the most common tests carried out in emergency laboratories. The test request is operated on inpatients, outpatients and through emergency service patients. Ensuring test results are taken on time and accurate is extremely crucial. The aim of this study is to conduct an annual analysis report in order to find out the reasons of sample rejection which are classified mostly as preanalytic errors.

Material and Methods: In this study, Ankara Numune Training and Research Hospital Emergency Laboratory's rejected ratios of coagulation tests of year 2017 were evaluated retrospectively.

Results: The Laboratory calculation includes ratios and numbers of accepted and rejected samples of all inpatients, outpatients and through emergency cases. Hemostasis samples are gathered, initially from the Emergency department including Internal and Surgery Services and from polyclinics as well. A total of 76167 Hemostasis samples sent to Laboratory in 2017. 576 samples were rejected, rated as (%0.76). Most of the samples were rejected due to being volume insufficient. 430 out of 576 samples (%74.7) as insufficient samples,53 out of 576 (%9.2) as hemolyzed samples, 24 out of 576 (%4.2) as excessive samples, 19 out of 576 (%3.3) as clotted samples, 6 out of 576 (~%1) as lipemic samples, 44 out of 576 (%7.6) are rejected for other various reasons. 196 samples that derived from Emergency, 371 samples(%0.9) from inpatients, 9 samples (%0.006) from outpatients were rejected.

Conclusions: From overall 76167 Coagulation Samples, just a ratio of (%0.76) was rejected samples.That can be considered as a satisfying result rather than acceptable. %74.7 of rejection was caused by insufficient sample volumes. Therefore, in order to present quicker and more accurate results these preanalytic failures must be identified and healthcare professionals should be routinely educated about blood sampling.

PP-03

Comparison of the Effects of Using SST and BD Barricore PST in Terms of Hs-CTnT's Turnaround Time

Uğurcan Eker, Çiğdem Yücel, Muhammed Fevzi Kilinçkaya, Turan Turhan

Department of Medical Biochemistry Clinic, Ankara Numune Training and Research Hospital, Ankara

Objectives: Nowadays, troponin measurement has a key importance for diagnosis of AMI (Acute Myocardial Infarction). Early diagnosis of emergency patients with chest pain and urgent hospital admissions and the provision of patient management by this result will enable the development of clinical and prognostic outcomes. This study was conducted to compare the TAT (Turnaround Time) of BD Barricore PST (Plasma Seperation Tube) and SST (Serum Seperator Tube) used for hs-cTnT measurement in our emergency laboratory.

Material and Methods: A total of 23851 hs-cTnT data were analyzed retrospectively in Ankara Numune Training and Research Hospital (ANEAH) Emergency Biochemistry Laboratory. These samples were collected to SST between July-September 2017 and to BD Barricore PST between November 2017–January 2018. We categorized these samples according to test request from Emergency, Cardiology and other services that might be a significant difference in TAT duration. These samples were analyzed by ECLIA (Electrochemiluminescent Immunoassay) method in Roche cobas e601 autoanalyzer at in the emergency Laboratory. The time between admission of the sample to the laboratory and the reporting of the result was defined as TAT. Statistical Analysis was made with SPSS 15.0. programme. The Mann-Whitney U test was used for comparison between groups. $p<0.05$ was accepted as statistically significant.

Results: Significant difference was found between TAT of hs-cTnT between the yellow cap SST and BD Barricore PST and compared services ($p<0.001$). When the samples were grouped according to services they requested from, there was also a statistically significant difference between TATs among groups ($p<0.001$).

Conclusions: It was expected that the TAT period of hs-cTnT worked with BD barricore PSTs to be shorter than SST. However, this difference is not sufficient to improve the prognosis of patients with AMI, but it is thought that it would be beneficial to consider other preanalytical factors clinically to improve this prognosis.

PP-4

Lipemia and Hemolysis Indices and Relationship with Triglyceride Levels

Özlem Doğan

Department of Biochemistry, Ankara University, School of Medicine, Ankara

Objectives: In the clinical laboratory setting, interferences can be a significant source of laboratory errors with potential to cause serious harm for the patient. After hemolysis, lipemia is the most frequent endogenous interference that can influence results of various laboratory methods by several mechanisms. Interference sources as lipemia, hemolysis and icter in automated systems are determined as serum index (SI). This study intends to identify the causes of severe lipemia and hemolysis index in Ankara University Cebeci Laboratory and to determine if there is any relationship between them.

Material and Methods: Retrospective study was done on the data from the Ankara University Cebeci Hospital Biochemistry laboratory at an School of Medicine. Lipemic and hemolysis index values and triglyceride levels were analyzed over a 12-month period from the automation system. We also determined 133.970 serum index values and 40.415 serum triglycerides levels with lipemia, hemolysis indeces. Lipemia and hemolysis indices were grouped acording to the values in the insert indicated Siemens Advia Centaur analyzers.

Results: The lipemia and hemolysis indices were found to be positive at 3118 (%2.3) samples of 133.970 samples. In the 13.722 (%10.2) samples, the lipemia index was positive, with only 39 lipemia indexes (++++) at the highest levels (300 mg/dL and over). The hemolysis index was positive in 16.285 (%12.1) samples and was over 379 mg/dL in 183 samples. Lineer regression analysis of triglycerides and lipids is y=4.0639x+103.55 R^2=0.2036. There was no correlation between triglyceride and hemolysis index. 173 patients hemolysis and lipemia index positive were observed to have increased y=170.7107+2.6824x R^2=0.3573 value of triglyceride and lipemia index linear regression analysis.

Conclusions: In this study it was found that there was a weak correlation between lipemia index and triglyceride levels. There was no correlation was found between the lipemia index and triglyceride levels of the hemolysis index. Lipemia and hemolysis is an important cause of interference for laboratory tests and will affect the results. Each laboratory should develop its own procedures by verifying the index values specified by the manufacturer.

PP-05

Relationship Between Serum Arginase Activity and Blood Lipids in Children with Hyperlipidemia

Özlem Bakırcı[1], İclal Geyikli Çimenci[1], Mehmet Keskin[2], Emel Hatun Aytaç Kaplan[2], Hasan Ulusal[1]

[1]Department of Medical Biochemistry and [2]Department of Child Health and Diseases, Faculty of Medicine, Gaziantep University, Gaziantep

Objectives: This study was planned to examine the activity of arginase, a hydrolytic enzyme that converts essential arginine amino acid, urea and ornithine, and to investigate its association with blood lipids in hyperlipidemic pediatric patients. Hyperlipidemia is a condition caused by elevated plasma lipids and atherogenic lipoproteins due to various causes.

Material and Methods: The study group consisted of individuals aged 0-18 years; 41 patients with hyperlipidemia and 50 healthy children. In the study, arginase enzyme activity was measured by thiosemicarbazide diacetyl monoxime urea (TDMU) method in serum samples taken from children included. The triglyceride, LDL-C, HDL-C and total cholesterol levels of the patient group and the healthy group whose diagnosis was previously determined by the pediatric clinic were measured and confirmed clinically.

Results: When arginase enzyme activity was examined between patient and control groups, although there were different results, this difference was not statistically significant (p=0.777).

Conclusion: In this study, it was concluded that hyperlipidemic patients had no significant association with lipid levels of arginase enzyme activity.

PP-06

Comparision of the Capillary Blood Samples with the use of Heparin and EDTA for Measuring Biotinidase Activity

Leyla Öz[1], Çiğdem Karakukçu[1], Pembe Soylu Üstkoyuncu[2], Selma Buldu[1], Derya Koçer[1]

[1]Departments of Medical Biochemistry and [2]Pediatric Metabolic Diseases, Health Sciences University, Kayseri Education and Research Hospital, Kayseri

Objectives: Biotinidase deficiency is an autosomal recessively inherited disorder caused by impaired biotinidase activity. There are some preanalytical error sources in using capillary blood samples, which is the recommended for screening biotinidase deficiency. Some preanalytical error sources such as; the inhomogeneity of the capillary blood samples saturated on filter paper, difficulties in taking appropriate amount of sample, the inexperience of the person who takes the sample, can be overcome by using the blood samples in the tubes having heparin and EDTA. The aim of this study is to compare the biotinidase activities of capillary blood with samples in heparin and EDTA tubes.

Material and Method: Samples from children having profound and partial enzyme deficiency and healthy individual are included in the study (n=3). Three different samples were taken from individuals; capillary, heparinized and EDTA. Capillary blood samples taken from each individual were applied directly to Gutrie papers. Heparinized and EDTA samples were applied in equal volumes (60 µL) in 30 min without delaying. Biotinidase activity was measured ten times in each sample. Biotinidase enzyme activity was measured by the colorimetric method using the Zentech brand kit and the results were given as Zentech Relative Unit (ZRU).

Results: In capillary blood samples, the enzyme activity was found to be 1.85 ZRU for the individual having complete deficiency, 44.69 ZRU for the individual with partial deficiency and 101.49 ZRU in healthy individual. Coefficiency of variation values of the measurements from samples taken from individual having complete enzyme deficiency, partial enzyme deficiency, and healthy individual, were calculated as 37%, 9.64%, and 8.23% in capillary samples, 21.4%, 4.49%, 5.78% in heparinized samples, and 19.8%, 8.91%, 5.13% in EDTA samples, respectively. There was no difference between capillary blood biotinidase activity levels and enzyme activities in samples in heparinized and EDTA tubes ($p<0,05$). The correlation coefficients between biotinidase activities of capillary-heparinized, capillary-EDTA and heparinized-EDTA samples were r^2=0.969, r^2=0.966 and r^2=0.980, respectively.

Conclusions: There was no difference in enzyme activity between the groups in the study. Additionally, %CV values of blood samples taken with EDTA and heparinized tubes were found to be lower than capillary blood samples, in all patient groups. The reasons of the high variation in capillary blood samples can be because of the preanalytical error sources such as the applicant dependency nature on the application and the subjectivity of the amount of the samples. As a result of the study, it has been observed that the application in the laboratory environment of samples in EDTA or heparinized tubes can reduce measurement errors in the measurement of biotinidase activity.

PP-07

Ankara University School of Medicine Cebeci Laboratory Quality indicators: Specimen Rejection

Özlem Doğan

Department of Biochemistry, Ankara University, School of Medicine, Ankara

Objectives: The IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) working group of 'Laboratory Errors and Patient Safety' (WG-LEPS) has identified several Quality Indicators (QIs) related with all stages of the total test period. 34 preanalytical phase quality indicators such as test selection, patient/sample identification, samples collected in inappropriate containers or with insufficient volumes, hemolyzed or clotted samples and 7 analytical indicators were selected. We aimed to classify the rejected samples registered to the automation system according to the quality indicators.

Material and Methods: Data of the rejected samples in Ankara University School of Medicine Cebeci Hospital biochemistry laboratory between January 2016-January 2017 was screened retrospectively from the laboratory information system. Errors are evaluated according to sample rejection rate, their type and working groups, clinical/outpatient.

Results: It was determined 10 sample rejection criteria in our laboratory. 8 of these criteria were preanalytical (hemolysis, lipemia, inappropriate sample volume, excess volume, improper sample, wrong record, sample did not come, duplicate recording) and 2 of them were the analytical period (device defective, incompatible with the old outcome) indicators. A total of 262.558 samples were admitted to the laboratory and 21.692 (%7.31) were rejected and 34.002 (%1.7) of 2.873.602 tubes were rejected for one year period. The most common reasons for rejection were 23.657 tests and 5384 patients with inappropriate samples. It was observed that the most common reason for inadequate sample rejection was coagulation tests and was caused by the pediatric clinic/polyclinic. In many publications, hemolysis is accepted as the prevalent cause of preanalytical rejection, it was the second most common cause in our study. The most common reason for rejection in our laboratory is 'inappropriate sample' because of he patient population that he serves may be due to pediatric, haematological and oncologic patients which are difficult to obtain blood.

Conclusion: Medical errors; inadequate treatment, time loss, additional cost and delay of diagnosis. On the basis of quality indicators, are the evaluation of potential errors and the frequency of observed errors. It is extremely important to keep the error prone preanaltyical phase that affects the quality of the results of the laboratory under control in order to produce accurate and qualified results. It is required to plan error proofing by taking into account the characteristics of the patient population of the laboratory.

PP-08

Determination of Sample Rejection Rates In Biochemical Test

Kamile Yücel, Ömer Kaya

Department of Medical Biochemistry, Konya Education and Research Hospital, Konya

Objectives: Errors in the preanalytical periods of the analyzes constitutes a large part of the total error. Our aim is to investigate the sample rejection rates determined in biochemical analysis.

Material and Methods: In the retrospective study, reject reasons of biochemical test samples were investigated between 01/01/2017-01/01/2018. The rejection criteria are as fallows: incorrect sample, hemolyzed sample, insufficient sample, empty tube.

Results: A total of 535867 samples were analyzed over a 1-year period and 421errors detected. The frequency of total errors was 0.08%. The most common faults were identified as incorrect sample 0.033 %, hemolyzed sample 0.032%, insufficient sample 0.011%, empty tube 0.002%

Conclusions: Determination of the causes of preanalytical errors is important in the development of the quality process. Laboratory errors that cause sample rejection are situations that prevent patients from getting results sick cases. Rejection rates can be further reduced by training blood draw staff about correct venous blood sample intake and transport.

PP-09

An Interference in Total PSA Measurement: Case Report

Abdulkadir Tekin, Murat Can, Berrak Güven

Department of Biochemistry, Bülent Ecevit University, Faculty of Medicine, Zonguldak

Objectives: Prostate cancer is the most common cancer in men. Total prostate spesific antigen (PSA) is a tumor marker which is used to follow patients with prostate cancer. This case report demonstrates a false positive PSA result caused by a interference in immunoassay.

Material and Methods: A 72-year-old man presented in 2014 with a palpable prostate nodule and a total PSA level of 7.6 ng/mL. It was found prostate cancer (Gleason 7) from his core biopsies and he was treated with radiotherapy. After treatment, he was taken the follow-up at 6-month intervals because of his total PSA levels decreased to 0,04 ng/mL and abnormal values did not detect until October 2017. During his scheduled clinical control in October 2017, the PSA and free PSA were measured 25.9 ng/mL and 0.04 ng/mL with Hybritech PSA (Lot No 771092) and fPSA assays using UniCell DxI 600 Access Immunoassay System (Beckman Coulter, USA). An error was suspected because there was a discrepancy between the test result and the patient's clinical status. Therefore, serial dilutions were made with calibrator S0 by diluting 1:1, 1:2, 1:4 ratio for hook effect. At the same time, serum was assayed with another immunoassay method using by Cobas e602 analyzer (Roche Diagnostics, Mannheim, Germany).

Results: Total PSA results of serial diluted samples were found 23.6 ng/mL, 30.9 ng/mL, 22.6 ng/mL, respectively. Total PSA level was measured 0,05 ng/ml in Cobas analyzer. We also have added test protocol that includes a heterophilic antibody blocking agent (Heterophilic blocking tube (HBT), Scantibodies Inc., USA) to neutralize heterophilic antibodies. Patient's serum was incubated in HBT and reanalyzed total PSA by UniCell DxI 600. The level of total PSA was found 1.54 ng/mL.

Conclusions: Laboratories should be aware of the potential for interference in all immunoassays. It is equally important that physicians communicate any clinical suspicion of discordance between the clinical and the laboratory data to the laboratory.

PP-10

Overview of the Delays of Blood Samples Send to Laboratory by Oncological Department

Emel Şahin, Ali Ünlü

Department of Clinical Biochemistry, Faculty of Medicine, Selcuk University, Konya

Objectives: We aimed to determine the preanalytical causes of the delays in the outcome of the blood samples sent to the laboratory from the Oncology Polyclinic.

Material and methods: Transfer information (delivery staff, delivery personel, delivery time) and sample acceptance information (sample acceptance laboratory staff, sample receipt time) and sample information of the blood samples sent to the laboratory from the Oncology Polyclinic during weekday daytime during the day are shown for 2 months was recorded. The difference between the sample delivery time and the sample acceptance time for the preanalytical process was calculated in minutes and the average was determined. In addition, the difference between the sample acceptance time and the result validation time of the analytical process and the average was calculated. The reasons for the delays in sample acceptance were investigated.

Results: A total of 1890 records were examined. The time period for which the sample barcode was printed and the sample was accepted by the laboratory was evaluated as overdue by more than 10 minutes. The acceptance period of 369 samples that were delayed was above 10 minutes (19.7%). 12 samples were above 30 minutes (0.63%). It was found that 58% of the blood acceptance delays were between noon and 25% of the evening shifts of staff shifts (16.00-17.00). The average acceptance time of all samples was 5.9 min and the yielding time was 50.4 min.

Conclusions: Delays in the preanalytical phase can be reduced by measures to be taken and the adverse effects of the patients can be prevented. Failure rates can be reduced by providing training to personel transferring laboratory samples to the clinics and to personel serving in the laboratory.

PP-11

Problems in the Urine Collection Process and Solution Proposals

Tuncay Seyrekel[1], Saadet Çelik[2]

[1]*Department of Medical Biochemistry, Yozgat City Hospital, Yozgat*

[2]*Department of Medical Biochemistry, Bilecik Public Health Laboratory, Bilecik*

Objectives: In some cases (getting information about kidney functions, determining the substances increased in urine) tests on 24-hours collected urine gives more useful information than tests on spot urine. As the amount of the substances that will be thrown away from the body through urine may vary from hour to hour, analysis of some substances must be based on all urine samples that is collected throughout 24 hours in order to achieve the most accurate results. For this to happen, all the urine that will come out in 24 hours must be collected. But this operation -because of its difficulties- is one of the least patient compatible methods. The aim of this study is to determine the difficulties and to solve problems in addition to implementation of corrective and preventive actions related to preanalytic phase.

Material and Methods: We studied with sampling unit for a month in order to determine the problems. We examined both patient's and laboratory staff's approach on the process once test request is made. Problems -according to degree of importance-are listed as such; 1. Lack of printed instructions of how to collect samples and verbal misguiding of patients by different people. 2. Use of improper container while collecting urine. 3. Delivery of the urine in a tube or cup. 4. Emptying of acid(preservative) because of its scent. 5. Conservation of the collected urine in improper conditions during the period before delivering it to the laboratory. After determining the problems, we started handling them one by one. These are the solutions we came up with at the end of our study: 1. We prepared a document called "24 Hours Urine Collection Procedure" and handed out to the patients. 2. We got in touch with the contractor and had every patient get a an uygun kap 3. We gave instructions to staff and patients in terms of proper collection, conservation and quick delivery of the urine. We kept tracking the appropriacy of incoming samples for a month after finishing our standardization study.

Results: In the patient group that is exposed to our study, properly collected sample rate was significantly higher in terms of statistics compared to the one before. (p=0.0001).

Conclusions: Preanalytic mistakes make up a big part of laboratory errors. Sometimes staff training and sometimes patient training is significantly important. In our study, there has been a meaningful increase in training efficiency and the number of successful delivery of the samples.

PP-12

Evaluation of Effects of Cyclosporine Administration on the Complete Blood Count

Hüseyin Yaman[1], Hatice Bozkurt Yavuz[1], Mehtap Esen[2], Mehmet Akif Bildirici[1], Asım Örem[1], Süleyman Caner Karahan[1], Yüksel Aliyazıcıoğlu[1]

[1]*Department of Medical Biochemistry, Karadeniz Technical University, Faculty of Medicine, Trabzon*

[2]*Bayburt State Hospital, Bayburt*

Objectives: Cyclosporine is an immunosuppressive drug which inhibits calcineurin. It can be used not only in patients with organ transplantation but also in diseases such as nephrotic syndrome, psoriasis and rheumatoid arthritis. Peak concentration may frequently occurs two hours after intake. Hematologic system related side effects such as hemolytic anemia, thrombocytopenia, hemolytic uremic syndrome are present. Changes in complete blood counts were observed when rats were given cyclosporine. There was a significant difference in the involvement of radioactive material in erythrocytes between basal and peak levels of cyclosporin concentration. Based on this information, we aimed to evaluate the drug administration before blood sampling as a pre-analytical error and to investigate the effects of drug use on erythrocyte indices, platelets and leukocyte counts in patients using regular cyclosporin.

Material and Methods: In our study, blood collected to K3 EDTA tubes from 41 patients who received regular cyclosporin treatment because of solid organ transplantation before and 2 hours after administration of the drug. Cyclosporine levels were measured on Roche Cobas e411 autoanalyser and complete blood count parameters were measured on Beckman Coulter DXH-800 autoanalyser from the blood samples taken before (0. hour) and 2 hours after (2. hour) drug administration and the significance of the results was assessed using the SPSS program. Distribution of the parameters was assessed by the Kolmogorov-Smirnov test. Parametric tests were assessed by paired-T test, nonparametric tests by Wilcoxon test, and $p<0.05$ was considered statistically significant.

Results: The mean level of cyclosporine was 145 mg/dL at 0.hour and 659 mg/dL at 2. hour. Erythrocyte indices were evaluated, hemoglobin and RDW measurements showed statistically significant difference

(p=0.033, p=0.034). The mean levels of HGB and RDW were 11.2 g/dL and 16.1% at 0. hour, 11.0 g/dL and 16 % at 2. hour, respectively. There was no statistically significant difference between RBC, HCT, MCH, MCHC, PLT and WBC levels (p>0.05).

Conclusions: Blood collection from patients after drug use is one of the significant preanalytical errors. Although there is a statistically significant difference between HGB and RDW values in our study, we think that there is no clinically significant difference. We were expecting a difference in erythrocyte indices according to cyclosporine levels because of preliminary studies about cyclosporin, but in our study, we found that cyclosporine levels increased 4-5 times after drug administration in patients who used regular cyclosporin but these levels did not cause any change in complete blood count parameters in the short term.

PP-13

Rejection Rates of Coagulation Tests with Respect to Preanalytical Error Sources

Emre Yalçınkaya, Hayriye Erman, Nevin Genç Kahraman, Afife Şerifoğlu, Eray Kıraç, Alperen Aksoy, Rabia Korkmaz, Ferruh K. İşman, Mustafa B. Çekmen

Department of Medical Biochemistry, Istanbul Medeniyet University Göztepe Training and Research Hospital, Istanbul

Objectives: It is very important to give accurate results in diagnosis, treatment and follow-up of the disease. Accurate results are not just about the performance of the laboratory. The quality of the laboratory sample, the test preparation and processing steps in the laboratory, and the accuracy of the results reporting and storage steps are of similar importance. In this study, it is aimed to evaluate the rejected coagulation samples retrospectively from the laboratory information system in order to plan the necessary corrective actions.

Material and Methods: We retrospectively analyzed the records held for rejected coagulation samples in our hospitals biochemistry laboratory in 2017. We categorized rejected samples according to their respective specific error sources and calculated sample numbers, error numbers, and percentages in the Microsoft Office Excel 2016 program (clotted sample, inappropriate sample volume, incorrect barcode, inappropriate sample tube, hemolyzed sample, lipemic sample, etc).

Results: During one year period, 111.817 coagulation tubes were accepted in our laboratory which 2.524 samples (2.26%) were rejected. When classified according to the reason for rejection, it was observed that inappropriate sample volume (1512-59.90%), clotted sample (801-31.74%) and inappropriate sample tube (71-2.81%) were in the first three orders.

Conclusions: It is very important to keep the preanalytical step which is most affected by the quality of the results produced by the laboratory for to produce the correct and quality results. For this purpose, necessary preventive measures should be taken by considering the characteristics of the patient population served by the laboratory.

PP-14

Effect of Preanalitic Conditions on Vitamin B12 Stability in Plasma and Serum Samples

Afife Serifoğlu, Eray Kıraç, Emre Yalçınkaya, Nevin Genç Kahraman, Alperen Aksoy, Rabia Korkmaz, Hayriye Erman, Mustafa Baki Çekmen, Ferruh Kemal İşman

Istanbul Medeniyet University Göztepe Training and Research Hospital Medical Biochemistry Laboratory, Istanbul

Objectives: The correct measurement of serum vitamin B12 deficiency is critical because of bone marrow failure and reversible demyelinating nervous system disease. Changes in test results can be induced by preanalytical and analytical processes or biological variations in addition to pathophysiological processes. Ideally, blood samples are collected at a central laboratory and processed immediately to avoid any unwanted changes in test results. We investigated the effect of centrifugation type (refrigerated and uncooled, storage temperature (2-8°C and 25°C) and storage time (4 hours and 24 hours) on vitamin B12 levels in this study.

Material and Methods: Blood was collected from 4 volunteers (3 male, 1 female) at the same time of the day (9:00 am) 6 tubes from each donor (4 tubes 5 mL SST, 2 tubes 10 mL K2EDTA). Samples from each patient were divided into two 3 tube groups and these were centrifuged at 1300 g for 10 minutes in refrigerated and uncooled centrifuges. Samples and plasma samples were separated into aliquots. Initially 0. minute measurements were performed. Aliquots were analyzed for storage at 2-8 °C and 25 °C and at 4 hours and 24 hours. Vitamin B12 analysis was performed using the chemiluminescence immunoassay method on Abbott Architect i1000. The results were evaluated using the Microsoft Excel 2016 software. The difference analysis was performed with Friedman test using the IBM SPSS 22.0 software.

Results: The percent change values for all of our parameters were within the allowed total error (TAE) limits and no statistically significant difference was found (p=0.084). Stability of vitamin B12 was not affected by different types of centrifugation in serum and plasma samples, storage up to 24 hours at 4°C and 25°C.

Conclusions: Vitamin B12 may tolerate rather long delays under different conditions without changes in the analyte content, suggesting that the effect of preanalytical conditions studied on the stability of vitamin B12 is not clinically significant. It may be useful to do this work in a larger population.

PP-15

Effect of Filling Ratio of Coagulation Tubes as Preanalytical Error Source on Coagulation Test Results

Nevin Genç Kahraman, Eray Kıraç, Hayriye Erman, Afife Şerifoğlu, Alperen Aksoy, Emre Yalçınkaya, Rabia Korkmaz, Mustafa Çekmen, Ferruh İşman

Department of Medical Biochemistry, İstanbul Medeniyet University, Göztepe Training and Research Hospital, İstanbul

Objectives: Coagulation tests are one of the most common test panels used in the biochemistry laboratory. Emergency, intensive care units, internal and surgical services, pediatric services and many outpatient clinics order coagulation tests. It is very important to report test results quickly and accurately. However the underfilling or overfilling of the blood in the sample disturbs the 1:9 citrate blood ratio in the tube and

causes preanalytical errors. The aim of our study is to compare the results of the coagulation tests performed by using the blue cap-citrate tubes drawn at different levels.

Material and Methods: Blood samples from 8 volunteers (4 female, 4 male) were obtained by filling 4 vacuette-greiner tubes from each volunteer with different volumes; (2 mL tube; 3.2 % sodium citrate) 50%, 75%, 100% and 125%. In this study, the tube filled up to the fill line was considered to be 100% full. The caps were closed and gently turned upside down 5-6 times. The samples were centrifuged at 2000 g for 15 minutes. The PT, aPTT, INR and fibrinogen parameters were studied in Stago-Sta Compact Max analyzer. The difference between the dependent multiple groups was analyzed by Friedman test and the difference between the two groups was analyzed by Wilcoxon test in PASW Statistics 18 program.

Results: The results of PT, aPTT and fibrinogen in 50% and 75% filled tubes were significantly higher than those of 100% filled tubes. In addition, the results of the aPTT test results of overfilled tubes which are 125% full were significantly lower than aPTT results of 100% full. No difference was found between the results of the INR test.

Conclusions: For accurate reporting of coagulation test results, the sources of preanalytical errors should be minimized. The aPTT test is influenced by both insufficient sample and overfilled sample volume. It is advisable to only accept tubes that are filled to the blood-filling line if the PT and aPTT tests are performed simultaneously.

PP-16

Ammonia Stability in Different Preanalitic Conditions

Rabia Korkmaz, Emre Yalçınkaya, Nevin Genç Kahraman, Afife Şerifoğlu, Alperen Aksoy, Eray Kıraç, Hayriye Erman, Ferruh Kemal İşman, Mustafa Baki Çekmen

Department of Medical Biochemistry, Istanbul Medeniyet University Göztepe Training and Research Hospital, Istanbul

Objectives: Preanalytical factors are a major source of variability for laboratory results. The neglect of these factors leads to erroneous outcomes and consequent erroneous clinical decision-making. In this study, we sought to test the stability of ammonia, depending on the temperature and duration of the run.

Material and Methods: Blood samples were collected from 8 healthy volunteers in EDTA tubes in the laboratory, centrifuged for 10 min at refrigerated (4 °C) and uncooled centrifuge at 2000g. Firstly, the plasma of 5 volunteers were separated into 6 aliquots each. Plasma separated for refrigerated centrifuge was kept refrigerated (4 °C) and the plasma separated by the uncooled centrifuge was kept at room temperature. Two measurements were made for each sample at 0-30-60-90-120-180 minutes. Secondly, plasma of 3 volunteers were not separated and refrigerated samples were centrifuged in the cooled centrifuge, and second group of samples kept at room temperature were centrifuged without cooling at room temperature. Two measurements were made for each sample at the 0-30-60-90-120-180. minutes. Ammonia was studied using the glutamate dehydrogenase method in the Abbott Architects ci4100 auto analyzer. The data was analyzed in Microsoft Office Excel 2016.

Results: The percent change in the 30-60-90-120-180. minutes was calculated with reference to the average value of 0. hour. When the optimal limits for total error limits based on biological variation are used, the plasma and whole blood samples kept at 2-8 ºC do not exceeded the limits; plasma and whole blood samples stored at room temperature were out of limits at 120 minutes and after. Based on desirable error limits data, plasma and whole blood samples at 2-8 ºC and room temperature, plasma ammonia did not exceed the limits, while whole blood samples waiting at room temperature were beyond the limit after 180 minutes.

Conclusions: In the ammonia results, there was no clinical difference between the stored plasma and whole blood samples at 2-8 ºC, while the deterioration was observed at 120 minutes for plasma and whole blood samples kept at room temperature. It may be advisable to work with a larger population and patient group to achieve optimal results.

PP-17

Drug Therapy as a Source of Preanalytical Error in Patients With Protein C and/or S Demand

İkbal Özen Küçükçetin[1], Kadriye Ece Ünüvar[2], Gültekin Yücel[2], Sadi Özdem[3], Sebahat Özdem[2]

[1]Department of Nutritional Sciences, [2]Medical Biochemistry and [3]Medical Pharmacology, Akdeniz University, Faculty of Medicine, Antalya

Objectives: Venous thromboembolism (VTE) often presents with deep veins thrombosis and/or pulmonary embolism and affects 1-2 out of every 1000 people in general population. Various hereditary and acquired conditions can lead to thromboembolism. Protein C, protein S or antithrombin deficiencies are leading hereditary causes. About 5-15% of patients with VTE show deficiencies of these proteins. Besides hepatic dysfunction, immobilization, surgery, malignancies, smoking, vitamin K deficiency and pregnancy; treatments with warfarin, L-asparaginase or estrogen are among reasons for acquired VTE. Identification of patients at risk is quite important due to high prevalence of VTE and frequency of adverse outcomes. Deficiencies of protein C and S can be observed both in hereditary and acquired conditions. Therefore, laboratory measurements of these proteins are particularly important. During course of the measurement, patients should be questioned about the presence of above-listed reasons that could cause acquired deficiencies. In this retrospective study, we assessed presence and relation of concurrent drug use with results in patients send to our laboratory for protein C and S measurements.

Material and Methods: Between July 2017-January 2018, we screened 729 files belonging to patients (F=446, M=283) with protein C and/or S measurement together with drugs received during course of sample collection. Protein C and S were measured using Siemens ®BCS-XP Coagulation Analyzer.

Results: 125 (17.15%) of 729 patients were on drugs known to affect protein C and/or S results during sample collection period and in 295 (40.6%) patients, protein C and/or S levels were below reference range. 25.8% (76) of these 295 patients with results below reference value and 49 (11.3%) of 434 (59.4%) patients with results within reference range were on drugs that could affect results.

Conclusions: In hemostasis tests, besides other clinical situations it is very important to determine whether patient is on anticoagulants during sample collection. We determined that approximately one-quarter of patients with protein S and/or C levels below reference value were on drug(s) that could affect results of measurements. False low levels, by necessitating repetition of and/or need for further tests, may reduce patient satisfaction and cause time, labour and prestige losses in laboratory.

PP-18

Evaluation of Preanalytical Error Sources in Our Medical Biochemistry Laboratory

Duygu Eryavuz, Sedat Abusoğlu, Büşra Ecer, Abdullah Sivrikaya, Ali Ünlü

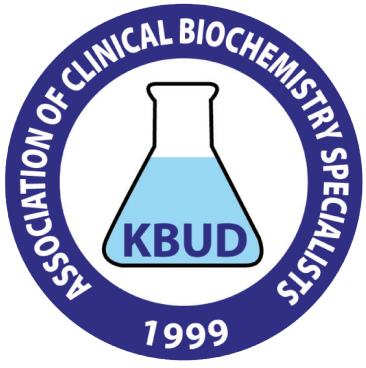
Department of Biochemistry, Selcuk University Faculty of Medicine, Konya

Objectives: Laboratory errors are divided into preanalytic, analytical and postanalytical faults.Pre-analytical steps, the major source of mistakes in laboratory diagnostics, arise during patient preparation, sample collection, sample transportation, sample preparation, and sample storage. Today, preanalytical errors account for more than 70% of laboratory errors. Our goal in our work is to determine the sources of major errors by determining the percentage distributions of error sources in our laboratory.

Material and Methods: In 2017, tests conducted in our hospital biochemistry laboratory were retrospectively screened from the Enlil system. Pareto analysis was performed for preanalytical error sources. Percentage rates of preanalytical errors are calculated according to error sources.

Results: The total number of tests tested is 3.931.033 while the rejected tests are 44.341 52% of the rejected tests were rejected because of preanalytical errors. The first three most common error sources are; hemolyzed sample (41%), insufficient sample (38%) and false sample (13%).

Conclusions: We found that preanalytical errors were the major error source among the error sources in our laboratory and that hemolysed samples (41%) were the most common preanalytical error sources. The faults that most affect the quality of the laboratory tests are the preanalytical faults and it is very important to keep these faults under control and to produce accurate, reliable and quality results. For this, necessary planning should be done to reduce and prevent mistakes such as education.



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Dear Colleagues,

As Board of Association of Clinical Biochemistry Specialists, we were pleased to be with you at KBUD Congress and Lab Expo 2018 with International participation and 1st Hereditary Metabolic Diseases Symposium that is held in Antalya between October 1-4, 2018

Scientific program was prepared to follow the scientific and technological developments in biochemistry and clinical biochemistry fields. With the courses, conferences, panel and satellite symposiums included in the scientific program, participants benefited from the knowledge and experience of the invaluable speakers in this field.

In the congress and symposium, there were a total of 6 panels including preanalytical, liquid waste management in health institutions, microbiota and diseases, kidney diseases, laboratory support system in laboratories and toxicology panels. The conferences on aging, biochemistry innovation, vitamin D, occupational health and safety, laboratory problems in hemoglobinopathy, lipids and cardiovascular diseases, Alzheimer's disease, detoxification and thioredoxin issues were presented. Courses on CLSI Document Training, Total Analytical Error, Hematology and Complete Urinalysis and Sediment enabled participants to reinforce their knowledge through practical applications as well as theoretical knowledge.

We believe that our congress and symposium made significant contributions to participants and the world of science. We would like to express our gratitude to our speakers, participants and diagnostic companies that sponsored our congress and symposium.

Best regards

Professor Dr. Dildar Konukoğlu

President

Association of Clinical Biochemistry Specialists

ULUSLARARASI KATILIMLI

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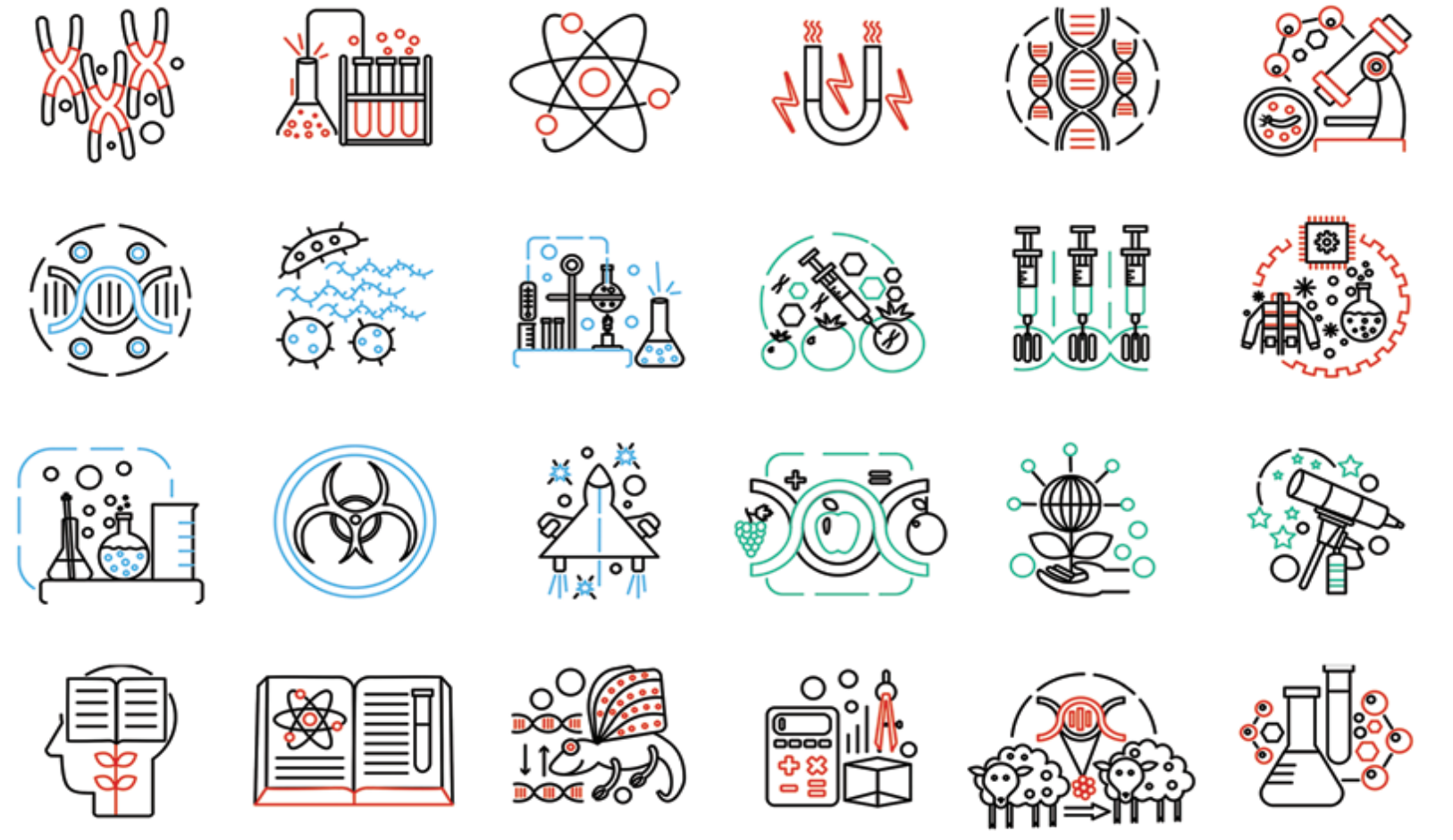

SCIENTIFIC PROGRAMME AND ABSTRACTS

Conference Abstracts

C-01

The Most Prevalent Type Of Dementia: Alzheimer's Disease

Kaya Emerk

Department of Biochemistry, Marmara University, Medical School, İstanbul

Dementia is a serious clinical condition leading to loss of intellectual skills and personality changes together with deterioration in memory, and it may even hinder daily functioning levels of the individual. The prognosis goes in parallel with the progressive deterioration of mental functions such as memory, attention, perception, speaking, planning, and decision making. It is one of the most significant health issues in geriatrics. The incidence of dementia increases with the increase in life expectancy.

Dementia may develop as a result of various causes. It may stem from a neurological or medical problem such as Vitamin B12 deficiency, insufficient function of the thyroid gland, neurovascular diseases etc. The incidence of dementia increases with age. Approximate distribution is 1% in those aged 60-65 years, 6% in 75-79 years and ≥20% in 80 years of age and above. The billions of cells in the brain gradually decrease with aging, leading to shrinking i.e. a smaller mass of the brain. The shrinking does not always occur at levels that lead to disease. A certain level of memory loss and reasoning skills is expected in old age. The sensory skills such as touch, taste, hearing, vision and smell may deteriorate as the communication between nerve cells slows down. Forgetfulness at a certain level (depending on slower brain functions) and requiring more time for problem solving are regarded as normal.

The causes of dementia include the following: Alzheimer's disease 50-80%; Lewy body dementia 20%; neurovascular diseases 5-10%; and Parkinson's disease <5%.

Alzheimer's disease affects the brain areas responsible for thinking, memory, language and skills. The initial phase is subtle and the destruction is usually slow-progressing. Currently, there is no definitive treatment approach to fully cure the disease.

What are the risk factors for Alzheimer's disease? Advanced age, family history (genetics), female gender, major head trauma, hypertension, diabetes, low education level, depression.

There may be a hereditary predisposition for Alzheimer's disease in some families; however, this is rather an exceptional. Alzheimer's disease should be suspected if the forgetfulness has become persistent and gets worse, affecting language, reasoning, understanding, and focusing; if behavior disorder (aggressive, anxious etc.) is observed; and if challenges in maintaining daily activities (cooking, traveling alone, driving, shopping) emerge and deterioration in memory and skills start interfering with daily life.

If life expectancy in humans had not increased, Alzheimer's disease would have remained a rare and interesting disease in the medical literature (Konrad and Ulrike Maurer).

Factors that provide protection against disease: Estrogen?, antioxidants, anti-inflammatory agents, statins, presence of APOE ε 2, education, mental and physical activities, sufficient social network. The relationship between education and dementia risk can be explained in two ways. Education has a protective effect according to the "Brain Reserve" hypothesis. This is likely to be resulting from the fact that education enhances synaptic density or activity or acquired skills, thereby enhancing cognitive functions beyond dementia threshold.

In Alzheimer's disease, the following non-genetic biological markers in plasma indicate high risk: Thrombocytes, APP level changes, high CRP and IL-6 while elevated cholesterol, LDL and HDL indicate increased risk and elevated homocysteine is effective especially in lower education levels.

In CSF, increased Tau and low Ab42 levels are observed in patients with Alzheimer's disease while this is not observed in the non-affected elderly. High Tau, low total Ab and increase in Tau/Ab42 ratio distinguish Alzheimer's disease from aging. High levels of phosphorylated Tau is considered as a risk factor for the transition from MCI to Alzheimer's disease.

There is no specific diagnosis method for Alzheimer's disease. The disease is diagnosed by means of clinical and assisting diagnostic methods. Acetylcholine in CSF decreases, and choline acetyltransferase enzyme activity in cerebral cortex and hippocampus decreases about 50-90%.

The following tests may be conducted depending on the clinical results: B12, folate, thiamine deficiency, blood glucose, hypoglycemia, full blood count, anemia, drug screening, drug toxicity, electrolytes, hypercalcemia, high manganese levels, hypernatremia, liver function tests, liver disease, lumbar puncture, normal pressure hydrocephalus, encephalitis, meningitis, thyroid function tests, hypothyroidism, VDRL, syphilis, and HIV infection.

In terms of the mechanism of Alzheimer's disease, the current understanding may be summarized as follows: The disease was defined by Dr. Alzheimer in 1958 for the first time. Neurovascular tangles and amyloid plaques were observed in postmortem brain histology. When the structures of the formations were examined, it was determined that the amyloid plaques consisted of a polymer of the β amyloid protein while the tangles were formed due to the clustering of Tau, an intracellular protein.

Amyloid plaques were shown to be formed as a result of consecutive APP gene product fragmentation. There are two major isoforms: Aβ42 and Aβ40. Although having only a 10% ratio, 42 is more toxic.

The α-secretase product of Amyloid Precursor Protein (APP) dissolves easily, and does not cause amyloid accumulation. β and γ secretase products, on the other hand, are less soluble and lead to β-amyloid protein accumulation. This accumulation starts the development of disease. Defects (mutations) of the gene coding APP on the 21st chromosome may lead to the excessive βAP production.

In AD, neurofibrillary tangles (NFTs) are increased in hippocampus, amygdala, and cortex. The tangles disrupt cholinergic transmission (nucleus basalis of Meynert) and other transmission channels (locus coeruleus). These are intracellular, and functions of double strand neurofilament fibers (abnormal phosphorylated forms of Tau protein) deteriorate, triggering cell death. The density NFTs and mental destruction progress in a parallel manner. Aluminum may be playing a role in AD development by enhancing the phosphorylation of Tau.

Neuritic plaques, on the other hand, are extracellular. These structures contain amyloid peptides with fragmented neurons around them. Plaque formation may precede the accumulation of NFTs. The density (number) of neuritic plaques and the severity of disease progress in a parallel manner.

A treatment method providing complete AD cure has not been discovered to date. Current pharmacological treatment approaches mostly aim to increase the functional capacity of remaining healthy neurons. The effective drugs for treatment may be classified as those effective on the cholinergic system, acetylcholine precursors, cholinergic agonists, and cholinesterase inhibitors. It should be noted that cholinesterase inhibitors need healthy cholinergic neurons in order to be effective. These drugs are only effective in mild and moderate cases. They should not be expected to be effective in advanced AD.

Drugs that decrease free radical formation such as antioxidants, Vit E, Vit C, superoxide dismutase, glutathione peroxidase, beta carotene, Vit E, (α-tocopherol) are used to delay clinical deterioration

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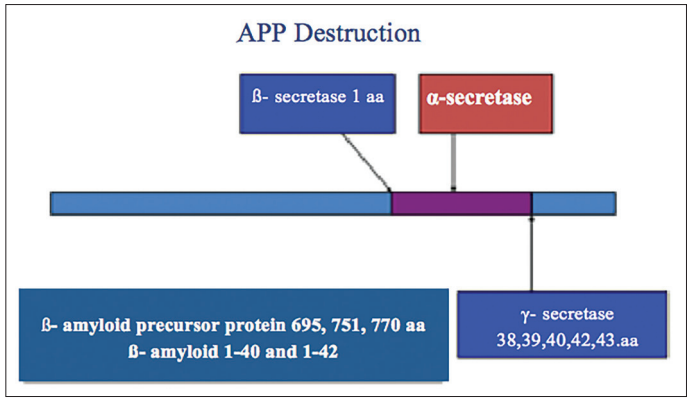

Figure 1.

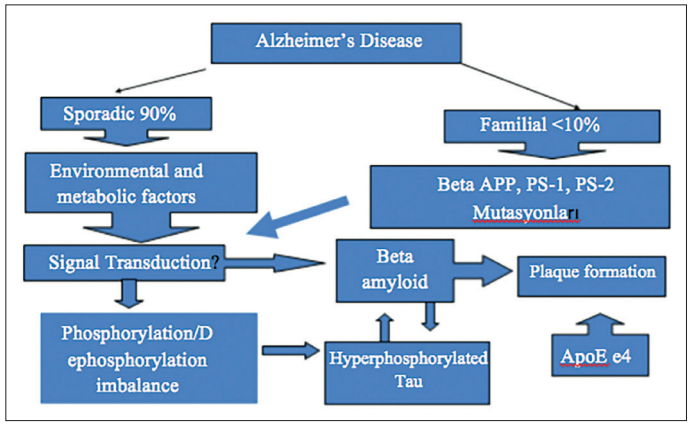

Figure 2.

C-02

Expanding Space for Next Generation Sequencing Diagnostics Applications

Maurizio Ferrari

Department of Genomic Unit for the Diagnosis of Human Pathologies, Vita-Salute San Raffaele University, San Raffaele Scientifi C Institute, Milan

The recent advances in the genomic field and the development of new technologies for DNA testing started the revolution of the diagnostic laboratory. For the diagnosis DNA-based diagnostics provide a sensitive alternative to protein-based diagnostics and the mutation detection is one of the most important areas of molecular diagnostics today. Advances in DNA analysis to develop methods, which are increasingly specific, sensitive, fast, simple, automatable, and costeffective, are considered paramount. These demands are currently driving the rapid evolution of a diverse range of newer technologies. Researchers have discovered hundreds of genes that harbour variations contributing to human illness, identifi ed genetic variability in patients' responses to dozens of treatments, and begun to target the molecular causes of some diseases. In addition, scientists are developing and using diagnostic tests based on genetics or other molecular mechanisms to better predict patients' responses to targeted therapy. For the future of genomics is demanding the rapid evolution of high-throughput genotyping technologies (next generation sequencing) toward increased speed and reduced cost. The speed, accuracy, efficiency, and cost-effectiveness of DNA sequencing have been improving continuously since the initial derivation of the technique. With the advent of massively parallel sequencing technologies, DNA sequencing costs have been dramatically reduced. The recent introduction of instruments capable of producing millions of DNA sequence reads in a single run is rapidly changing the landscape of genetic diagnostics, providing the ability to answer questions with heretofore unimaginable speed.

C-03

Current Developments in the Relationship of Lipids and Cardiovascular Disease

Sebahat Özdem

Department of Medical Biochemistry, Akdeniz University, Faculty of Medicine, Antalya

Atherosclerosis-related diseases such as cardiovascular disease and stroke are among the most significant reasons for morbidity and mortality in all over the world, particularly in developed and developing countries [1]. Atherosclerosis is accepted as a chronic inflammatory disease of artery wall arising from inappropriate inflammatory and unbalanced lipid metabolism. According to our current information, vascular endothelium, monocytes, macrophages, T lymphocytes, smooth muscle cells, cytokines, and lipids participate in the course of this process.

Lipids and metabolism products have a role in organizing several cellular processes like cell growth, proliferation, differentiation, survivability, apoptosis, inflammation, motility, membrane homeostasis, chemotherapy response and drug resistance. Lipid metabolism is regulated by multi signal pathways; it produces various bioactive lipid molecules. These bioactive lipid molecules, also known as signal molecules include eicosanoids, diacylglycerol, phosphatidic acid, lysophosphatidic acid, ceramide, sphingosine, sphingosine-1-phosphate, phosphatidylinositol-3 phosphate and cholesterol and fatty acids activate and/or organize different signal pathways [2].

Although epidemiological studies indicate that many of genetic and environmental factors contribute in formation of atherosclerosis, it has been known for many years that increased serum cholesterol levels have a great contribution in development of atherosclerosis [3]. Besides, it is well-known that HDL-cholesterol (HDL-C) is an independent protective factor for coronary artery disease. This effect of HDL was revealed for the first time by Framingham heart study by showing the reverse relationship between HDL-K level and cardiovascular diseases [4]. Upon demonstration of high LDL-cholesterol (LDL-C) and low HDL-C levels, the interest has focused on reducing the risk factors such as hypertension, smoking, diabetes mellitus in prevention and treatment of atherosclerosis in addition to regulation of abnormal lipid levels. Within this scope, one of the most emphasized targets is to decrease LDL-C. There are different approaches and treatment choices for decreasing LDL-C. It is proved by clinical studies that statins that have been used for this purpose since 1988 provide beneficial effects in primary and secondary prevention of coronary artery disease. Apart from statin treatment for decreasing LDL-C; there are other measures such as life style changes, diet (feeding with low cholesterol and low saturated fatty acids), ileac bypass surgeries, inhibition of intestinal absorption of cholesterol (with ezetimibe), use of monoclonal antibodies developed against proprotein convertase subtilisin/kexin type 9 protein to increase hepatic LDL receptor [5].

Even though LDL-C is reduced in new studies on atherosclerosis, there are two important problems in terms of cardiovascular events. One of them is that a great majority of cardiovascular events develop in people with normal LDL-C and HDL-C levels. The second problem is that cardiovascular events continue to develop despite aggressive therapy for reducing LDL-C in a majority of subjects.

The studies performed to clarify these problems revealed the possibility of differences in qualitative characteristics of both LDL and HDL molecules by showing sub-types of these lipoproteins with different sizes, shapes, antigenicity and load attributes. Through these studies small dense LDL (sdLDL) found its place in atherosclerosis while it was shown that HDL has heterogeneous sub-types and this heterogenicity directly affects the biological activity and metabolism of HDL.

Besides HDL's capacity to avoids cholesterol deposition in the artery wall by transferring the cholesterol from the periphery to the liver, the demonstration of its strong antioxidant and anti-inflammatory effects supported the idea that this particle is an anti-atherosclerotic molecule. However, the recent studies showed that HDL may become a pro-inflammatory particle through acute and chronic inflammation-induced changes in its structure and function, which was named as dysfunctional HDL. Later on, studies also showed that this dysfunctional HDL may be directly and/or indirectly involved in progression of atherosclerosis.

However, the studies revealed the necessity for discriminating between functional loss of HDL and its conversion to dysfunctional form. Indeed, HDL may completely lose its anti-inflammatory effects and gain pro-inflammatory characteristics by dysfunctional gains. However, in particular situations, there might be partial functional loss in HDL [6].

The fact that cardiovascular events continued to develop in many of the subjects despite aggressive LDL-C reducing treatments caused the inclusion of triglyceride, that was mostly ignored, into the game again in addition to LDL-C and dysfunctional HDL. Recent meta-analysis results showed that high triglyceride (TG) and TG-rich lipoprotein level is an independent risk factor as atherogenic structures apart from the risk caused by high LDL-C for cardiovascular diseases.

The frequent occurrence of high TG levels with low HDL levels is interpreted as atherogenic dyslipidemia. ATP III (ADULT TREATMENT PANEL III) defines this situation as a significant risk factor for coronary artery disease [7].

Large-sized chylomicrons and very low-density lipoproteins (VLDL) cannot enter into arterial lumen because of their sizes. However, remnants of VLDL and TG-rich chylomicron and VLDL rapidly penetrate into artery wall and contribute to cholesterol in atherosclerotic lesions. A unique aspect of of these remnants compared to LDL particles is that they do not require oxidative modification for their uptake by macrophages and that they may be associated with higher levels of inflammation. Lipoprotein lipase enzyme produces proinflammatory mediators including free fatty acids by hydrolyzing TG within the remnant lipoprotein in subendothelial space. These increased fatty acids contribute to development of atherosclerosis by various mechanisms such as stimulation of proinflammatory cytokines, procoagulant factors, inhibition of fibrinolysis and upregulation of endothelial adhesion molecules. Some population studies concluded that TG associated cardiovascular risk results for the relation between VLDL particles/metabolic remnants and sdLDL particles. This relation is the view that continued presence of VLDL in circulation may result in formation of more atherogenic sdLDL particles. Hypertriglyceridemia is also associated with particles with higher apoC-III concentrations apart from low HDL particles and apoA-I concentrations and high sdLDL particles [8].

A recent study showed that high TG levels particularly those >200mg/dl causes atherosclerotic plaque progression and reduction in TG level induces regression of plaques. Another study concluded that high TG is an independent causal factor for endothelial dysfunction that is accepted as one of the initial steps of atherogenesis [9].

2016 guidelines of European Society of Cardiology recommends that TG level reducing treatments can be used in combination with statins in high risk patients with TG levels >2.3 mmol/L (200 mg/dL) despite statin treatment (patients with documented cardiovascular disease, diabetes, and chronic kidney disease). 2017 Diabetes Guideline of American Clinical Endocrinologists Association states that measuring TG levels should be a part of routine lipid scanning. This guideline expresses that moderate elevations (≥150 mg/dL) in TG define the individuals with insulin resistance syndrome; and levels ≥200 mg/dL define individuals who have substantially increased risk for atherosclerotic cardiovascular disease [8].

Despite their wide usage, all the well-known lipid biomarkers such as total cholesterol, LDL-C, HDL-C, and TG can reveal increased sensitiveness against cardiac events, although they still remain insufficient in predicting cardiovascular events. Recent studies revealed that ceramides could be used as very reliable diagnostic tests to predict undesirable major cardiac events.

Ceramides are synthesized in all the tissues by using saturated fatty acids and sphingosine. They are lipid structures of which synthesis is stimulated by inflammatory cytokines. Ceramides playing a role in platelet activation and endothelial dysfunction keep lipids in vascular wall by inducing transcytosis of oxidized low-density lipoproteins from endothelium (9). Moreover, ceramides also contribute to plaque formation by promoting adhesion of monocytes to vascular wall [10]. Adiponectin receptors have a natural ceramidase activity and decrease ceramide levels. Ceramidase activity is dependent on adiponectin levels and regulated by binding to the receptors. Adiponectin stimulates the ceramidase activity by binding to AdipoR1 and AdipoR2 receptors; accordingly, sphingosine formation is stimulated by ceramide catabolism. Sphingosine produced is phosphorylated by sphingosine kinase to create sphingosine-1 phosphate (S1P) that is a bioactive sphingolipid metabolite with anti-apoptotic and antidiabetic effects. S1P transferred to the extracellular space binds to S1P receptors, increases intracellular calcium and activates AMP-dependent kinase pathway (AMPK). Contrary to the effect of ceramide, S1P activates Akt and promotes cellular proliferation. These findings suggest that inflammatory cytokines are closely related to the modulation of sphingolipid metabolism. S1P and ceramide have opposite roles; 'reostat theory of sphingolipids' in body metabolism regulates the fate of the cells to survive or die [11].

Studies show that three ceramides in circulation are particularly associated with cardiovascular mortality. These ceramides are N-palmitoyl-sphingosine [Ceramide (16: 0)], N-stearoyl-sphingosine [Ceramide (18: and N-nervonoyl-sphingosine [Ceramide (24: 1)].

Recognition of the prominent role of inflammation in every step of atherosclerotic plaque development triggered the preclinical and clinical

studies investigating the potential relationship between systemic inflammation and atherogenesis. Studies revealed the residual inflammatory risk concept. The residual inflammatory risk is a term used for cardiovascular events (e.g. myocardial infarction, stroke and cardiovascular death, etc.) occuring despite 'optimal' medical treatment. In current practices for treatment of atherosclerosis it is recommended that residual inflammation needs to be treated in addition to desired targets in lipid levels [12].

Lastly, as we have a look at omega-3 fatty acids, there are contradictory results on effects of supplemental omega-3 fatty acids on cardiovascular disease although omega-3 fatty acids have reported to play a protective role against atherosclerosis with their effects on lipid metabolism, thrombosis and inflammation [13, 14].

Dyslipidemia and inflammation display a complex interaction in pathophysiology of atherosclerosis; so, they should be evaluated together.

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C-04

Laboratory Management of HbA_{1c} Test in Patients with Hemoglobinopathies

Fikriye Uras

Department of Biochemistry, Marmara University, School of Pharmacy, Istanbul

HbA1c is glycated hemoglobin, a fraction of hemoglobin (Hb)-reflecting the average glucose concentration over the preceding 2-3 months. Utility of the HbA1c test for diagnosis and follow-up of diabetes is based on several assumptions:

1. Hemoglobin lifetime is same as the erythrocyte lifetime of 120 days.
2. Hemoglobin fractions in the blood of healthy adults are approximately 95-98% HbA, 1-2% HbA2 and 1% HbF (fetal hemoglobin).
3. The structure and amount of the peptides in hemoglobin molecule are normal.
4. The International Federation of Clinical Chemistry and Laboratory Medicine has defined HbA1c as 'Hb that is irreversibly glycated at one or both N-terminal valines of the beta chains. This does not exclude hemoglobin that is additionally glycated at other sites on the alpha or beta chains.' But this does not include lysine glycation alone.

If at least one of these assumptions fails, HbA1c test becomes problematic to use in diagnosis and follow-up of diabetes.

Hemoglobinopathies

Abnormalities in the structure of hemoglobin chain for various reasons such as genetic mutations, deletions, and insertions, lead to hemoglobinopathies, which are usually examined in two main groups, hemoglobin variants and thalassemia. 70% of the mutations are in the beta chain [1]. The four most common variants in the world are hemoglobin S (HbS), hemoglobin E (HbE), hemoglobin C (HbC) and hemoglobin D (HbD). Generally, HbA1c measurement is not reliable in homozygotes because they cannot produce HbA. However, it can be measured in heterozygotes using an appropriate assay. Alpha or beta chain synthesis is reduced or lack in thalassemia. The average incidence of thalassemia and hemoglobinopathies in Turkey was reported to be 4.3%. Beta thalassemia is most frequently seen in Antalya (13%), sickle cell anemia in Mersin (13.6%), Hatay (10.6%) and Adana (10%) [2].

Hemoglobinopathies can make measurement and interpretation of HbA1c quite challenging. They can have either falsely increased or falsely decreased HbA1c levels. Some hemoglobinopathies reduce the erythrocyte lifespan and HbA1c concentration.

Factors affecting the interpretation of HbA1c results regardless of the method

HbA1c is not affected by blood glucose levels alone. Other factors affect the interpretation of HbA1c results regardless of the assay method used [3, 4]. The most common factors are:

1. Erythrocyte lifespan
2. Age and race
3. Iron deficiency anemia
4. Chronic renal failure
5. Glycation changes
6. Hemoglobinopathies

1. Erythrocyte lifespan

Mean erythrocyte lifespan is around 120 days. Conditions that increase survival of erythrocyte increase the HbA1c concentration, and vice versa. Exposing the erythrocyte to glucose for a longer period of time, HbA1c levels may be falsely elevated in polycythemia, iron and vitamin

B12 deficiency, alcoholism, and after splenectomy, not reflecting the patient's true glucose control [5]. Beta-thalassemia major, acute and chronic blood loss, splenomegaly, and hemolytic anemia can cause falsely lowered HbA1c values because of shortened erythrocyte lifespan.

2. Age and race

Significant ethnic and racial differences seem to exist in HbA1c values for a given average glucose value. After 30 years of age, HbA1c concentrations increase by 0.1% every 10 years [6]. Caucasians' HbA1c levels are approximately 0.1 %-0.4 % lower for the same average glucose levels in comparison to other ethnicities such as African Americans, Asians, or Hispanics [7].

3. Iron deficiency anemia

Iron deficiency is a common situation. Two systematic reviews have reported contradictory results [8-11]. In iron deficiency, diagnosing prediabetes/diabetes may be problematic where patients' HbA1c levels are near the decision limit.

4. Chronic kidney disease

In chronic kidney disease, a common complication of diabetes, erythrocyte lifespan and HbA1c values are shortened [12]. Where erythropoietin is used as a drug, the number of reticulocytes increases and erythrocyte survival is reduced. HbA1c test may not accurately reflect glycemic control.

5. Glycation rate

Each person has small differences in the rate of hemoglobin glycation. However, significant differences exist between patients, resulting in different HbA1c concentrations despite similar average glycemia [8].

6. Hemoglobinopathies

Hemoglobin variants are common in some communities. HbA1c measurement is problematic as homozygotes cannot produce HbA [13]. Method-specific effects of hemoglobinopathies are summarized below.

Effects of hemoglobinopathies on HbA1c measurement

Hemoglobinopathies affect HbA1c measurement. In some variants, erythrocyte lifespan is shortened. In common variants, erythrocyte lifespan changes are not significant in heterozygotes. Therefore, accurate and reliable HbA1c measurement may be possible by selecting the appropriate method [8, 14].

Ion exchange chromatography-HPLC separates hemoglobin species based on charge differences. Apart from the fractions A0 and A1c, it separates other hemoglobin species: HbF, HbA1a/b, carbamylated-hemoglobin, HbA2, labil A1c and HbS. Peaks of Hb variants can usually be detected but HbA1c values are falsely elevated or reduced depending on the technique [15].

Capillary electrophoresis also separates according to electric charge, providing very good separation of A0 and HbA1c. Minor hemoglobins and variants can also be detected by this method. This brings advantages and challenges together. Common heterozygous variants such as HbS, HbC, HbD and HbE do not disrupt the HbA1c measurement [16].

Immunoassay methods are based on recognizing of antibodies specific for the N-terminal glycated amino acids on the beta chain of HbA. Antibodies used in the first generation methods recognize the N-terminal 4-10 amino acid sequence. These were affected by HbS, HbC and 25 other hemoglobin variants. In the second- and third-generation methods, new antibodies recognize a few amino acids at the N-terminal. Immunoassay methods may provide reliable HbA1c measurement in HbS carriers and some other heterozygous variants that do not shorten the RBC lifespan [17]. However, some variants may disrupt this measurement. It is believed that antibodies bind to HbS similar to HbA.

Immunoassay methods cannot detect the presence of hemoglobin variants. Unless HbA1c values are outside the clinical range, it does not give a clue about a possible disruptive condition. Since the results obtained from hemoglobin variants are not always at such dramatic limits, they may create a situation that misleads the diagnosis or treatment.

In the boronate affinity method, m-aminophenylboronic acid reacts with the cis-diol configuration of glucose attached to hemoglobin. This method measures total glycated hemoglobin including HbA1c and Hb glycated at other sites, regardless of hemoglobin species. Glycation is not limited only to the N-terminal valine of the beta chain, including some of the 10 lysines in the alpha and beta chains (40%). The device is calibrated and the corrected HbA1c equivalent is calculated [17, 18]. The precondition is that the beta chain exists.

For some time it was assumed that boronate affinity method is not affected by HbF (2 alpha and 2 gamma chains). HbF presumably is gycated with the gamma chain; however, the rate is lower than HbA. Therefore, HbA1c results are falsely low related to the amount of HbF [17-19]. As with immunoassay and enzymatic methods, the boronate affinity method cannot detect hemoglobin variants either.

In the enzymatic HbA1c measurement, oxidizers in the lysis buffer remove impurities. "Fructosyl valine oxidase" enzyme cleaves the N-terminal glycated valines; H_2O_2 occurs. Except for HbF and A2 elevation in beta-chain deficiency, Hb variants do not affect the measurement.

Conclusions

None of HbA1c methods are appropriate for the assessment of glycemic control in homozygous for HbS or HbC, with HbSC disease, or with any other condition affecting erythrocyte lifespan.

In thalassemic syndromes and sickle cell anemia, HbF may be variable. When HbF <5%, most of the chromatographic methods are generally not influenced. HbA1c is not measurable and cannot be reported if beta chain is low in samples with high HbF.

What are the options to reduce misinterpretation of HbA1c results?

1. When using ion exchange chromatography-HPLC or capillary electrophoresis, abnormal peaks should be carefully examined visually. If an obvious variant is detected, the following ways can be chosen:

a) The laboratory does not report the HbA1 result and can write a statement: "HbA1c result could not be reported due to hemoglobin variance. Further research should be done to determine the variant ". If laboratory facilities are available, an alternative method can be used.

b) If possible, medical laboratory specialist can require tests to determine the variant. If heterozygous HbS, HbC, HbD, HbE or Hb O-Arab is detected, then interferences on the HbA1c method should be investigated. If there is no interference, the result can be reported. If the variant is less common, the possibility of comorbidity due to hemolytic anemia, and other conditions are not known well, then it is not easy to decide what to do. Samples with high HbF should be carefully evaluated.

2. If there are apparent differences between HbA1c and glycemic control (e.g. fasting glucose) or other laboratory tests, then the hemoglobin variant should be suspected if HbA1c<4.0% or >15.0%.
3. In situations where HbA1c test result may not accurately reflect glycemic control, the clinician would be advised to prefer glucose measurement. Additionally, fructosamine and glycated-albumin, and 1.5-anhydroglucitrol may be considered. However, the lack of standardization and clinical guidelines of these tests should be considered. Only HbA1c has been validated as an indicator of long-term glycemic control and risk assessment for development of complications.

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C-05

Innovative Biochemistry

Özcan Erel

Department of Medical Biochemistry, AYBU. Faculty of Medicine, and Ankara Ataturk Training and Research Hospital, Ankara

An innovation is the implementation of a new or significantly improved product (good or service), or process, a new marketing method, or a new organizational method in business practices, workplace organization or external relations (Oslo Manual/OECD, EU-2005). The fundamental dynamics of innovation are the "improvements that are transformed into an economic and social value". A development that does not provide an economic and social value is not considered innovation. Innovation has product innovation, process innovation, organizational innovation, distribution and marketing innovation, and business model innovation processes. Innovation involves critical, analytical thinking, RD, integrative solution creation and value production.

Innovation is the symbol of competitive power. Today, developed countries are investing large amounts in innovation. The investments that countries make in the field of innovation also define their role in the world of technology and science. Our country ranks 54th in 2014, 58th in 2015, 42th in 2016, 43th in 2017 and 50th in 2018 in the order of global innovation among 126 countries while it ranks 18th in the world in the number of international academic publications and 17th in the world in economic magnitude.

The number of success stories in innovation in biochemistry is too small in our country. Stimulating innovation programs in undergraduate, postgraduate and specialist educations in biochemistry and clinical biochemistry areas that have the potential to encompass all types of innovation should be developed and should be promoted at the scientific meetings and encouraged in academic life. Innovation is a matter of culture. Innovation is not a destination but a journey that will never end.

C-06

Growing Older Wihout Aging: A Biochemical View

Abdullah Olgun

Department of Biochemistry, Prof. Dr. İstinye University Faculty of Pharmacy İstanbul

A short answer to the question "Is growing older wihout aging possible?" can be "Yes". This "yes" answer or growing older without aging means that although it is not possible at this time, it can be accomplished by scientists who believe that this is technically possible and work hard.There are "almost ageless" organisms in nature (i.e. Pinus longaeva, Arctica islandica, Somniosus microcephalus). This suggests the presence of living organisms having biochemical systems which are growing older without aging. It is a technical issue to make the human organism gain similar system.

Aging is a primary risk factor for many chronic diseases (diabetes, cancer, cardiovascular diseases, neurodegenerative diseases, arthritis, etc.). Aging can be described as changes that accumulate over time and increase the risk of death of the organism. For some diseases, there is a higher risk of mortality in elderly compared with young people. For this reason, all diseases, including colds and influenza in the elderly, should be considered more important.

Life span is species specific and categorized as average and maximum life span. Average life span is the arithmetic mean of the life span of individuals born at the same time. The maximum life span is the average life span of the longest living 10% of the individuals born at the same time, or the life span of the longest living individual (122 years 164 days, Jeanne Calment). While the advances in the prevention and treatment of diseases that increase the risk of mortality as a result of aging extend the average life span; the most effective method known to prolong the maximum life span in almost all species tested, including primates, is long term caloric restriction.

Some of the major theories that try to explain how aging occurs are; accumulation of damage as a byproduct of enzymatic or spontaneous biochemical reactions causing free radical production, glycation, protein deamidation, and DNA deamination; the accumulation of senescent cells over time, especially due to the shortening of telomeres in cells having a limited divisison potential; changes in hormones, and environmental factors (natural radiation sources such as radon, toxic substances, etc.).

Biogerologologists who try to explain why aging occurs, focus on the natural history of man on earth. The fact that the features that are useful in the early stages of life can be harmful in older ages, is described as "antagonistic pleiotropy" theory which is an important theory that explains why we age. For example, testosterone in males and estrogen in females are very important for reproduction and health in the early stages of life and can be harmful by increasing the risk of cancer (prostate in men, breast cancer in women) in late periods. Life spans of species that can not survive for a long time due to predation, environmental risks and diseases, have a short life span, because, they can not find a chance for genetic selection to make them healthy in later ages.

A good example for healthy aging is the preventive and therapeutic applications of dentistry. We can have healthy teeth even at advanced ages. With a similar approach, rejuvenating medicine can be applied at the molecular, cellular, tissue and organ levels to extend the life span or health span.

Health professionals are expected to act in accordance with the principles of "evidence-based medicine" in order to increase the accuracy of the decisions they make and to enforce the principle of "first, do not harm". Because the human body is a very complex system and every individual is unique. A solution that is appropriate for one person can be harmful to someone else, and a solution that is now good for one person can be harmful in the future.

By also taking into consideration individual differences; it is necessary to consume foods in accordance with the principles of healthy nutrition, to avoid unnecessary calories, and to correct deficiencies of micronutrients. There might be a need for a population level fortification programs for micronutrients, of which deficiencies are common in the population, and if not taken, could lead to the severe chronic diseases, and not having toxicity problems. Examples of such micronutrients are vitamin B12, magnesium and zinc.

First, diseases that shorten average life span; such as cardiovascular diseases, cancer, diabetes, osteoporosis, and hypertension can be diagnosed early through health screening in accordance with age and gender. It is possible to supplement micronutrients that are found to be deficient. If, through biochemical markers, the risk of having some diseases or the rate of aging is found to be high, then interventions can be made to slow down or prevent the process. For example, vitamin B12, which is very commonly deficient, can be supplemented very cost effectively, easily and without side effects; thanks to this intervention, an individual may be protected from depression, forgetfulness, aphtous ulcers, atherosclerosis, some early dementia problems, even paralysis, and some cancers that may be caused by its deficiency.

Some people might have "functional deficiency" even though the blood levels of some micronutrients are in the reference range. Those deficiencies can be detected by "functional laboratory tests". About 1% of the population has celiac disease. This disease can lead to vitamin and mineral deficiencies that can lead to unhealthy aging and an increased risk of cancer. Cancer can be diagnosed only a few years after the emergence of the first cancer cell. Approaches such as liquid biopsy for early diagnosis are very important nowadays. In some cells having a limited division potential, telomeres at the ends of chromosomes shorten after each cell division. This causes the senescence of these cells and the increase of the number of senescent cells in our bodies. In some people, the shortening of telomeres, for example due to viral infections, can cause problems in the immune system. Telomere length can be measured and it is possible to use telomerase (the enzyme that elongates telomeres) activating supplements in an evidence-based manner, if necessary. To prevent wrinkles caused by aging of skin, some vitamin A derived cosmetic products are proposed in evidence-based databases.

Conclusions

There are anti-aging strategies having a promising potential to be used widely in the near future. It has been shown that the new group of drug candidate molecules called senolytics, which selectively remove senescent cells that increase in number by age, can restore many age-related pathologies in experimental animals. Some of these candidate compounds are also found in some plants that we consume as food. For example, quercetin, which is a senolytic, is abundant in capers. Fisetin and piperlongumin are also some other plant-derived senolytic compounds studied on.

With partial reprogramming, changes that occur during the aging process in mice and human cells can be erased. It has been shown that transient reprogramming of cells through the expression protein transcription factors, called Yamanaka factors (OSKM), improves some age-related signs and significantly prolongs the life span, in the progeroid mouse model. Research is also being conducted on the use of artificial intelligence for the discovery of compound cocktails mimicking OSKM proteins.

The discovery of the factors that are the very first triggers of the aging process at the biochemical level is very important. In addition to classical factors such as free radicals; coenzyme Q side chain length, deuteronation, and cardiolipin profile changes may also be triggering factors.

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C-07

Why Detoxification Program is Needed?

Güler Buğdaycı

Department of Medical Biochemistry, Faculty of Medicine, Bolu Abant İzzet Baysal University, Bolu

Detoxification is the entire extent of a physiological and psychological process in which the body's metabolic byproducts and toxic substances are neutralized and eliminated. The metabolic end products of the human body are nitrogen, carbon dioxide, bile, urea, free radicals and stool. Exotoxins taken by respiration and oral route are drugs, heavy metals (mercury, arsenic, lead, cadmium and aluminum), chemicals (pesticides, herbicides, cleaning products, coatings, solvents and adhesives), antinutrients (high fructose corn syrup, trans fats, caffeine, alcohol and processed foods), infectious agents (bacteria, viruses, yeast and parasites), allergens (pollen, dust) [1]. The social, emotional and spiritual challenges that effect health and well being activates the sympathetic system. Under normal circumstances, the body and mind are homeostases, a state of a biological and mental balance. For this reason, mainly liver, gallbladder, kidney, gastrointestinal system, skin, lungs, circulation and lymph system, mind and brain coexist together to maintain the continuation of health [2-4].

Detoxification and biotransformation are predominantly in the liver. Furthermore Phase-I and Phase-II enzymes are present in the intestinal mucosa cell, lung, epidermal, kidney. All reactions of Phase-I and Phase-II occur in the intestinal epithelium, which is coordinated with the liver. Microbiota is considered as an integrated part of biotransformation [4, 5]. Fat-soluble toxins sre oxidized within Phase-I enzymes. If consisted intermediates are not transformed into water-soluble products in Phase-II, they will remain as more toxic ones.

The toxins are mainly oxidized by Phase-I enzymes in the liver, digestive system, lung epithelium, and the intermediate formed may remain in the form of more toxic intermediates if not converted to water-soluble by Phase-II immediately. If a healthy working system is encountered, the xenobiotic is made ready to be thawed through the water and therefore through the urine, bile, stool and sweat. One of the problems is the imbalance in the presence of overstimulated Phase I systems in which the Phase II system is inadequate. Micronutrients that are required in Phase I and II processes; certain vitamins (B2, B3, B6, B12, C, E), magnesium, zinc, iron, copper, branched chain amino acids, flavors found in fruits and vegetables in particular, phospholipids and glutathion [6]. The difference in detoxification one person to another changes. The filling of each individual 'toxic load barrel' is variable. The toxicity of the detoxification system discharging is as effective as the exposure to the toxin. Nevertheless, those who are sensible to toxins; Polymorphisms in Phase I and Phase II detox enzymes, dysbiosis, cumulative heavy metal load, high carbohydrate and protein intake, chronic stress, micronutrients and vitamins deficiencies [7].

Symptoms indicating detoxification insufficiency can be summarized as; irritability, irritable bowel, malodorous stools and dark urine, muscle tone and loss of weight, heartburn, repetitive inbreeding, permanent infections, infertility, dyspareunia and low libido, premature aging and unfairness, edema and excessive weight gain, rash and thrush, bad breath and body odor. If an individual is insensible to these symptoms and if necessary detoxification is not provided, autoimmune diseases, cancer, endocrine disorders, mitochondrial and metabolic problems, neurological and psychiatric problems will be inevitable [6].

Laboratory tests, which is be used to study the detoxification performance of a person, can be more likely related to the clinical presentation of the patient. These tests include; absorption and microbiota assays; heavy metal tests, vitamins and trace element levels, urine organic acids, detox genetics. Unfortunately, there are many fraudulent, expensive and potentially unnecessary applications when detoxification is main subject [8, 9]. The following application is the fundamental component for any detoxification program:

1. Fasting protocols
2. Healthy nutrition with organic vegetables and fruits, protein intake not exceeding 10%, 40 ml filtered water per weight
3. Daily regular physical activity, especially outdoors activities such as yoga and walking
4. Acupuncture, massage, manual therapies
5. Exercise programs with regular sweating such as sauna, steam room, high rhythm exercise
6. Meditation, mindfullness, diary and relaxation techniques such as breath-focused retention techniques
7. Aromatherapy
8. Spending regular and supportive, social time with friends, family and society (8-10).

The CYT P450 system processes up to 200000 endogenous substances, all steroid hormones and eicosanoids, as well as toxins. Considering the number of toxins we are exposed to in the 21st century, bioactive molecules that are formed within Phase I are increased. The toxins that cannot be defeated with detoxification cause chronical diseases by storing in connective tissues. In this case, detoxification program is a must for each individual.

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C-08

D Vitamin Deficiency: The Age Pandemic?

Ayfer Çolak

Department of Medical Biochemistry Specialist, University of Health Sciences Tepecik Training and Research Hospital, İzmir

Vitamin D deficiency is a global health problem caused mainly by insufficient exposure to sunlight. It is estimated that 1 billion people have vitamin D deficiency or insufficiency worldwide [1]. Vitamin D is a steroid hormone synthesized in the skin under the effect of sun light or it is taken with meals. The most important effect of vitamin D involves calcium homeostasis, and bone metabolism. Vitamin D deficiency is caused by rikets

in children and osteomalacia in adults.Vitamin D deficiency is associated with musculoskeletal diseases, as well as extraskeletal diseases, such as cancer, cardiovascular diseases, and infections [2]. Epidemiological studies indicate a relationship between vitamin D deficiency and cancer incidence [3].

Approximately 80 to 90% of vitamin D requirement is provided by sun rays and 10 to 20% from diets such as fish oil, eggs and liver. Solar ultraviolet B radiation penetrates the skin and converts 7- dehydrocholesterol to previtamin D3, which is rapidly converted to vitamin D3. Vitamin D from the skin and diet is metab-olized in the liver to 25-hydroxyvitamin D. The 25-hydroxyvitamin D is metabolized in the kidneys by the enzyme 1α- hydrox-ylase to its active form, 1.25- dihydroxyvitamin D. The active form, 1.25-dihydroxyvitamin D markedly increases the efficiency of intestinal calci-um and phosphorus absorption [4]. Consequently, major risk factors for vitamin D deficiency include inadequate sunlight exposure, inadequate dietary intake of vitamin D-containing foods, and malabsorption syndromes such as Crohn's disease and celiac disease [5].

The best parameter showing the body's vitamin D status is serum 25 (OH) vitamin D level. Although there is no consensus on the optimal level of 25 (OH) vitamin D, most researchers have found that vitamin D,

- Levels of 30 ng/ml (75 nmol/L) were adequate,
- Inadequate levels between 20 and 30 ng/ml (50-75 nmol/L)
- The level below 20 ng/ml (50 nmol/L) is considered as deficiency [1].

Despite the widespread vitamin D deficiency, community screening is not recommended and the evaluation of high-risk individuals is recommended.

There are two main types of assays used for measuring 25OHD-the immune-based assay (commonly used in clinical practice) and the chromatography-based assay (commonly considered the gold standard for research). Estimating the prevalence of vitamin D deficiency, requires the accurate and precise measurement of 25-hydroxyvitamin D in serum or plasma. The utilisation of different methods among laboratories obviously leads to a great variability in test results. A reference method and a standard reference material (NIST SRM 972a) for the measurement of 25 (OH) D have been developed [6]. In addition, the Vitamin D Standardization Program (VDSP) has been launched with the goal to improve accuracy and comparability of analytical methods. Such a programme is anticipated to eliminate the inaccuracies surrounding vitamin D quantification. The use of standardized assays in large population studies will allow comparisons to be made between populations and the prevalence of vitamin D deficiency will be more accurately predicted.

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Panel - Abstracts

P1 - Preanalytic

P1-01

Management of hemolyzed samples in clinical chemistry tests

Asım Örem

Department of Medical Biochemistry, Karadeniz Technical University, Faculty of Medicine, Trabzon

According to a report from the United States in 2000; approximately 44.000-98.000 people die due to preventable medical errors annually. In terms of laboratories: The erroneous result is the most important cause of medical error. Therefore, the goal in the laboratory is to produce reliable and accurate laboratory test results.

Sample quality is the cornerstone of total quality in our clinical laboratories and constitutes a large part of our daily laboratory activity. Hemolysis is one of the most important indicators of sample quality. Preanalytical errors are the highest for analytical and postanalytical errors. In addition, hemolysis is about half of preanalytical errors.

Although hemolysis may interfere with many mechanisms, perhaps the most important of these is that the potassium in an erythrocyte leaks into plasma or serum and makes a height of pseudo-potassium. For this reason, laboratory management of samples affected by hemolysis is of great importance in reporting the results of potassium especially in patients with high risk such as intensive care and emergency services. Hemolysis is the most common error cause to malpractice by affecting misdiagnosis. CLSI C56-A defines interference mechanisms for serum indexes, their intended use, study in automated systems, management and reporting of positive samples in serum indices. Although this is the case today, the laboratory needs a good harmonization in this regard. Some factors that can be harmonized can be summarized as follows;

1. Systematic assassment of serum hemolysis index (HI);

Measurement of hemolysis index should be done with standardized automated systems. The numerical values obtained should be transferred to the LIS used and should be the decision maker to accept or reject the test result. A common perception is that the use of these automated systems prolongs the turnaround-time (TAT) of the desired tests, but according to present data, this is not true. In the absence of these automated systems, the hemolysis should be standardized to a certain extent by using a color scale.

2. Defining of H-index cut-offs for flagging, alarming or suppressing test results;

Test-specific cut-offs of HI values above which an analytically significant bias may accur cen be either adopted from manufacturer' assay sheets, when available, or can be locally calculated. Clinical significant error should be expressed as Reference Change Value (RCV).

RCV is a specific formula that includes a person's biological variation (CVi) and analytical variance (CVa). The formula was recently recommended by Sumindic et al. and approved by the EFLM biological variation study group (WG-BV).

$$RCV=\sqrt{2}\cdot 1.96\cdot\sqrt{(CV_I)^{\wedge 2}+(CV_A)^{\wedge 2}}$$

RCV, Reference change value

CV, Within-subject biological variation

CV_A, Analytical imprecision

$$CV_A=\frac{CV_A\ QC\ Level_1+CV_A\ QC\ Level_2+...CV_A\ QC\ Level_n}{n}$$

3. Reporting flagged or alarming test results;

a. Test results should be reported if the HI values are between analytical and clinical significance limits

b. If the test result is influenced by HI, Increasing/reducing effect of HI should be clearly stated in the test report. This should be placed just below the given numerical value or at the end of the report and it should be suggested to take another sample sample.

4. Suppressing of test results significantly affected by hemolysis;

a. Results that are affected by the hemolysis that exceed the clinical error limit according to the test specifically calculated RCV are suppressed.

b. Instead of the result, "Hemolysis influenced the decision limit level determined for this test." It is recommended to take another sample.

c. For hemolysis influences not exceeding the clinical significance value, the report of the test should be given clearly indicating the direction of impact.

5. Suppression of all test results significantly affected by hemolysis;

If the cell-free Hb values are >1000 mg/dL (10 g/L), all clinical chemistry tests are suppressed and a new sample is requested. In this case, "hemolyzed sample and a new sample requested" should be written in report.

6. Correcting data for the H-index;

Using corrective formulas for adjusting test results of hemolysis-sensitive test is inaccurate and strongly discouraged.

7. Data of hemolysis index in laboratory reports;

a. The degree of hemolysis should be converted from the device-specific unit into g/L of cell-free hemoglobin to improve harmonization.

b. Degree of hemolysis index should also be expressed as g/L in the test report.

c. Clinical laboratories should use special control materials for the H-index to continuously monitor the analytical performance of the H-index.

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P1-02

Pre-ve Post-Analytic External Quality Control KBUDEK Pre->Post Analytic External Quality Control Programmes

Erhan Cüneyt Canbulat

Coordinator of KBUDEK Pre->Post Analytic External Quality Control Programmes, İstanbul, Turkey

The majority of errors in total testing processes are observed in pre-analytical (62-76%) and post-analytical phases (18-30%). Our point of view for quality should be to produce accurate and error-free results at the first time. We need to focus on quality in all of our processes. Therefore, monitoring performance in pre- and post-analytic processes is as important as analytical process monitoring. External Quality Control (EQC) programs are needed to accurately monitor these processes. The majority of EQC programs are only involved in ensuring the control of the analytical phase. ISO 15189:2012 (E) "Medical laboratories: requirements for quality and competence" standard states that "Interlaboratory comparison programme(s) chosen by the laboratory shall, as far as possible, provide clinically relevant challenges that mimic patient samples and have the effect of checking the entire examination process, including pre-examination procedures, and post-examination procedures, where possible."

Today, a small number of External Quality Control Programme providers run programmes that control the pre-analytical or post-analytic phase. Three different programme models can be used to monitor these phases.

Type I: Registration of procedures: In this type, the participants are sent various surveys or asked questions about the procedures they have applied in the laboratory. The procedures applied in the laboratory can be questioned by giving a case and asking questions. In the reports to be given to the participants after the cycle, both the results between participants are compared and recommendations are given to improve the processes.

Type II: Circulation of samples simulating errors. In this type, real samples containing interference are sent to participants like analytical EQC to find out how laboratories deal with these samples and how they give the results of these samples to physicians.

Type III: Registration of errors/adverse events. It is implemented as a monitoring of quality indicators in a certain period of time. The advantage of the implementation of the Type III model is the use of the laboratory's own system for recording errors. However, harmonization of quality indicators is required for comparison.

ISO 15189: 2012 states that "The laboratory shall establish quality indicators to monitor and evaluate performance throughout critical aspects of pre-examination, examination and post-examination processes". Quality indicators available for use by laboratories are published by IFCC Laboratory Errors and Patient Safety Working Group (WG-LEPS). In the article published in 2017 by Plebani et al 53 quality indicators (QI) are defined. These quality indicators are related to pre-analytical phase (28 QI), analytical phase (6 QI), post-analytical phase (11 QI), support processes (5 QI) and output processes (3 QI).

The EQC programmes to be used by the laboratory should include pre- and post-analytical phases. For this purpose, KBUDEK EQC Programme which has been in service since 2006 launched the KBUDEK Pre-> Post Analytical Programme (www.kbudekpreandpost.com) in 2018, The program will allow the comparison of preanalytical, analytical and postanalytical errors among programme participants and statistical evaluation. In KBUDEK Pre->Post Analytic Programmes, the methods of Type I and Type III mentioned above will be used. For type I currently 2 Surveys related to "Oral Glucose Tolerance Test" and "Hemolysis Index" are in progress.

In the Type III method used in the KBUDEK Pre-> Post Analytical Program, the classification system used by WG-LEPS is used in the classification of

quality indicators. There are 53 indicators related to preanalytical, analytical and postanalytical phases.

All questions are expected to be answered for surveys. For quality indicators, the participants can only enter the results of the quality indicators that are used in their institution.

In addition to data comparisons in the EQC program reports, it is aimed to contribute to the development of laboratory processes by giving information from relevant guides and current publications.

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P2 - Waste Water

P2-01

Liquid Waste and Wastewater Management in Health Facilities

Selda Murat Hocaoğlu[1], İrfan Baştürk[1], Recep Partal[1], Mehtap Dursun[1], Oltan Canlı[1]

[1]TUBITAK Marmara Research Center, Environment and Cleaner Production Institute, Kocaeli

[2]Marmara University, Pendik Education and Research Hospital, İstanbul

Introduction

Healthcare facilities represent an incontestable release source of many chemical compounds in the aquatic environment due to laboratory activity or medicine excretion into wastewater (Gupta ve diğ., 2009). Wastewaters from healthcare facilities could be dangerous to the environment and human health. Pathological, radioactive, chemical, infectious, and pharmaceutical wastes, if left untreated, could lead to outbreaks of communicable diseases, diarrhea epidemics, water contamination. These chemicals may contaminate the city's drinking water system. For these reasons, hospital wastewaters contains pollutants that are hazardous and require on-site treatment to prevent contaminating the city's sewerage system and environment (Gautam ve diğ., 2007).

Although the composition of wastewater in health facilities is similar to domestic wastewater; These wastewater are contaminated with a wide range of chemicals and disinfectants, which are used for diagnostic purposes, and can contain many chemicals. In addition, these wastewaters have mutagenic and bacterial toxic properties (Jolibois and Guerbet, 2005; Ferk ve diğ., 2009).

Among the liquid wastes generated in health facilities are chemical wastes with different characteristics and dangerous substances, medical devices containing liquid substances with high and different characteristics, liquid wastes, sterilization liquid wastes and so on is located.

At present, it is tried to determine whether liquid wastes are hazardous waste with comprehensive, costly and long-term experimental studies. On the other hand, the absence of a representative sampling method for the analyzers, imbalances in the characterization of the liquid waste (the number of tests and the variables being tested, etc.), the absence of a method of measurement for all pollutants, and/or interference effect (matrix effect) lead to problems. However, very different results are obtained for the same analyzer.

In our country, there is a great deal of confusion and chaos about the method of disposal of analyzer liquid wastes. Due to these insufficiencies, only a few part of the liquid wastes in health facilities in our country which contain dangerous substances can be collected and the wastewater is discharged directly into the sewer after the pH adjustment.

The separate collection and/or purification of all liquid waste sources in health facilities is not sustainable interms of technically and cost-effective. The prevention of pollution caused by the wastewater generated in these establishments can be achieved by deciding how to manage the liquid wastes with a large number of different properties. In this study, whole liquid waste sources and formations were examined in pilot facilities, and it was estimated the amount of liquid waste generated if the World Health Organization (WHO) approach would be implemented. Moreover, hazardous wastes and ecologically hazardous pollutants identified and liquid wastes proposed for separate collection have been determined, considering formation of wastes. With the WHO approach, separate collection of liquid wastes and on-site treatment in cost was compared.

Materials and Methods

In this study, whole liquid waste sources and formations were examined in pilot facilities, and it was estimated the amount of liquid waste generated if the World Health Organization (WHO) approach would be implemented. Moreover, hazardous wastes and ecologically hazardous pollutants identified and liquid wastes proposed for separate collection have been determined, considering formation of wastes. With the WHO approach, separate collection of liquid wastes and on-site treatment in cost was compared.

Results

Biochemistry laboratory produces most liquid waste, when compared to other units, analyzers generate wastewater 150-850 m3/year in labs, according to the WHO approach (separate collection of all liquid wastes containing hazardous chemicals/wastewater) as hazardous waste disposal cost of these waste is about 350 thousand-2 million TL/year. Furthermore, on-site treatment of all liquid waste/ wastewater in healthcare facilities requires 2-10 MTL investment per hospital, depending on treatment technology and hospital size. On the other hand, it is predicted that in case of separate collection of liquid wastes which are carcinogenic, toxic, mutagenic and ecologically harmful to the reproductive system, health facilities will dispose of very low volumes of liquid waste, on average 4-15 m^3/year. Among the liquid wastes that need to be collected separately include formaldehyde, xylene, ethylbenzene, halogenated solvents, dyes and analyzer wastes. Furthermore, at the end of the study, the liquid wastes/wastewater generated in the health facilities were evaluated individually on the basis of units and it was prepared a document whose name is "Health Facilities Wastewater/ Liquid Waste Management Handbook". This handbook is guide for the health facilities. The handbook includes which liquid wastes/wastewater will be collected separately and which liquid wastes/wastewater will be discharged into the sewer. Prepared handbook, liquid wastes and wastewater from health facilities will be helped reduce the risks on human and environment and will be thought to be contribute to the implementation "Environmentally Friendly Hospital" approach and reduction of liquid waste/ wastewater disposal costs.

Conclusions

The most economical and effective solution in terms of cost and applicability is collection the waste at the source and disposed. In this way, water resources will be protected while contributing to reduction of disposal costs. This study was supported the Ministry of Environment and Urbanization and guideline prepared, containing liquid wastes resources, collected separately (http://cygm.csb.gov.tr).

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P3 - Microbiota

P3-01

Gut Microbiota and Its Importance

Nevin İlhan

Department of Medical Biochemistry, Faculty of Medicine, Fırat University, Elazığ

All of the microorganisms (bacteria, viruses, fungi, archaea and micro-eukaryotes) that are symbiotic relationship with people and settled in different parts of the human body (skin, urogenital system, respiratory system, digestive system, especially intestine) are called microbiota, and the total genomes of all microorganisms in a microbiota is called microbiome. The human body contains 10 times more microbial cells than human cells (10^{14}) and the number of microbiome is 150 times higher than the human genome. The surface area of the bacteria in the human body is 400 m^2 and the bacterial mass is approximately 1.5-2 kg. The human gastrointestinal system has a complex, highly variable microbial population, and the structure of the microbial community is influenced by endogenous and exogenous factors that vary throughout a person's life, such as host genetics, mode of delivery, diet, lifestyle, antibiotic use, diseases, the geographic region and the species of bacteria. The gut microbiota is like a fingerprint, and it has a unique composition, diversity and functional competence. In healthy humans, Firmicutes and Bacteroidetes dominate the gut microbiota (90%), whereas Proteobacteria, Actinobacteria, Fusobacteria and Verrucomicrobia species are the minor components of gut microbiota. In pathological conditions, the dominant bacterial population may change and in particular their “variability and diversity” may be reducing. Any change in environmental factors, lifestyle, disease, and infections leads to alteration of the composition of bacterial populations, that is to say, disruption of the microbiota balance and this process is called dysbiosis. This complex microorganism community interact with each other and the host, and includes a certain percentage of beneficial/harmful bacteria and there is a dynamic balance between the microorganisms and the host. The gut microbiota maintains symbiotic relationship with the host, and provides important metabolic, immunological and intestinal protective functions in the healthy individual. They act as a "metabolic organ" through energy metabolism, metabolism of dietary components, feeding of the host by interaction with intestinal epithelial cells, physiological, metabolic and immune system modulation, as well as by a broad metabolic capacity and by a significant functional plasticity on host’s behavior, motor system and endocrine functions.

The gut microbiota mediates the systemic immune response primarily by producing metabolic products (interleukin (IL)-1, IL-18, interferons, tumor necrosis factor (TNF), IL-10, serum amyloid A) and microbial-associated molecular patterns (MAMPs). Microbiota plays an effective role in various metabolic functions (energy harvest and storage) including fermentation and absorption of undigested carbohydrates, maturation and functioning of immune cells through interaction with the immune system, and brain growth and behavioral regulation. Gut microbiota derives its nutrients mostly from dietary carbohydrates. The fermentation of complex polysaccharides and complex glycans containing resistant ligands that escape from the host digestive enzymes in the part of the diet reaching the large intestine by the colonic organisms, such as Bacteroides, Roseburia, Bifidobacterium, Fecalibacterium and Enterobacteria, results in synthesis of SCFAs (acetate, propionate, butyrate) and of various metabolites, that are rich energy source for the host. SCFAs initiate various metabolic activities in the host (such as lipid and glucose synthesis) and provide about 10% additional calories per day of calories. The energy balance of the host is mediated by a G protein-coupled receptor Gpr41 and a ligand receptor interaction of the SCFAs. This interaction triggers secretion of peptide tyrosine tyrosine/ pancreatic peptide YY3-36 (PYY), which is another enteroendocrine hormone. Moreover, butyrate can also prevent toxic metabolic accumulation through prod-

ucts such as D-lactate. Members of the genus Bacteroides, the dominant organisms involved in carbohydrate metabolism, do so with enzymes such as glycosyl transferases, glycoside hydrolases and polysaccharide lyases. Oxalate synthesized in intestines as a result of carbohydrate fermentation and bacterial metabolism is met by microorganisms like Oxalobacter formigenes, Lactobacillus, Bifidobacterium and thus the risk of oxalate stone formation in the kidneys is reduced. Not only complex carbohydrates escaping digestion, but also various polyphenols, fats, amino acids, proteins, fermentation of proteins, deconjugation of bile acids, various components of vitamin B (biotin, cobalamin, folate, nicotinic acid, pridoxin, riboflavin, thiamine) and vitamin K synthesis is of the important metabolic functions of intestinal microbiota. It has also been shown that the intestinal microbiota has a positive effect on lipid metabolism by suppressing the inhibition of lipoprotein lipase activity in adipocytes and up regulating the expression of AMPK (It decreases fat and glycogen stores by increasing beta oxidation of fatty acids). In addition, Bacteroides thetaiotaomicron has been shown to increase lipid hydrolysis by regulating the expression of colipase, which is required for lipid digestion by pancreatic lipase. The intestinal microbiota is an active protein metabolizer that functions through microbial proteinases and peptidases along with human proteinases. Different amino acid transporters located on the bacterial cell wall facilitate amino acid entry into the bacteria from the intestinal lumen; here, several gene products convert amino acid to small signaling molecules and antimicrobial peptides (bacteriocins). For example, conversion of L-histidine to histamine by the bacterial enzyme histamine decarboxylase that is encoded by bacterial hdcA genes, and conversion of glutamate to γ-amino butyric acid (GABA) by glutamate decarboxylases that are encoded by bacterial gadB genes. The synthesis of vitamin K and various vitamin B components is another important metabolic function of the gut microbiota. Bacteroides species members have been shown to synthesize conjugated linoleic acid (CLA), which is known to be antidiabetic, antiatherogenic, antibiogenic, hypolipidemic and known to have immunomodulatory properties. The gut microbiota, in particular Bacteroides intestinalis, and to a certain extent, Bacteroides fragilis and E. coli, are capable of deconjugated and dehydrating primary bile acids and converting them into deoxycholic and lithocholic acids which are secondary bile acids in the human column.

Recent researches have shown that human gut microbiota also plays a role to cleavage of various polyphenols (phenolic compounds) consumed in diet. Polyphenolic secondary metabolites are found in various plants, fruits and plant-derived products (tea, cocoa, etc.) such as flavanols, flavanones, flavan-3-ols, anthocyanidins, isoflavones, flavones, tannins, lignans and chlorogenic acids. Of these, flavanoids and flavanoid subgroups are the most commonly absorbed by the intestine. Polyphenols are found as glycosylated derivatives limited to sugars such as glucose, galactose, rhamnose, ribulose, arabinoprinose and arabinofuranose. Polyphenols, which are generally inactive in the diet, are converted to active compounds after elimination of the sugar residue by gut microbiota. The structural specificity of polyphenols as well as richness of the individual microbiota determine the level of biotransformation occurring in the intestine. The active end products are absorbed by the portal vein, and goes to other tissues and organs, so, these products exhibit antimicrobial and other metabolic effects.

Conclusion

Nutrition, microbial diversity, intestinal barrier permeability, immune functions, energy harvesting, metabolism of macromolecules and enzyme activities regulate composition and function of intestinal microbiota consisting of trillions of microorganisms in equilibrium under normal conditions. The deterioration of this homeostasis, the differentiation of the microbiota content, the change of microbial metabolites and the effects of new and different signals will prepare the ground for many chronic and metabolic diseases (obesity, Type 2 DM, Metabolic Syndrome, CVS diseases, cancer etc.).

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P3-02

Microbiota and Relation with Obesity, Prebiotics, Probiotics and Food Additives

Fatih Gültekin

Department of Medical Biochemistry, Prof. Dr., University of Health Sciences, School of Medicine, Istanbul

Food additives are substances that are added during the production process to improve properties of food like the color, taste, odor, nutritional value and shelf life. These substances are indicated on the label of food packages under "ingredients". Many toxicological studies are conducted before food additives are allowed to be used. After these tests, the additives that are allowed to be used are considered safe. Additionally, as new techniques and research topics emerge, new discoveries can be made about the side effects of additives. The topic of microbiota has started to be studied more intensively in recent years. The relationship between microbiota and food additives is also a subject of new research.

Intestinal microbiota has considerable importance in individual health. It is involved in the regulation of many physiological events. They settle in the mucus layer of the intestines and have a role in forming its composition. They assist in the digestion of food such as fiber; synthesize some vitamins and amino acids; play an important role in the metabolism and storage of energy, the regulation of the immune system, growth and neural development, and may even have a role in the regulation of our behavior.

The effects of food additives on microbiota have been investigated in a limited number of studies. The additives detected in reviews can be listed according to their function as follows:

1. **Sweeteners:**
   - Artificial Sweeteners :Saccharin (E954), sucralose (E955) and Aspartame (E951), Neosperidine DC (E959), Splenda
   - Sugar Alcohols: Maltitol (E965), Xylitol (E967) ,Sorbitol (E420), Erythritol (E968)
2. **Emulsifiers:** Carboxymethyl cellulose (E466) and Polysarbot 80 (E433) (10).
3. **Nanoparticles:** Silver (E174) and Titanium dioxide (E171) (11).
4. **Flavor enhancers:** Monosodium glutamate (E621) (12).
5. **Stabilizers:** Pectin (E440) (13), Polydextrose (E1200) (PDX) (14), Alginic acid (E400) (15).
6. **Anti-Caking Agents:** Bentonite (E558) (16).
7. **Preservatives:** Benzoic acid (E210) (17).

After evaluating all the research carried out in this area, the vast majority of microbiota-related additives are sweeteners. Synthetic sweeteners affect the microbiota and the resulting change in microbiota leads to glucose intolerance and probably weight gain. These results are actually the opposite of what is expected from synthetic sweeteners with no calorific value. Moreover, several studies have shown that there is no benefit to using synthetic sweeteners to lose weight. Sugar alcohol sweeteners, in contrast to synthetic sweeteners, affect microbial growth in a positive way and behave like prebiotics. If we overlook exceptions like erythritol, the use of these additives has a positive effect in terms of microbiota.

Lastly, obtain clear results is challenging due to the differences between experimental animals and models used in research. We need to increase the amount of research to obtain clearer results.

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P3-03

Microbiota and Neurodegenerative Diseases

Nevin İlhan

Department of Medical Biochemistry, Faculty of Medicine, Fırat University, Elazığ

The gut-brain axis and the regulation of this axis through microbiota plays a key role in the biological and physiological basis of neurodegenerative disorders. The gut microbiota affects not only the gastrointestinal physiology but also the central nervous system (CNS) function by modulating the microbiota-gut-brain axis signaling pathways. Brain-gut-microbiota axis is controlled at various stages by the sympathetic and parasympathetic branches of the autonomic nervous system (ANS), the enteric nervous system (ESS) and the CNS, neuroendocrine and neuro-immune pathways. Bidirectional communication along hormonal, neural and immune pathways affects the motor, sensory and secretory functions of the gastrointestinal tract of CNS and conversely gastrointestinal tract also causes signals to affect the CNS function.. These systems together form a highly integrated molecular network linking the development of neurodegeneration with systemic imbalances. Gut--brain axis functions are affected at any level of neuronal control disorder. It is thought that gut microbiota is in communication with the intestinal epithelium and immune system cells, and also this communication causes many neuropsychiatric and metabolic disorders, especially autoimmune diseases. This connection is established in the intrauterine period and lasts a lifetime. The harmful substances formed by the deterioration of the intestinal microbiota balance (microbial dysbiosis), which plays a key role in microglia activation, are transferred to the systemic circulation. The liposomal vesicles called 'exosomes' which transcend the blood brain barrier with a series of events caused by the dendritic cells, one of the gut cells of the immune system, cause changes in the membrane potential of neurons. This situation contributes to the pathology of many neurological diseases including depression, anxiety, Alzheimer's and Parkinson's disease. The intestinal microbiota can give signals to the brain by regulating the production of proinflammatory cytokines and the activity of neuro-immune pathways, microbial metabolites such as short-chain fatty acids (SCFAs) and microbial derived neurotransmitters, afferent sensory neurons of the vagal nerve, neuroendocrine pathways. Proinflammatory cytokines stimulate the hypothalamic–pituitary–adrenal (HPA) axis to produce either CRH, ACTH and cortisol or may have a direct effect on CNS immune activity. The direct effect occurs by production of SCFAs such as propionate, butyrate, and acetate; production of neurotransmitters (GABA, NE, Dopamine) which may enter the circulation and cross the blood brain barrier; and by modulating tryptophan metabolism and metabolites such as serotonin (5-HT), kynurenic acid (KYNA), and quinolinic acid (QUIN). Because of tryptophan metabolism regulated by intestinal microbiota, the levels of 5-HT and other metabolites are affected. 5-HT is the basic neurotransmitter and modulates a number of physiological processes such as mood, appetite, aggression and sleep Metabolites occurring as a result of other pathways in tryptophan metabolism are thought to play a role in important psychiatric disorders, including schizophrenia and depression. KYNA is the only endogenous the N-methyl-D-aspartate (NMDA) receptor blocker found in the central nervous system and is also an antagonist of the alpha-7-nicotinic acetylcholine receptor (α7nAChR). The QUIN and 3-hydroxykynurenine (3-OHKY) have neurotoxic properties. In animal studies, it was shown that tryptophan levels and the conversion rates of tryptophan to serotonin and other metabolites were different in gram-negative mice when compared to colonized-mice, and that added probiotic therapies also caused changes in tryptophan metabolism. For example, it has been argued that rats with bifidobacterium infantis for a long period of time, increased tryptophan levels, decreased kynurenine-tryptophan ratios and lower levels of 5-HIAA in the frontal cortex of the rats, may affect the central serotonergic transmission. The increase in metabolites of peripheral and central kynurenine has been reported in diseases such as autism, schizophrenia, depression, and Alzheimer's disease.

Considering that microbiota can regulate the pathway of tryptophan / kynurenine; microbiota is a new treatment target. Gut microbiota affects the production of neurotransmitters and the expression of neurotrophic factors (such as BDNF). Brain-induced neurotrophic factor (BDNF) and NMDA are known to be important in brain plasticity, memory, neuronal health and pathophysiology of schizophrenia. Studies have shown that BDNF expression is under the influence of gut microbiota, decreases the expression of hippocampal BDNF mRNA by leading to a depletion of intestinal microorganisms in chronic antibiotic-used mice and also leads to deterioration of cognitive functions. It has also been shown that hippocampal BDNF expression and N-methyl-D-aspartate (NMDA) receptor functions decrease in germ-free mice compared to normal-grown mice (Fig. 1).

The changes in the microbiota can alter the stress response or the stress itself (early life, prenatal stress, psychological stressors, etc.) changes the structure of the microbiota. Psychological/physical stress induces glucocorticoids that secreted from HPA axis. Pathological processes such as oxidative stress and inflammation increase the cytokine and inflammatory mediators and cause inflammaging, which is defined as a chronic low-grade inflammatory condition. Inflammaging is involved in various age-related cellular and molecular mechanisms including cellular aging, mitochondrial dysfunction, defective autophagy and mythophagia, activation of inflamasomas, irregularity of the ubiquitin-proteasome system, activation of DNA damage response, dysbiosis and neurodegeneration. A variety of neuropsychiatric disorders such as sensitivity to stress, anxiety-like behavior, sociability and cognition as well as anxiety, depression and autism have been associated with changes in microbiota population. Because of the structure and neurochemical similarity of ESS neurons with the CNS, enteric symptoms may occur in the pathophysiology of CNS (eg constipation in neurodegenerative diseases, loss of appetite, chronic pain, etc.). Neuron connections and immune system may have a role in the distribution of diseases in the gut into the CNS. Activation of highly conserved neuronal and hormonal communication pathways in mammals causes symptoms triggered by inflammatory cytokines, called disease behavior, including fever, neurogenic inflammation, fatigue, sleepiness, lack of appetite, depression, lack of concentration. Cytokines both co-ordinate the fight against infection in the periphery of the body and send signals from the periphery to the brain via the vagus nerve or can directly access the brain through circumventricular hormones and initiate behavioral changes. However, these behavioral effects of cytokines are not always useful. When the cytokine signal is too strong or prolonged, these effects may become incompatible and lead to more chronic and pathological behavioral changes such as depression. For this reason, the rate of get into depression is higher in situations characterized by low-grade inflammation than in the general population. For example, depression is seen 20-30% of obese individuals while this prevalence in the general population is 5-10%.

Patients with various psychiatric (depression, anxiety) and neurological disorders (Parkinson's disease, autism spectrum disorders) have significant gastrointestinal (GI) comorbidities, and many recent studies show that the gut microbiota plays a potential role not only in the pathophysiology of GI symptoms but also in the primary disorder. However, despite the significant advances that have characterized the interaction between gut microbiota and CNS for the last 10 years, questions about the pathogenesis, pathophysiology and treatment of human brain-gut disorders have been continuing. Efforts are being made to identify not only the microbial community structure, function and contributions of individual taxa, but also the communities such as viromes and mushrooms (mycobiomas) that have been ignored until recently due to technological limitations. The reduced costs of new multi-omic analyzes facilitated data-based approaches to identify subgroups of patients with different patterns of dysbiosis, and the response hypothesis of these subgroups to personalized treatment using diet, prebiotic or probiotic interventions was tested. However, large-scale, randomized controlled study, long-term human studies are needed, and causes and sequelae of dysbiotic bowel status, inter-individual variability in susceptibility to brain-gut microbiome-related diseases are tried to be explained. This newly discovered secret organ in the past decade may play a role that the diagnosis and in the targeted manipulation for the therapeutic intervention of many diseases over the next decade.

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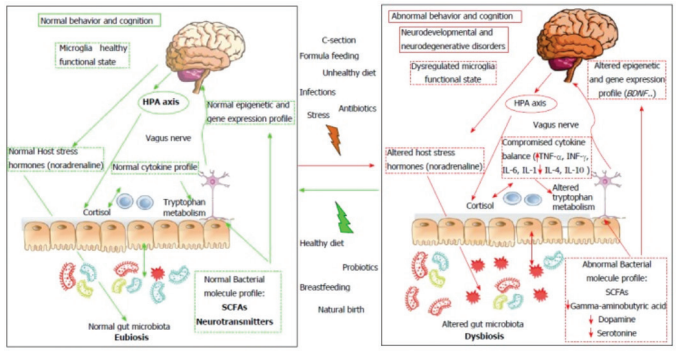

Figure 1. The modified intestinal microbiota composition increases the risk of neurodevelopmental and neurodegenerative disorders from microbiota-derived products such as short-chain fatty acids (SCFAs) and neurotransmitters. HPA: Hypothalamic-pituitary-adrenal.

P4 - Renal Diseases

P4-01

Kidney Diseases: Classification and Molecular Mechanisms

Dildar Konukoğlu

Department of Medical Biochemistry, İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, İstanbul

Kidney diseases are a group of disorders affecting kidney structure and function. The Centers for Disease Control and Prevention estimates that in the United States, more than 10% of people 20 years and older have chronic kidney disease. For the year 2015, general incidence and general prevalence of end stage renal disease in Turkey were 147.3 and 935.4 per million population. Kidney diseases are classified according to etiology, pathology, or location of involvement. According to the KDIGO guidelines kidney diseases are classified as acute kidney injury (AKI), chronic kidney injury (CKI) and acute kidney diseases (AKD). Criteria included the measures of kidney damage and function are given in Table 1.

On the other hand, classification of kidney diseases according to morphological components, such as glomeruli, tubules, interstitium, and blood vessels may provide greater convenience in approaching these diseases. However, some disorders affect more than one structure. Whatever the origin, all forms of chronic kidney disease ultimately damage all four components of the kidney. The most common causes of and main risk factors for kidney disease are given in Table 2. Some factors affecting the kidneys or patterns of kidney disease are given in Table 3. These factors can cause different patterns of injury to the kidneys and can affect kidney function. Some of them affect nephrons, or parts of the nephrons (glomeruli or the tubules). Some factors affect the passage of urine from the kidney or cause damage to the kidney(s). The clinical manifestations of renal disease can be grouped into well-defined syndromes. While some renal diseases only contain glomeruli, some renal diseases may involve more than one morphological component.

Azotemia is a biochemical abnormality associated with an elevation of blood urea nitrogen (BUN) and creatinine levels, and decreased glomerular filtration rate (GFR). It is a consequence of several kidney disorders, but it usually arises from pre or post kidney disorders. A typical characteristic of azotemia is acute or chronic kidney damage.

Acute Kidney Injury (AKI) is a syndrome associated with rapid decrease in glomerular filtration rate (hours to days). Previously it is known as acute renal failure. In AKI, the changes in kidney function evolve within one week. Retention of the nitrogenous waste products, and disturbance in homeostasis of electrolytes and asid-base develop. Oligouria is seen in the 50% of these patients. Symptoms may include: Urinating less frequently, fluid retention, causing swelling in the legs, ankles or feet, drowsiness, fatigue, shortness of breath, nausea, confusion seizures or coma and chest pain. Most of the patients are admitted to intensive care units. AKI can result from glomerular, interstitial, vascular or acute tubular injury, and may divided into three classes as prerenal renal, and postrenal.

Prerenal AKI, called Prerenal azotemia, is a most common form of acute kidney failure (AKF). Represents a physiological response to moderate renal hypoperfusion. Since renal tissue is not damaged, the majority of AKI is reversible. But severe hypoperfusion may lead to ischemic injury of renal parenchyma. The most common cause of hypoperfusion is hypovolemia. Hypovolemia may due to the hemorrhage, burns, dehydration, gastrointestinal fluid loss (eg. vomiting, diarrhea),renal fluids loss (eg.diuretics, osmotic diuresis) or sequestration in extravascular space (eg. Pancreatitic, trauma, burns). The other causes of AKI are low cardiac output, elevated renal vascular resistance (eg. systemic vasodilatation in sepsis or antihypertensives) and hyperviscosity syndromes (eg. multiple myeloma, polycythemia).

Intrinsic renal AKI can be complication of many diseases. Intrinsic AKI can be a progression from a prerenal phase, but many conditions causing AKI do no have a prerenal component. According to the causes of ınjury, it can be divided into four groups as diseases of larger renal vessels, disease of the renal microcirculation and glomeruli, ischemic and nephrotoxic AKF, and tubulointerstitial inflammation. Majority of AKF is triggered by ischemia or nephrotoxins.

Ischaemic injury and many nephrotoxins can cause acute tubular necrosis. The renal vasoconstriction due to the intrarenal release of vasoactive substances (eg.endothelin and prostaglandins) and to angiotensin II are main involved in the pathogenesis of acute tubuler necrosis.

Postrenal AKI, called postrenal azotemia, occurs usually due to the urinary tract obstruction. Bladder neck obstruction is most common cause of postrenal AKF and is associated with prostatic disease (e.g. hypertrophy,neoplasm or infection) or neurogenic bladder.

CKD is a pathophysiologic process with multiply etiologies leading to end-stage renal disease (Table 4). It is progressive disease leading to reduction in renal mass which causes structural and functional hypertrophy of surviving nephrons as an adative responce againts to the injury. It has been demonstrated that If 80% of renal mass was removed, it develops proteinuria, hypertension and progressive renal failure. Before these changes develop, there is a massive increase in renal blood flow. This leads to an increase in capillary hydrostatic pressure, increased capillary permeability and passage of macromolecules, (plasma proteins and lipoproteins) through the capillary wall. Finally, this adaptive responces are disrupted, because of the sclerosis of the remaining nephrons.

Major causes of CKD are diabetic renal disease, hypertension, nondiabetic glomerular disease (nephritic or nephrotic), cystic kidney diseases and tubulointerstitial diseases. It is essential for the diagnosis of the CKD that the pathophysiologic process should be last than 3 months. KDIGO 2012 guidelines classifies CKD based on cause, Glomerular Filtration Rate (GFR) category, and albuminuria category, thus emphasizing the role of laboratory medicine in manage¬ment of CKD. One of the major laboratory tests involved in CKD management is serum creatinine (SCr) and consequently estimation of GFR via estimating equations. KDIGO 2012 guidelines also recognize the value of estimating GFR using Cystatin C measurements as a biomarker alternative to creatinine. Since CKD can progress silently over many years, with no signs or symptoms or with ones that are too general for a person to suspect as related to kidney function, routine blood and urine tests are especially important.

Nephrotic syndrome is characterized by the loss of too much protein in the urine. It is caused by damage to the glomeruli and can be a primary disorder of the kidney or secondary to an illness or other condition, such as cancer or lupus. Along with a high amount of protein in the urine, signs and symptoms of nephrotic syndrome include a low amount of albumin in the blood, higher than normal lipid levels in the blood, and swelling (edema) in the legs, feet, and ankles. The condition may be acute or chronic, and the outcome can vary.

Nephritic syndrome is a clinical entity caused by glomerular disease and is dominated by the acute onset of either gross hematuria or microscopic hematuria with dysmorphic red cells and red cell casts on urinalysis, diminished GFR, mild to moderate proteinuria, and hypertension. It is related to acute poststreptococcal glomerulonephritis.

Kidney failure, also called end-stage renal disease or ESRD, is the total or near total loss of kidney function and is permanent. Treatment with hemodialysis or kidney transplant is the only option at this stage of kidney disease to sustain life.

Conclusion, the functional reserve of the kidney is large, and much damage may occur before there is evident functional impairment. For these reasons the early signs and symptoms are of particular clinical importance.

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Table 1. Criteria for the Definitions of Kidney Diseases and Disorders (KDIGO guidelines)

	Functional Criteria
Acute Kidney Injury (AKI)	Increase in serum creatinine by 50% within 7 days or increase in serum creatinine by >0.3 mg/dL within 2 days, or oliguria
Chronic Kidney Injury	Glomerular Filtration Rate <60 mL/min for 3 months.
Acute Kidney Diseases	AKI, or Glomerular Filtration Rate <60 mL/min/1.73 m^2 for 3 months, or decrease in GFR by >35% or increase in serum creatinine by >50% for 3 months
Normal	GFR >60 mL/min/1.73 m^2, stable serum creatinine

Table 2. The most common causes of and main risk factors for kidney disease

Diabetes mellitus	Uncontrolled diabetes can over time damage the nephrons in the kidneys
High blood pressure (hypertension)	Hypertension can damage blood vessels within the kidneys, preventing them from filtering wastes from the blood
Family history of kidney disease	For example, polycystic kidney disease

Table 3. Some factors affecting the kidneys or patterns of kidney disease

Glomerulonephritis (chronic nephritis or nephritic syndrome)	A group of diseases that cause inflammation and damage to the blood filtering units of the kidneys (glomeruli) and the third most common type of kidney disease.
Obstruction	The urinary tract can become blocked, or obstructed, from such things as a kidney stone or tumor. The blockage can lead to infection and injury of the kidney.
Autoimmune disease	Systemic lupus erythematosus or Goodpasture syndrome can lead to glomerular disease and affect the kidneys
Infections	Certain bacteria and viruses
Immune response	Some infection such as impetigo, endocarditis, HIV, hepatitis B, or hepatitis C has an adverse effect on the kidneys.
Congenital defects	Defects that impede the normal flow of urine.
Injury	It can cause acute kidney diseases that can lead to chronic kidney disease
Toxins	Some contrast dyes used for imaging procedures and certain medications
Drugs	Use and/or overuse of non-steroidal anti-inflammatory drugs (NSAIDS)
Pre-renal azotemia	Severe blood loss or reduced blood flow
Interstitial nephritis	The spaces between the kidney tubules become inflamed and swollen.
Acute tubular necrosis	Most common causes of kidney failure. It is caused by a lack of oxygen to the kidney tissues or from damage to the kidneys by toxic substances

Table 4. Risk factors and Sociodemographic factors for chronic kidney disesase

Risk factors	Sociodemographic risk factor
• Diabetes	• Older age
• Hypertension	• Black race
• Autoimmune diseases	• Smoking
• Systemic infections	• Heavy alcohol use
• Urinary tract infection, nephrolithiasis, lower urinary-tract obstruction	• Obesity
• Hyperuricemia	• NSAIDs
• Acute kidney injury	
• Family history of chronic kidney disease	

P4-02

Evaluation of Renal Function Tests in Pediatric Population: Estimation and Measurement of Gfr and Problems

Mine Kucur

Department of Medical Biochemistry, İstanbul University, Cerrahpaşa Faculty of Medicine, İstanbul

Aeliable and accurate assessment of glomerular filtration rate (GFR) is critical for diagnosing acute and chronic kidney impairment, intervening early to prevent endstage renal failure, prescribing nephrotoxic drugs and drugs cleared by a failing kidney, and monitoring for side effects of medications. Estimation of GFR using exogenously administered substances is well established and precise, but these methods are cumbersome and time consuming. Plasma creatinine is the most commonly used index for estimating renal function in the clinical practice. Due to its small size and lack of protein binding, it is freely filtered through the glomerulus. However, it is also actively secreted by the proximal tubules at unpredictable rates. Moreover, with decreasing GFR, the fraction of tubular secretion increases, leading to an over-estimation of 10-40% when compared to that of inulin clearance. Especially in children, estimation of creatinine is difficult, as there is a muscle mass related increase in plasma creatinine in children after 2 years of life. Moreover, plasma creatinine may change in cases of excessive dietary intake of meat, malnourished children and anorectic adolescents [1]. On the other hand, cystatin C is produced endogeneously at a constant rate, is freely filtered by the glomerulus, and is completely reabsorbed and catabolised by the renal tubule cells. Blood levels of cystatin C have been found to be a reliable indicator of renal function. The levels of cystatin C are independent of age, height, obesity and malnutrition. Recent studies also suggest that serum cystatin-C is better than serum creatinine in detecting acute kidney injury in critically ill children [2]. Due to high cost, difficult assay methodologies and standardization, and non-availability of definite cut-off values, cystatin C has still not replaced creatinine in the clinical practice. To compensate for the increasing muscle mass during childhood, creatinine based formulae which include height and muscle mass have been developed. The most commonly used formula is the Schwartz formula. The low muscle mass in malnourished children, may influence the value of k, and may affect the GFR estimation, and thus may lead to over-estimation of GFR in this subset. Moreover, the value of k should be different based on the method of estimation of serum creatinine. Schwartz, et al., using the enzymatic method of creatinine estimation, recently proposed a new k value of 0.413. To improve the bias and accuracy of the GFR estimation, it is important for all the pediatricians to understand that the value of k should be locally derived based on the method of creatinine estimation, reference GFR estimation and the local population characteristics. Hari, et al., based on the regression analysis, found the value of k to be 0.42 in Indian children where the creatinine was estimated by kinetic Jaffe method and 99mTc-DTPA GFR was the reference GFR. Cystatin-C based equations have been found to have better accuracy of predicting GFR, as compared to the creatinine based equations. The combined equations have generally been found to have better accuracy in the estimation, than individual equations. In the current issue of Indian Pediatrics, Hari, et al. prove that cystatin-C equations have better accuracy. They also found that the combined cystatin-C and creatinine-based equation was not better than only cystatin-C or creatinine based equation. The strengths of the study are testing the equation in the GFR 60-90 mL/min/1.73 m^2. Early detection of chronic kidney disease and monitoring of renal function deterioration requires an equation which works well in early stages of chronic kidney disease. Another strength of this study is its relevance for the pediatricians in India which can help in the current clinical practice. There is a need to have more studies in children and adolescents with an early chronic kidney disease, to enhance the use of these equations. It is important for pediatricians to understand that children and adolescents with early chronic kidney disease and a well-maintained fluid and electrolyte balance, the urinalysis may be entirely normal. Therefore, a reduced GFR may serve as the only clinical sign of kidney damage. Early intervention in the course of renal impairment offers the best chance of preventing end stage renal disease in children. There currently exists no equation for monitoring acute changes in GFR. However, the equations developed till now, may be able to determine longitudinal changes in GFR over time. The parameters used in the equation may be used on the locally available marker, which has been standardized according to the local laboratory.

As in adults, GFR estimating equations incorporating creatinine and/or cystatin C have been developed for children over the past 4 decades that attempt to account for the influence of age, body size, and/or sex on these markers, thus improving accuracy. But the limitations of these equations must be recognized. First, the laboratory methods to determine creatinine and cystatin C have changed over time, and thus estimating equations using creatinine or cystatin C derived from a different laboratory method may yield different, and less accurate, results. Second, the equations were developed in small groups of children, primarily with decreased GFR. GFR estimating equations in adults, also primarily developed in populations with decreased GFR, have been shown to underestimate GFR among those without kidney disease.

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF/DOQI) Clinical Practice Guidelines, published in 2003, recommend that the formulas by Schwartz et al. or Counahan-Barratt et al. be used to estimate GFR. Both formulas account for the relationship between creatinine production and muscle mass by using height as a surrogate. The differing constants used in these formulas highlight the significant effect of the laboratory method for creatinine determination on GFR estimating equations. The original Schwartz equation was derived using Jaffé (alkaline picrate) creatinine methodology, and the Counahan-Barratt using the Jaffé reaction after serum adsorption onto an ion-exchange resin to remove noncreatinine chromogens. If the same laboratory method is used for creatinine determination, the difference between the constants leads to a 22% and 39% reduction in eGFR by the Counahan-Barratt compared with the Schwartz equation in adolescent females and males, respectively. The recently published GFR estimating equations from the CKiD Study were derived using creatinines determined by an enzymatic assay that is more specific and sensitive than the Jaffé method. Compared with the Jaffé method, the enzymatic method results in lower creatinine values; hence, the lower constant in the bedside CKiD estimating equation, compared with the original Schwartz equation, reflects this.

Accurate estimation of GFR in children has obvious clinical and research benefits. This analysis underscores that appropriate application of pediatric estimating equations requires an understanding of the creatinine and cystatin C laboratory methods used in a given clinical or research setting and the methods used to develop the equations. Efforts by NKDEP to standardize laboratory assay calibrators will help minimize the measurement variation that affects the accuracy of all GFR estimating equations. The novel CKiD GFR estimating equations have been shown to have excellent precision and accuracy at GFRs between 15 and 75 ml/min per 1.73 m^2. The precision and accuracy in children with higher or normal GFRs cannot be fully addressed in this analysis because of the lack of formally measured GFR. The population-based eGFR percentiles for each equation provided in Table 1 may help clinicians determine the normal range of eGFR, and thus better identify children at risk for loss of kidney function. However, clinical validation of eGFR in the general pediatric population is needed before using these equations to screen for CKD whenever a serum creatinine or cystatin C is obtained.

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Table 1. Percentile distribution of creatinine, cystatin C, and eGFR in adolescents aged 12 to 17 years, NHANES

	1st	5th	10th	25th	50th	75th	90th	95th	99th
Serum creatinine, mg/dl	0.5	0.5	0.6	0.6	0.7	0.8	0.9	1.0	1.1
Serum cystatin C, mg/L	0.57	0.65	0.68	0.75	0.83	0.91	1.01	1.06	1.21
Bedside CKiD	62.9	71.1	75.6	84.4	96.6	108.8	122.1	131.6	149.1
Counahan et al.	65.5	74.0	78.7	87.8	100.5	113.3	127.2	137.0	155.2
Leger et al.	77.6	87.7	94.4	105.8	122.2	139.2	156.9	170.7	195.7
Schwartz et al.	96.0	106.8	113.4	125.4	140.0	159.1	180.6	193.2	229.0
Filler et al.	74.0	85.8	90.6	101.9	112.9	126.6	141.3	148.6	172.2
Grubb et al.	62.3	80.6	90.7	106.3	130.1	157.1	189.1	208.4	261.7
Bouvet et al.	72.3	79.6	83.6	92.4	104.6	116.6	128.5	134.3	150.6
CKiD	72.9	79.5	84.1	89.5	96.6	105.6	115.1	121.3	131.6
Zappitelli et al.	69.0	74.8	78.5	87.2	97.6	110.0	119.1	126.8	140.2

Nhanes: National health and nutrition examination survey

P4-03

Proteinuri: Algorithmic Approach

Dildar Konukoğlu

Department of Medical Biochemistry, İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, İstanbul

Introduction

Proteinuria is often transient and benign, but persistent proteinuria is not only a marker of early kidney disease, but also an independent risk factor for athero-sclerotic diseases, such as coronary or cerebrovascular arterial diseases. Individuals with proteinuria are at increased risk of death (Table 1).

Proteinuria

Normally urine contains less than 150 mg protein per day, with only 20% of it as albumin (less than 30 mg/day) and 40% as Tamm-Horsfall mucoproteins, which are secreted by the distal tube. This protein originates from the ultrafiltration of plasma and from the urinary tract itself. Proteins of low molecular weight readily pass through the glomerular filtration barriers and are reabsorbed. Because of their low plasma concentration, only small quantities of these proteins appear in the urine. In contrast, albumin, a moderate molecular- weight protein, has a high plasma concentration. Combined with its ability to pass through the filtration barriers, the small amount of albumin present in normal urine. Microalbuminuria is defined as a urinary excretion of albumin between 30-300 mg/gün. It is recognized to be an early marker for nephropathy associated with type 2 diabetes mellitus or hypertension, and also is an independent marker for cardiovascular disease. Proteinuria is defined as urinary protein excretion at levels higher than 150mg /day and can be represent a glomerular disease (Table 2).

Classification of Proteinuria

Proteinuria can be classified into four categories: prerenal or overflow proteinuria, glomerular proteinuria, tubular proteinuria, and postrenal proteinuria (Table 3). This differentiation is based on a combination of protein origination and renal dysfunction; together, they determine the types and sizes of proteins observed in the urine (Table 4). Therefore there are four mechanisms of excessive protein excretion in urine; glomerular proteinuria, inadequate tubular reabsorption, increased tubular secretion, and overflow proteinuria.

Glomerular proteinuria occurs in primary glomerular diseases or disorders that cause glomerular damage. It is the most common type of proteinuria encountered and is the most serious clinically. The proteinuria is usually heavy, exceeding 2.5 g/day of total protein, and can be as much as 20 g/day. Glomerular proteinuria can be occur in nephrotic syndrome. The hallmark of glomerular proteinuria is presence of albuminuria. However, albuminuria is not diagnostic for glomerular proteinuria. Albuminuria can also occur in the tubular proteinuria.

Overflow proteinuria results from increased levels of plasma proteins in the blood readily passing through the glomerular filtration barriers into the urine. Increased excretion of low-molecular-weight proteins can occur with marked overproduction of a particular protein, leading to increased glomerular filtration and excretion. This is generally due to immunoglobulin light chains in multiple myeloma.

Tubular proteinuria occurs when normal tubular reabsorptive function is altered or impaired. When either occurs, plasma proteins reabsorbed normally are can be increased in the urine. The urine total protein concentration is usually less than 2.5 g/day. Tubular protein is not determined by urine dipstick test since the dipstick for protein is not sensitive for the detection of proteins other than albumin.

Postrenal proteinuria can result from an inflammatory process in the urinary tract or the leakage of blood proteins into the urinary tract as a result of injury and hemorrhage. Contamination of urine with vaginal secretions or seminal fluid can also result in a positive protein test or proteinuria.

Proteinuria can be classified as transient or persistent. Transient proteinuria is caused by a temporary change in glomerular hemodynamics that in conditions such as orthostatic (postural) proteinuria, dehydration, fever, exercise, and emotional stress. Postural (orthostatic) proteinuria is considered as functional proteinuria. It is associated with the urinary excretion of protein only when the individual is in an upright (orthostatic) position. Protein content is normal in the first morning urine specimen whereas during the day obtained urine samples contain elevated quantities of protein. Persistent proteinuria is defined as 1+ protein on a standard dipstick (which corresponds to approximately 30 mg/dL) two or more times over a three-month period. It indicates a pathologic process such as genetic, infectious, metabolic, or vascular diseases. The most common type of persistent proteinuria is glomerular proteinuria.

Determination of protein in urine

The urine dipstick colorimetric test is the usual first line screening test for the detection of proteinuria/albuminuria, but false positive reactions are common. Positive reactions can be confirm by sulfosalicylic acid (SSA) turbidimetric test. Proteinuria detected by dipstick and/or SSA screening tests and is often confirmed and quantitated using the urine protein/creatinine ratio (UP/C). The dipstick colorimetric test for proteinuria is inexpensive, easy to use, and primarily measures albumin, but sensitivity and specificity are relatively low. The dipstick, SSA, and UP/C tests are more sensitive for albumin than for other proteins. False negative results (decreased sensitivity) may occur with Bence Jones proteinuria, low concentrations of albuminuria, and/or dilute or acidic urine. The lower limit of detection for the dipstick test is approximately 30 mg/dl. In addition to albumin, the SSA test can detect globulins and Bence Jones proteins to a greater extent than the dipstick test. False positive results may occur if the urine contains radiographic contrast agents, penicillin, cephalosporins, sulfisoxazole, or thymol (a urine preservative). The protein content may also be overestimated with the SSA test if uncentrifuged, turbid urine is analyzed. The reported sensitivity of the SSA test is approximately 5 mg/dl. Albuminuria can be also measured by quantitative immunoassays.

Assesment of proteinuria

The first step in the evaluation of patients with proteinuria should include a comprehensive history and physical examination focusing on the various possible causes as applicable based on the clinical context including drugs and evidence of systemic diseases. The assessment should also include a search for other cardiovascular risk factors. In the next step, glomerular filtration rate and fasting blood glucose should be determined and urine and plasma protein electrophoresis as well as urine microscopy and specific serological tests (autoantibodies, complement levels, cryoglobulins, hepatitis, HIV serologies) should be performed.

Conclusion

Since proteinuria is a surrogate marker for progressive atherosclerosis and a marker of widespread vascular inflammation and endothelial dysfunction, reducing proteinuria is of paramount importance in retarding the progression of chronic kidney disease. Screening for proteinuria is recommended in all subjects with diabetes, hypertension, vascular disease or autoimmune disease.

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Table 1. Risk Factors for Proteinuria

- Male Sex
- Diabetes Mellitus
- Advanced age
- Hypertension
- High Body Mass Index (BMI)
- Elevated systolic blood pressure
- Smoking

Table 2. Definitions of albuminuria and proteinuria

Nephropathy	Urine dipstick for protein	24- urine collection for albumin (mg/day)
Normal	Negative	<30
Albuminuria	Negative	30-300
Overt nephropathy-proteinuria	Positive	>300

Table 3. Classification of Proteinuria

Prerenal-Overflow proteinuria	An increase in plasma low MW proteins leads to increased excretion in urine	• Muscle injury • Intravascular hemolysis • Infection • Inflammation • Multiple myeloma
Renal proteinuria-Glomerular	Glomerular filtration barrier is defective, allowing plasma proteins to enter ultrafiltrate. It can be selective or non selective. In selective proteinuria albumin and moderate molecular weight. Plasma proteins increase In nonselective proteinuria all proteins, including high molecular weight. Plasma proteins increase	***Primary glomerular diseases:*** • Glomerulonephritis • Glomerulosclerosis • Minimal change disease ***Glomerular damage due to:*** • Poststreptococcal glomerulonephritis • Diabetes mellitus • Lupus erythematosus • Amyloidosis • Sickle cell anemia • Transplant rejection • Infectious disease (malaria, hepatitis B) • Preeclampsia • Cancers (leukemia, lymphoma) • Drugs (penicillamine, lithium) • Toxins (heavy metals) ***Transitory glomerular changes:*** • Strenuous exercise • Fever, dehydration • Hypertension • Postural proteinuria • Postpartum period • Extreme cold exposure
Renal proteinuria-Tubular	Defective tubular reabsorption of protein. The low molecular weight proteins including albümin increase	• Acute/chronic pyelonephritis • Interstitial nephritis • Renal tubular acidosis • Renal tuberculosis • Fanconi's syndrome • Systemic diseases–sarcoidosis, lupus erythematosus, cystinosis, galactosemia, • Hemoglobinuria–hemolytic disorders • Myoglobinuria–muscle injury • Drugs (aminoglycosides, sulfonamides, • penicillins, cephalosporins) • Toxins and poisons (heavy metals) • Transplant rejection • Strenuous exercise
Postrenal proteinuria	Urine includes proteins produced by the urinary tract or the urine is contaminated with proteins during excretion	• Inflammation • Malignancy • Injury/trauma • Contamination during urination

Table 4. Principal Proteins in Glomerular and Tubular Proteinuria

Glomerular Proteinuria	Tubular Proteinuria
• Albumin • Transferrin • α_1-Antitrypsin • α_1-Acid glycoprotein	• Albumin • β_2-Microglobulin • Retinol-binding protein • α_2-Microglobulin • α_1-Microglobulin • Lysozyme

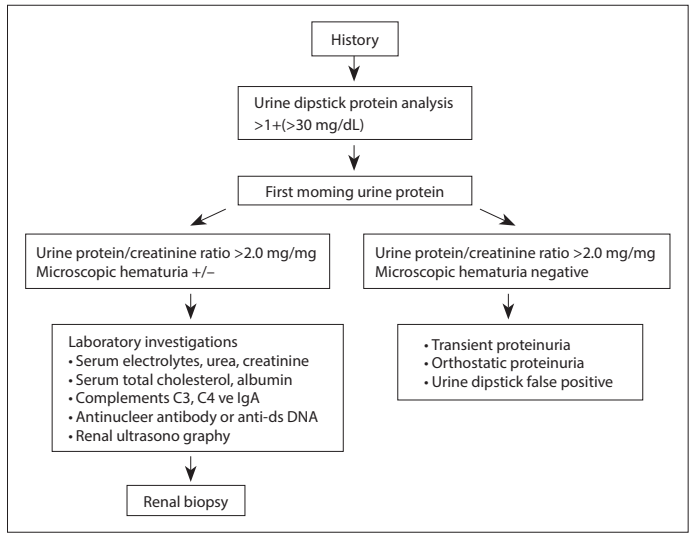

Figure 1. Proteinuria algoritmia.

P4-04

Biomarkers in Acute Kidney Diseases: Which and When

Banu İşbilen Başok

Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, İzmir

Acute kidney diseases and disorders are an important health problem with high morbidity and mortality due to acute kidney injury. Today, avoiding the use of potentially damaging agents such as nephrotoxic drugs and contrast agents and supportive care is the basis of patient care. The most likely reason why the treatments developed in animal experiments are not effective in humans is the lack of biomarkers that will detect acute injury in the reversible phase of kidney function. Therefore, it is important to develop new biomarkers and make them widely available, such as conventional renal function tests, to provide early diagnosis.

Acute kidney injury (AKI) is diagnosed by increasing serum creatinine (SCr) and/or decreasing urinary output in the direction of guidelines such as "Acute Kidney Injury Network (AKIN)" or "Kidney Disease Improving Global Outcomes (KDIGO)". However, SCr measurement in the early phase of AKI has some limitations: (i) increased pre-renal azotemia in spite of no tubular damage, (ii) the undesirable effects of non-renal factors such as body weight, muscle metabolism, drug use, (iii) no increase up to 72 hours after the injury starts, and (iv) due to its tubular excretion no increased levels despite the injury. To reduce the effect of delayed SCr elevation after the actual decrease in glomerular filtration rate, which is

the most important limitation, it is suggested to put AKI diagnosis according to individualized SCr levels. Oliguria is a sensitive and specific marker of AKI, but only when the urine output is correctly monitored in an intensive care unit by monitoring urine output hourly by using a leakproof catheter; or in case of no taking any diuretic drugs. Moreover, each case may not be presented with oliguria.

AKI is characterized by vascular and tubular alterations, which can synthesize various molecules up to 3 days before the presentation of clinical findings. In this critical period, a molecule that can be measured in serum and/or urine might be a biomarker that will contribute to the management of the disease by showing an early damage. Among the molecules suggested in the literature as biomarkers are: tubular enzymes (α and π glutathione S-transferase, N-acetyl beta glucosaminidase), cytokines (IL-18, IL-1, -6, -8), low molecular weight proteins (cystatin C, hepatocyte growth factor, alpha1-microglobulin, beta2-microglobulin), proximal tubule proteins (KIM-1, NGAL, cystatin C, L-FABP), cell cycle arresting proteins (IGFBP7, TIMP-2), and microRNAs. Among the most researched biomarkers, NGAL, TIMP-1, and IGFBP7 have the potency to be used in early AKI. KIM-1, L-FABP, and IL-18 have also been shown to be effective in predicting renal injury and prognosis. The most studied biomarkers in the literature and their potential use in AKI will discuss in the conference in detail.

It is also possible to use biomarkers for risk assessment, differential diagnosis, positive or negative prognosis determination, and the right time for treatment or intervention as well as diagnosis and staging. However, it is unlikely that all of these needs will be realized by a single biomarker in AKI, which arises from diverse pathologies of pre-renal, renal and post-renal diseases. Just as in the case of SCr, the above-mentioned biomarkers also have limitations. For example, the most studied AKI biomarker is NGAL. NGAL has been found to be effective in the AKI of pediatric population after long-term injury in case of cardiopulmonary surgery. However, since NGAL is an acute phase reactant, if the patient has pyelonephritis, its specificity is reduced. For this reason, it may be more useful to use biomarkers together to represent the underlying functional change, damage, or combination of these two, instead of a single biomarker. For example, measuring the level of NGAL in combination with SCr after using a nephrotoxic agent may reveal kidney injury before measuring the SKR alone. Thus, a damage that leads to functional impairment can detect at an early stage without clinical signs. Alternatively, an elevated level of SCr may indicate a reversible dysfunction while NGAL in an oliguric and dehydrated patient is at a normal level. In conclusion, it seems appropriate to establish a panel of biochemical markers consisting of traditional and new molecules for early diagnosis and effective follow-up of the disease. It would be more appropriate for this panel to be structured according to the age of the patient, the accompanying clinical condition (such as sepsis, cardiac surgery, the use of nephrotoxic agents) and the timing of the illness (emergency department referral, intensive care hospitalization, beginning of AKI clinic) rather than a standard panel. The major challenges we face as medical biochemistry specialists at this stage will be in identifying the right biomarkers, standardizing their measurement methods and hence ensuring reliable results at the right time.

Conclusion

Biomarkers recommended for use in AKI are currently not widely available in medical laboratories. However, it is important to bring these markers to a level that can be widely used, such as existing renal function tests. Moreover, an effective preventive treatment may require an AKI staging which includes new biomarker/s that will identify early onset of acute renal disease, such as in chronic kidney disease.

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P4-05

Laboratory Evaluation of Dialysis Adequacy

İkbal Özen Küçükçetin

Department of Nutrition and Dietetics, Assist. Prof. Dr., Akdeniz University, Faculty of Health Sciences, Antalya

Despite the widespread use of peritoneal dialysis and renal transplantation, hemodialysis (HD) remains the main renal replacement therapy in our contry and in the most countries in the worldwide. In spite of our better understanding of the development of chronic renal disease (CKD) and the advances in dialysis technology, annual mortality in HD patients is 15-25% at the international level, depending on demographic factors [1, 2].

The concept of Dialysis Adequacy has been developed to reduce the morbidity and mortality associated with CKD and HD and to increase the quality of life of the patient. Dialysis Adequacy is evaluated by the patient's clinical evaluation, biochemical parameters and kinetic markers. In time, calculations involving many kinetic approaches have been developed to quantify the delivered dialysis dose in a reproducible manner and to correlate the delivered dialysis dose with clinical outcomes [3, 4]. The clearance calculations to determine the dialysis dose include urea, which is the principal representative of both protein uptake and water-soluble small uremic toxins. Some of the different calculation methods based on BUN (Blood Urea Nitrogen) measurement in the clinic are: spKt/V (singlepool Kt/V), Urea Kinetic Model (UKM), eKt/V (equilibrated/V), Online Clearance Measurement, Urea Reduction Ratio (URR) [1, 3].

The Kt/V and URR methods are the most often used for Dialysis Adequacy measurement. Kt/V is a ratio representing fractional urea clearance, where K is the dialyzer urea clearance (expressed in liters per hour), t is the time on dialysis (expressed in hours), and V is the volume of distribution of urea (expressed in liters). A value of Kt/V of 1 implies that the total volume of the blood completely cleared of urea during a dialysis session would be equal to the volume of distribution of urea. It is recommended that for both adult and pediatric HD patients have Kt/V of at least 1.2 [1, 3, 5].

Another measure of the delivered dialysis dose is the URR. It is the percentage expression of the decrease in urea concentration during dialysis. It is formulated as URR (%)=((1-postdialysis BUN/predialysis BUN)X100). For dialysis adequacy, the URR should be at least 70% and above, which corresponds to an average Kt/V of 1.3 [1, 3, 5].

In HD patients, it is recommended that certain laboratory tests be measured at specific time intervals for monitorization. Serum BUN, creatinine, potassium, phosphorus, calcium, bicarbonate, albumin, cholesterol, hematocrit, aminotransferase levels should be measured once a month in samples taken before dialysis. Serum ferritin, iron, alkaline phosphatase and PTH levels should be monitored at intervals of three months [4, 5].

Dialysis Adequacy can be affected by many factors such as dialysis frequency and duration, residual renal function, dialysis application technique, dialyzers, nutritional status of the patient. In order for all calculations and evaluations to be done correctly, the results of the parameters to be measured in the laboratory must also be reliable. The collection of blood samples at the appropriate time and frequency, as indicated in the guidelines, correctly is important. Pre- and post- dialysis blood samples should be collected in the same session. The pre-dialysis samples should be collected before dialysis is started, if catheter is used to collect blood sample the first part of blood sample which contains heparin should not be used for measurement. After dialysis, samples should be collected after the blood flow rate is reduced to 100 mL/min or the dialysate flow is stopped for 3 minutes [4].

The optimal time and dose for hemodialysis remain controversial, but the determination of the dialysis dose and prescription of dialysis should be done according to the individual needs of the patient.For this, it should be decided with the help of the guidelines and formulas and considering all clinical factors of the patient.

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P5 - Toxicology

P5-01

Ethanol and the Role of Laboratory

Turan Turhan

Deparment of Clinical Biochemistry, University of Health Sciences Ankara Numune Training and Research Hospital, Ankara

Introduction: Ethanol is a commonly used addictive substance on which the highest money is spent on. It has been reported to affect 140 million people all over the world in year 2013. The cost of alcohol addiction is around 166 billion dolars in United States. Problems emerging from alcohol abuse are one of the most important problems of our era. Alcoholism causes health problems, traffic accidents, self-destruction, guilt tendency, family break-ups, economical problems and problems in occupational life. In year 2009, 18.7 million individuals which makes 7.4% of the population over 12 years of age was reported to be alcohol users or alcohol abusers.

Sources of Ethanol: Beer, wine and other distilled beverages contain different concentrations of ethanol in them. Ethanol ratios in beers (volume/volume) can differ accordingly as shown by Logan et al.'s work ranging between 2.9%-12.7%. Wine is generally produced from fermented grapes and unless there is an addition of extra pure ethanol, alcohol content of wines range between 7-15%. Cognacs and liquors have much higher ethanol. Ethanol can be found in some products besides alcoholic beverages, which are shown in Table 1.

Epidemyology of ethanol usage and heath-related consequences: Major causes of ethanol-related morbidity and mortality are chronic illnesses or traumas. Ethanol related injuries include motor car accidents, drawning, workplace accidents, judicial crimes and suicide cases. Mortal traffic accidents is the leading cause of individuals up to 35 years of age and in year 2009, in 32% of mortal traffic accidents blood ethanol levels of drivers and other passangers were reported to be over 80 mg/dL. Ethanol consumption is also a risk factor in mortal drawnings and half of fire cases. In violence crimes, near the quarter of 11.1 million crimes ethanol consumption was detected. Besides these judicial crimes, ethanol consumption is also known to be related with medical conditions like hepatitis, cirrhosis, oral, larynx and osephagaus cancers, cardiomyopathy, hipertension, arythmia, Korsakoff syndrome and fetal alcohol syndrome.

Acute effects of alcohol consumption: Social problems related with alcohol abuse can be listed as treatment expenses, productivity loss caused by alcohol based mortality and morbidity, crimes committed related to alcohol and traffic accidents. Alcohol consumption has several effects on various disorder categories. ICD-10 defines more than 60 disorders which may potentially caused by alcohol abuse. Table 2 lists the acute effects of alcohol consumption.

Absorption and metabolism of ethanol: Orally taken ethanol is quickly metabolized by 10% in stomach and 90% in colon lumen by passive diffusion. Absorbtion is quicker in alcoholic beverages containing 15-30% alcohol. It can be detected in blood after 5 minutes of oral consumption. In an avarage adult, it reaches it's maximum blood concentration after 30-60 minutes following a single dose. This time is also dependent on the duration of alcohol consumption. While the peak value is reached quickly in consumption in a short time, the peak value is reached slowly in long interval consumptions. Absorption phase takes 30-90 minutes. Alcohol is easily passed in to fetal circualtion and fetal blood alcohol concentration equals maternal blood alcohol concentration. Consumption of foods containing carbohydrates, proteins and especially fats delays the absorbtive phase. Consumption with beverages containin CO_2 facilitates the absorbtion. Distilled beverages containing more than 20% alcohol are absorbed quickly by diffusion due to concentration difference. But beverages containing higher amounts of alcohol may cause muscle spasm

and absorebd slowly as their passage to small intestine is delayed. Once alcohol is in the blood stream, as it is distributed equally in body fluids, tissues with high liquid content will retain more alcohol. Ethanol has low solubility in lipids and it does not bind to plasma proteins so it's distribution in the body is basically related with body's water content and differs according to age and gender. Alcohol concentration is low in bone and fat tissues which contain low amount of water. Volume of distribution is assumed as 0.68 L/kg in males and 0.55 L/kg in females. Body fat ratio is higher, distribution volume is lower and gastric ADH aktivity is also lower in females. Alcohol elimination ratio is increased by 14% in luteal phase.

The primary organ responsible for ethenol metabolism is liver as 90% of oxidation takes place there, but ethanol is also partially metabolised in the gastrointestinal tract (GI). GI mucosa has alcohol dehydrogenase (ADH) activity. Gastric ADH takes place in the first pass metabolism of ethanol. 10% of ethanol is excreted by urine, airway, sweat, saliva and tears.

Ethanol is metabolised in the hepatocytes by three different mechanisms. It is metabolised to acetaldehyde by alcohol dehydrogenase in cytoplasm. It is converted to acetaldehyde in the endoplasmic reticulum by mikrosomal oxidation system. Also it is reduced to acetaldehyde in peroxisomes by ethanol catalase enzyme. Generated acetaldehyde is oxidized to acetic acid by aldehyde dehydrogenase enzyme. Acetic acid then enters the Creb's cycle. The rate-limiting step of these reactions is conversion of alcohol to acetaldehyde. Alcohol dehydrogenase enzyme metabolizes alcohol up to 100% mg blood level by first order kinetics but in higher concentrations, it metabolizes with zero order kinetics. In an avarage person 150 mg/kg-hour alcohol is metabolized. Mikrosomal enzyme system is used only in very high blood alcohol levels. ADH is a dimeric molecule coded by 7 genes, subcategorized by catalytical activity (Km and Vmax) and different organs it is found. There are 6 ADH subunits ALDHG has two isoenzymes.

MEOS activity is decreased by age. MEOS activity may also be induced by some drugs. Main components of MEOS are CYP2E1 and NADPH but it also includes cytochrome c reductase and phospholipids. CYP2E1 isoenzyme has the highest metabolic activity for ethanol. In cirrhosis, hepatic artery blood flow is diminished so the first metabolic affect of liver is reduced.

Ethanol assays: Clinical laboratories need fast and trustable methods for detection of ethanol in biological fluids like plasma, serum and urine. If remains unnoticed, interferences can lead to important clinical and legal consequences. Restrictions of these tests should be known and guidelines about questionable results should be followed. Various methods are available with different spesificity and cost for ethanol analysis. Gas chromatography is the specific method for detection of ethanol together with volatile compounds like methanol, isopropanol and acetone. Widely used methods for alcohol analysis are enzymatic methods using alcohol dehydrogenase (ADH) and alcohol oxidase (AOD).

Enzymatic methods have several advantages over gas chromatography. They are fast, can be easily automated, widely used and have helped saving lots of lives up to date. Automated ADH methods are under the risk of two potantial interference sources. First one is the cross-reactivity with other toxic alcohols and second one is the positive bias caused by increased lactate an/or lactate dehydrogenase concentrations.

Point-of-care tests are generally AOD based, this enzyme is unstable in solutions but when it is applied to a solid resin or dry dipsitck pads, it's tability is increased.

Automated test methods can analyse more than one body fluids. Generally the specimen of choice are serum/plasma and urine. Commercially available quality control materials can be used as there is legal restriction about usage of matrix-compatible controls. Besides internal quality controls, performance of labortaries can be monitored by external quality control programmes like CAP. CAP's acceptable performance value under CLIA'88 guidelines is ±25% for ethanol for all methods and 0-9 mg/dL for specimens containing no alcohol.

Urinary ethanol: after alcohol consumption in the post-absorptive phase, urinary ethanol level is 1.3 times higher than blood ethanol level. Some legal authorities accept blood ethanol level calculated from urinary ethanol level based on this formula. A good correlation between urinary and blood alcohol levels can be obtained by collecting urine 20-30 minutes after emtying of bladder. Detection of alcohol in urine shows alcohol consumption in the previous 8 hours.

Common Interferences seen in ethanol measurement and solution strategies used: Common interferences in ethanol measurement are; cross-reaction with other alcohols, and interferences seen with high lactate and LDH levels. Most commonly applied solution strategies to avoid interference are questioning the harmony between data, controlling the rightheousness of analysis units, checking correlation between consumed alcohol level and analyzed ethanol level with Widmarck Formula, and questioning consumption of alcohols other than ethanol.

Conclusion: Ethanol is the most frequently encountered toxic substance both clinically and legally as it is easily obtainable. Ethanol analyses are needed to be carried out for several reasons. Biochemistry specialists have to be careful in evaluating ethanol results both by the means of sensitivity and spesificity and also personal data of the individual from whom the sample is collected.

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Table 1. Ethanol contents of some non-beverage products

Products other than alcoholic beverages	Ethanol content (volume/volume)
Mouth wash solutions	10-27%
Shaving lotions	15-80%
Paint removers	25%
Cough syrups	2-25%
Parfumes and colognes	25-95%

Table 2. Acute effects of ethanol consumption

Blood alcohol level (mg/dL)	Clinical symptoms
<25	Feeling hot, slowing of reflexes, lowering of inhibiton, chattiness,
25–50	Euphoria, increased self confidence, decreased evaluation,
50–100	Decrease in critical performance tests, decrease in reaction time, decrease in concentration and coordination, aphasia
100–250	Emotional instability, balance problems, apathy, decreased perception,
250–400	Orientation problem, confusion, dizziness, exeggarated emotional expressions (fear/anger), color perception problems,
>400	Significantly reduced response to stimuli, motor function loss (walking, standing still), vomitting, urine and feces incontinens, loss of conciousness, sleepiness, stupor, loss of reflexes, lowering of body temperature, lowering of breath, death (respiratory arrest)

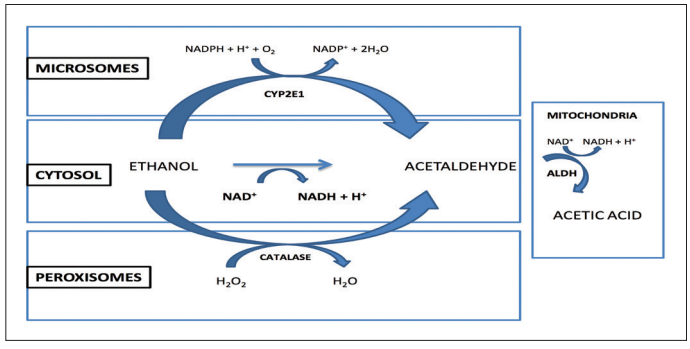

Figure 1. Oxidative pathways of alcohol metabolism.

P5-02

Analysis of Ethylene Glycol, Methanol and Isopropyl Alcohol and the Role of Laboratory

Halef Okan Doğan

Department of Biochemistry, Sivas Cumhuriyet University, School of Medicine, Sivas

Ethylene glycol, methanol, isopropyl alcohol, propylene glycol, and diethylene glycol are called toxic alcohols. Among these, the most common toxicants are ethylene glycol, methanol and isopropyl alcohol. Studies on the epidemiology of poisoning incidents due to toxic alcohols have been carried out in different countries. However, there is no exact information about the poisoning incidents in our country [1-3]. Toxic effects occurs related with the effects of the alcohol itself such as isopropyl alcohol and their metabolites as in methanol and ethylene glycol. Alcohol dehydrogenase catalyzes the first oxidation of the toxic alcohols. The resulting aldehydes (except for acetone from isopropanol) undergo further oxidation by aldehyde dehydrogenase to form carboxylic acid metabolites. Formic acid, which is the result of methyl alcohol metabolism and glycolic acid which is the result of ethylene glycol metabolism are the main metabolites that play role in the formation of clinical findings [4]. Methyl alcohol is metabolized mainly in the liver, ethylene glycol and isopropyl alcohol are metabolized in the both liver and kidney [5]. Loss of cellular function and death can occur in toxicities caused by these substances. Since nonspecific clinical findings such as visual disturbances, loss of pulmonary function, impaired renal function, nausea, vomiting, abdominal pain and neurological symptoms occur in alcohol toxicities, the diagnosis of these cases may be delayed and non-recurring damage may be encountered [6-8]. Among toxic alcohols, methanol toxicity is the most common toxicity. Ethylene glycol and isopropyl alcohol toxicities are less common than methyl alcohol toxicities. For diagnosis, physical examination findings and some biochemical analyzes are used [5]. Diagnostic biochemical assays are divided into two groups: direct and indirect analyzes. Direct tests are gas chromatography and enzymatic methods. Gas chromatography is the gold standard method in the determination of toxic alcohols. In direct methods, the levels of methylene, ethylene glycol and isopropyl alcohol and their metabolites found in serum or plasma samples can be quantitatively determined [9, 10]. There are also enzymatic methods that can be used to determine the metabolites of methanol and ethylene glycol levels. However, the results obtained with these methods need to be confirmed by gas chromatography [11-13]. Indirect methods are the determination of the calcium oxalate crystals, osmolar gap, pH, anion gap, lactic acid levels and urine fluorescence. Determination of the level of toxic alcohols is one of the important factors in determining the treatment protocol [5]. Gas chromatograph cannot be used every center due to the need for trained stuff and system cost. For this reason, indirect tests are more commonly used in the diagnosis of ethylene glycol, methanol, and isopropyl alcohol toxicities [10]. However, there are important limitations because the results are also affected by different diseases and the results vary according to the duration of admission to the hospital [5]. For this reason, there is a need for fast and reliable methods that can be used with toxic alcohol poisoning in clinical biochemistry laboratories. With the development of these methods, clinicians can intervene to patients more rapidly and therefore the most possible complications can be minimized.

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P5-03

Case Reports About Toxic Alcohol

Turan Turhan

Deparment of Clinical Biochemistry, University of Health Sciences Ankara Numune Training and Research Hospital, Ankara

Alcohol reports can often be requested to detect the condition of people after traffic accidents or people acting against the social order. Knowledge about the rate of alcohol elimination in the evaluation of blood alcohol concentration is important for forensic medicine and law. The body can metabolize an average of 15 mg/dL (10-34 mg/dL) ethanol in an hour. The elimination rate of 10 mg/dL/hour is used in forensic medicine applications. Crime time, alcohol intake time, measurement time, test result, sex, weight, height, food intake, number of beverages, amount of beverages, alcohol concentration in beverages, history of alcohol intake, medications taken together with alcohol, body temperature, gastric first pass effect is important in elimination.

Legal Issues Associated with Ethanol

The breath alcohol concentration of drunk drivers are measured by a device and in the case of the objection to the result of the device, blood sampling will be done by an authorized and trained staff in order to determine the amount of alcohol in blood and it will be sent to the police criminal laboratory for analysis. If it is not available in police criminal laboratories, blood sample will be sent to the Forensic Medicine Centers and to the nearest health institutions of Ministry of Health with technical and medical facilities capable of analysis. According to the regulation, in cases where the measurement of alcohol concentration is not available by the device or the laboratory, the drivers who are found to drive with alcohol will be referred to the nearest health institution and they will be passed the routine alcohol examination by the physician.

Alcohol reports can often be requested to detect the condition of people after traffic accidents or people acting against the social order. The general appearance of the person, the hyperemia of the face, incoordination of movements, the deterioration and delay in reflexes, the lisping in speech, the zigzag-like and irregular formation of the walk, difficulty of standing, tremor of hands and presence of alcoholic smell are expected to be found in people according to the amount of alcohol consumed. Findings of people should be mentioned in the report and it should be indicated to which opinion the person is alcoholic. Also alcohol level can be determined by alcohol meter if applicable. In cases where it is not decided by examination, blood sampling is done from the person and the situation could be reported to the related judicial authorities and the analysis of the blood can be performed. The blood taken should be approximately 15 mL and divided into two portions. It is also useful to add 1% sodium fluoride as an additive for accurate determination of alcohol content. In cases where sodium fluoride can not be found, blood samples should be sent to the laboratory without delay and judicial authorities should be warned. The person who is examined during the report should be carefully investigated and the time of examination or blood collection should be specified. In the conclusion part of the report, it should be stated whether the persons are alcoholic or not according to the findings. If there is an event that disrupts the social order, in addition it should be mentioned whether they are intoxicated. According to the regulation published in OFFICIAL GAZETTE dated 11.06.2013; ARTICLE 48-Drivers who have taken drugs or stimulants and drunk drivers are prohibited. If a driver is found to be driving with alcohol over 0.50 promile, even if it doesn't constitute an actual offense, an administrative penalty of 700 Turkish Liras will be issued and the driver's license will be withdrawn for six months. For drivers who use non-automobile vehicles, the higher limit of promile is applied as 0.21.

Conclusion

"Circular on Procedures and Principles of Ethanol Analysis Procedures in Blood Samples" dated 11/07/2017 and numbered 2017/12 were published and put into practice by medical laboratories in order to conduct the standardization of ethanol analysis in blood samples. Medical laboratory specialists are evaluating alcohol results of mostly forensic cases, traumatic events and alcohol abuse treatment follow-up and use their knowledge in practical life situations.

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P5-04

Drugs Used in Central Nervous System Diseases and Therapeutic Drug Monitoring

Necip İlhan

Department of Medical Biochemistry, University of Fırat, Faculty of Medicine, Elazığ

TDM in practice is performed by collection of a blood sample at a known time relative to administration of the last (or next) dose. The concentration of drug and/or metabolite is measured in the sample and compared to a target range or predicted pharmacokinetics for the drug. In order for TDM to be effective and necessary, several criteria must be met: [1] The drugs must have a narrow therapeutic index (the difference between the minimum effective concentration and the toxic concentration, relative to the pharmacokinetic variability), [2] the relationship between the drug dose and concentration in blood must be highly variable and/or not predictable, [3] the relationship between blood concentration and clinical or toxic effect must be well defined, [4] there should be serious consequences for under-or overdosing, and [5] the result of TDM testing must be interpretable and actionable–there should be an effect on clinical outcomes. It should answer a clinical question.

The introduction of 18 new antiepileptic drugs (AEDs) since 1989 has led to increasingly widespread application of therapeutic drug monitoring (TDM) in the clinical management of patients with epilepsy. TDM provides a pragmatic approach to epilepsy care, Special dose adjustments are made through drug concentrations to optimize clinical outcomes. Plasma or serum samples for TDM are preferred and unstimu-

lated saliva samples are used more often. Plasma AED concentrations correlate much better than dose with the clinical effects. Assessment of therapeutic response on clinical grounds alone is difficult in most cases because AED treatment is prophylactic, and seizures occur at irregular intervals. It is thus difficult to ascertain whether the prescribed dose will be sufficient to produce longterm seizure control. It is not always easy to recognize signs of toxicity purely on clinical grounds. AEDs are subject to substantial pharmacokinetic variability and thus, large differences in dosage are required in different patients. There are no laboratory markers for clinical efficacy or toxicity of AEDs.

For a number of antidepressants incurrent clinical use, concentrations in serum or plasma are a more reliable index of target drug concentrations than is dosage. For such drugs, therapeutic drug monitoring (TDM) may be a useful clinical guide for the purpose of maximizing the likelihood of favorable therapeutic outcome while minimizing the probability of clinical ineffectiveness or adverse side effects. TDM is of greatest benefit when a therapeutic range of serum concentrations has been well established. Even if such a range is not definitively determined, TDM can be of help in situations in which patients are refractory to therapy despite adequate or high dosages, when adverse events supervene even with low doses, or when noncompliance with the intended dosage plan is suspected. Serum antidepressant concentrations from TDM should be interpreted in the full context of the patient's demographic characteristics and clinical status, along with an understanding of the pharmacokinetics of the medication being taken, the timing of the sample in relation to the dosage regimen, and the specific laboratory assay procedure. TDM measurements may be costly, and the potential benefits of the information need to be weighed against the cost to the patient or to the health care system.

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P5-05

Drugs Used in Cardiovascular System Diseases and Therapeutic Drug Track

Can Duman

Department of Medical Biochemistry, İzmir Demokrasi University Faculty of Medicine, İzmir

The goal of new drug development is to put drug treatments in the clinic with a high therapeutic effect, but with the least side effects and/or toxic effects. Both the therapeutic and unwanted effects of drugs are closely related to drug dosing. Standard dosing for many drugs is safe for different individuals. On the other hand, the situation is much more complicated for drugs used in heart diseases, bacterial infections, epilepsy, asthma and immunosuppression with COPD or in psychiatric disorders. Therapeutic Drug Monitoring (TIDI)-Therapeutic Drug Monitoring is very important in terms of follow-up.

TIDI is the measurement of drug levels in body fluids in order to obtain information about the plateau concentration reached during treatment and to increase the effectiveness of the treatment or to prevent toxicity by checking whether the drug concentration has reached a sufficient level.

It is known that the drug concentration in the circulation, and hence the drug effect, varies depending on many factors affecting the elimination and/or metabolism of the drugs. In relation to all these factors, close monitoring of the level of circulating drug, especially for certain drugs or drug groups, is a necessity for the clinical follow-up of the patient. Otherwise, serious complications such as death from organ failure, cardiac disorders, arrhythmia, epileptic seizures to organ rejection are inevitable results.

In which situations is TIDI application required?

- When the therapeutic window (safety interval) is narrow,
- A weak relationship between the drug level and the dose.
- If there is a direct relationship between drug and/or drug metabolites in the plasma and therapeutic or toxic effects,
- If the therapeutic effect can not be assessed by clinical observations,
- If the plasma steady-state concentration shows large differences between individuals,
- If targeting a range of therapeutic concentrations,
- If the response is unresponsive, the suspicious suicide problem, the signs of toxicity,
- In diseases where therapeutic efficacy can have serious consequences,
- In addition to the conditions mentioned above, the existence of an appropriate analysis method is an essential condition or requirement for TIDI.

Apart from the situations described above, there may be a need for TIDI in a variety of situations which may in general affect the pharmacokinetics of the drugs. Side effects may occur or hypersensitivity reactions may occur in cases of kidney and liver failure that adversely affect drug elimination and metabolism, or in the presence of disease or factors that may cause the drug effect to change.

Monitoring of therapeutic drug levels is of even greater importance, especially in these and similar situations when using newly introduced medicines.

In what situations does TIDI make sense?

- In the case of drugs with a very wide therapeutic range,
- On conditions where the inter-person variation is not intensive)
- If the pharmacological effect can be monitored clinically,
- If the serum concentration of the drug is not associated with a therapeutic or toxic effect there is no need to monitor drug levels.

Medications followed up at the therapeutic level:

1. Cardioactive drugs: Digoxin, digitoxin, amiodarone, lidocaine, procainamide, propraconazole, flecainide, disopramide
2. Antibiotics: Amikacin, gentamycin, tobramycin, vancomycin, netilmisin
3. Antidepressants: Lithium, tricyclic antidepressants
4. Antiepileptic drugs: Phenytoin, phenobarbital, carbamazepine, valproic acid
5. Immunosuppressive drugs: tacrolimus, sirolimus, cyclosporin
6. Drugs Used in Cancer Chemotherapy: Methotrexate
7. Bronocodilator drugs: Theophylline, aminophylline
8. Abused Drugs: Amphetamine, methamphetamine, cocaine, methadone, codeine, morphine, meperidine, oxycodone, propoxyphene, LSD, phencyclidine
9. Toxicologically monitored: Paracetamol, salicylic acid, ethanol
10. Protease inhibitors: Indinavir, ritonavir, lopinavir, atazanavir, nelfinavir,

Unless the physician has a specific reason, it is important that he or she is willing to appeal after the drug reaches a stable level (4-5 half-life). For example, the time of receipt is an important part of TIDI. Digoxin should be taken as a sample for measurement after 6 hours to avoid toxic levels.

The knowledge that 70-80% of drug adverse effects are dose-dependent is a currently accepted thesis. On the other hand, the pharmacokinetic properties of drugs are predominantly responsible for the same dose interindividual variation. The pharmacokinetic parameters that may be associated with TIDI are absorption, distribution, biotransformation and elimination, respectively, from the main steps that determine these properties of the drugs.

Absorption order is the most important reason for interpersonal variation. In fact, the same patient also has variability in different disease episodes. Blood digoxin level shows a relatively rapid decline and subsequently draws a concentration-dependent concentration curve with a slower decline. The rapid decline in the first period is the "distribution phase" of digoxin, while the second and relatively slow decline reflects predominantly the "elimination phase" of the drug. In contrast to the blood level, tissue digoxin level gradually increases inversely to the blood digoxin level in the distribution phase, and then, in the elimination phase, the blood undergoes a parallel decrease with the digoxin level. The level of myocardial tissue that digoxin will show is also following this kinetics, and the effect of the drug is also evident over time. The therapeutic window defined for digoxin reflects the level of elimination phase in which the distribution phase ends and the level of myocardial tissue and blood is balanced.

Unlike our habits, it is not possible to draw an ideal picture, such as the optimal therapeutic effect and minimal adverse effects, by measuring the blood level of all medicines. An example of digoxin can be given to reveal the complexity of the variation between individuals. Steady state for digoxin is considered to be effective and non-toxic when the valley blood level is in the range of 0.8-2.0 ng/ml. However, toxic effects can be detected in approximately one-tenth of patients even in this concentration range. This can be minimized if the therapeutic range is narrowed (eg, 0.8-1.6 ng/ml). When trying to determine which subset of toxic findings are present, it is seen that all of the toxic patients between 1.6 and 2.0 ng/ml have coronary heart disease causing myocardial sensitization at the same time. This interpretation of the level of medication in the light of knowledge suggests that situations such as coronary artery disease which are present in the patient's medical history and which can change the current situation should be considered.

It should not be forgotten that many plants interact with warfarin. The use of certain herbal substances increases the risk of bleeding in patients receiving antithrombotic therapy such as warfarin.

It is also known that many plants act like digoxin-like substances, and that these plants may increase the digoxin effects. Chinese silk vine (Periploca Sepium) is a poisonous plant containing cardiac glycosides.

TIDI is a system that has serious economic contributions in terms of hospital and social security institutions expenditures. Effective and regular control of post-treatment drug levels that patients have received can provide significant cost effectiveness by preventing toxic effects or inadequate treatments. By preventing toxic effects, social security institutions prevents additional costs on hospital and patient by reducing the complications and serious risks that may arise. Detection of ineffective treatments for several reasons, such as compliance problems, subtherapeutic dose, bioavailability differences, drug interactions, is also important in preventing unnecessary drug treatment and ultimately economic loss.

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Symposia

SMP-01

Laboratory for Inborn Errors of Metabolism

İncilay Lay

Department of Medical Biochemistry, Hacettepe University Faculty of Medicine and Hacettepe University Hospitals Clinical Laboratory, Ankara

Hereditary metabolic disorders are caused by the interruption of a metabolic pathway through genetic mutations, as a result of an enzyme or activator protein or transport protein. In the last decade, it has been revealed that dysfunction of organelles such as peroxisomes, mitochondria and lysosomes also cause inborn errors of metabolism and the spectrum has expanded. To date, approximately 1000 hereditary metabolic diseases have been described. As a result of interruption of the related pathway, the unmetabolized substance accumulate or lack of the synthesized metabolic substance is seen. A wide clinical spectrum with chronic, progressive, multi-system involvement is seen. Clinical diagnosis is difficult, therefore laboratory for inborn errors of metabolism involving screening and diagnostic tests is important for early diagnosis and early treatment. Laboratory for inborn errors of metabolism is a specialized clinical laboratory unit where screening and diagnostic tests of metabolic diseases are performed. It differs from the clinical laboratory that it includes tests that require specific knowledge, experience and interpretation. In recent years, the name of biochemical genetic laboratory is in usage for laboratory of inborn errors of metabolism. Biochemical genetic laboratory is an interdisciplinary entity in which specialists of biochemistry, genetic and pediatrics metabolism are involved. A comprehensive laboratory of inborn errors of metabolism should consist of three units: 1) Metabolite laboratory, 2) Enzymology laboratory and 3) Molecular genetic laboratory. Metabolite laboratory measures the accumulation or the impaired metabolites in body fluids. In this context, basic laboratory tests such as glucose, lactate, pyruvate, ammonia, simple metabolic screening (FeCl3 test, reducing substance in urine, DNPH test, keto acids, nitroprusside test) as well as quantitative amino acid, carnitine and acylcarnitine, long chain fatty acids and organic acids analyzes are performed. Analysis of disease-specific metabolites such as typing of glycosaminoglycans, analysis of oligosaccharides can also be performed. In the enzymology laboratory, specific enzyme activity measurements are performed in leukocyte or fibroblast cultures, especially which are the gold standard for laboratory diagnosis of lysosomal storage diseases. Laboratory diagnosis is made by looking at the defective enzyme activity. In the last decade, enzyme activity measurements with tandem mass spectrometry method in dry blood samples for some types of lysosomal storage diseases have been in usage. Analysis of known or unknown mutations is performed in the molecular genetic laboratory. Molecular genetic laboratory is important to confirm the enzymatic diagnosis, in cases where enzymatic analyzes cannot be performed, for determination of pseudodeficiency and for carrier and prenatal diagnosis. Capillary sequencing, next generation sequencers and re-sequencing arrays are used for molecular analysis. These methods have advantages and disadvantages. Reporting should be carried out together with authorized genetic counseling. Laboratories that carry out screening and diagnostic tests of hereditary metabolic diseases should be a member of external quality control programs; ERNDİM and CDC. A wide range of screening and diagnostic tests of inborn errors of metabolism are carried out at Hacettepe University Hospitals Clinical Laboratory and our laboratory is a member of ERNDİM. In recent years, the development of technology and progress in screening and diagnostic tests have allowed early diagnosis and early treatment of patients. It is important to provide early diagnosis and early treatment in these disorders where the incidence is high in Turkish population due to consanguineous marriages. In the future, it is predicted that algorithms of laboratory analysis for inborn errors of metabolism will be changed with the developments in genetic analysis methods and in metabolomics field.

SMP-02

Analytical Techniques in the Laboratories for Inherited Metabolic Disease

Canan Çoker

Department of Medical Biochemistry, Dokuz Eylül University, Faculty of Medicine, İzmir

Inherited diseases of metabolism are typically caused by recessive mutations in genes encoding metabolic enzymes or transmembrane transporters and spans a wide clinical spectrum. Multiple specimen types and analytic approaches are currently used in laboratory investigations for hundreds of recognized metabolic diseases. The diagnosis of these disorders is performed at three stages, measurement of the metabolites, measurement of the activity of the responsible enzyme and the analysis of the specific mutation. The diagnosis of inherited metabolic disease requires the use of numerous different techniques for the analysis of molecules representing different biochemical pathways [1].

Tandem Mass Spectrometry with electrospray ionization (ESI-MS/MS) is being widely used for the analysis of amino acids and acyl carnitines in dired blood spots for newborn screening of inherited metabolic diseases. Mass spectrometry is an analytical technique in which molecules or fragments are defined and measured quantitatively according to mass-charge ratio. MS/MS performs a secondary fragmentation of selected precursory ions for more accurate definition of analytes. MS/MS enables a multianalyte approach to obtain a metabolic profile and can detect inherited metabolic disease as well as examine the effect of acquired diseases or pharmacologic intervention on intermediary metabolism. It is possible to screen for many metabolic diseases including primary aminoacidemias, urea cyle disorders, organic acidemias and fatty acid oxidation disorders by MS/MS, yet it is important to define the cut off values and it is necessary to quantitate the relevant metabolites in plasma and urine samples to verify the diagnosis [2-4].

The reference method for quantitative analysis of amino acids consists of ion exchange liquid chromatographic separation followed by photometric measurement of ninhydrin reaction and is performed by amino acid analyzers. Recently, Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) is being more widely preferred for amino acid analysis due to its speed. Urinary organic acids are analysed by Gas Chromatography Mass Spectrometry (GC-MS). In the preanalytical phase, sialylating reagents are very commonly used for derivatization of organic acids with carboxylic and hydroxylic groups and optimization of conditions are of particular importance in routine analysis when no stable-isotope labeled analogues are used. More than one hundred metabolites are analysed with this method and the metabolic profile obtained is evaluated regarding the biochemical pathway and the related metabolic disease [1, 5].

High performance liquid chromatography is used for the analysis of oxalate and sitrate, glycosilated proteins, electrophoresis is used for separation of mucopolysaccharides and thin layer chromatography is used for separation of oligosaccharides in metabolism laboratories. Spectrophotometric and spectrofluorimetric methods are also still valid for measurement of enzyme activity eg. biotinidase and for measurement of some metabolites eg. sialic acid, mukopolysaccharides [1].

In addition to these basic analysis; many other metabolites are analysed using mass spectrometric techniques eg. fatty acids and bile acids by GC-MS; purins and pyrimidines, bile acids and steroids by LC-MS/MS. In some storage disease, the abnormal metabolites are difficult to analyse, thus direct measurement of the enzyme activity is performed in leucocyte or fibroblast homogenates or in serum or plasma. In recent years multiplex LC-MS/MS is being applied for measurement of lysosomal enzymes in dried blood spots [6].

Mass spectrometry has become the most widely used platform in proteomics and metabolomics because of its ability to analyze a wide range of molecules, its optimal dynamic range, and great sensitivity. Both focused and untargeted metabolics by LC-MS/MS, together with bioinformatics is a rapidly advancing analytical technique [7]. There is expanding research on MALDI-TOF/TOF MS or UPLC-MS/MS measurement of the macro molecular substrates of lysosomal enzymes and biomarkers reflecting the cytopathological events [8]. Global metabolic profiling currently achievable by untargeted mass spectrometry-based metabolomic platforms has potential utility in the detection and understanding of novel and known inherited metabolic disease [9].

Recently, digital techniques are being developed and "digital microfluidics", based on the control of surface tension of liquid droplets by electrodes is taking its place in laboratories with its advantages of low sample volüme, short analysis time and ease of use [10].

As advances in laboratory technology and knowledge of the molecular basis of disease increase, the number of laboratory tests in the screening, diagnosis, and treatment of inherited metabolic diseases also increase. Thus, guidelines are necessary for quality assurance and quality improvement in these areas of laboratory testing. The guidelines prepared with this purpose address the benefits of using a quality management system approach, factors to consider before introducing new tests, establishment and verification of test performance specifications, the total laboratory testing process (which consists of the preanalytic, analytic, and post-analytic phases), confidentiality of patient information and test results, and personnel qualifications and responsibilities for laboratory testing for inherited metabolic disease [3, 11].

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SMP-03

Biomarkers in Inherited Metabolic Disease

Eser Yıldırım Sözmen

Department of Medical Biochemistry, Ege University Faculty of Medicine, Bornova, İzmir

Inborn errors of metabolism (IEM) that are genetic disorders (more than 400 human diseases), are related to deficiency of specific enzyme proteins, transport proteins or other functional proteins resulted to clinical aspects due to accumulation of substrates/metabolites in different tissues [1].

Diseases are diagnosed by determination of accumulated molecules and/or deficient protein levels especillay enzymes and diagnosis is verified by determination of genetic mutation in gene of enzyme protein which is specific for disease. However, a variety of problems such as low accuracy of enzyme activity methods, unknown genetic mutations, high ratio of false positive diagnosis due to methods, complicate the correct diagnosis of these patients. Therefore, clinicians need new biomarkers other than enzyme activity to diagnose and monitor of treatment of the patients.

Biomarkers are described as molecules which can be determined in blood or body fluids, reflect the presence of a given disease (diagnostic biomarkers),the prognosis or response to therapeutic intervention or risk of complications or survival (surrogate biomarkers). [1, 2].

Recently two types of biomarkers have been suggested for IMD. 1) Primer (Direct) biomarkers which are metabolites accumulated in tissue due to enzyme deficiency, found in plasma and/or urine, e.g. glycosaminoglycan in urine of patients with mucopolysaccharidosis, tetrasaccharide in urine of patients with Pompe disease. 2) Secondary (Indirect) biomarkers which are non-specific, increase in serum/urine resulted from damaging of other tissues due to a disease. e.g. biomarkers of liver damage and renal damage. Some biomarkers in this group are partially specific to a disease. e.g. chitotriosidase which is a macrophage activation marker, increases in blood of patients with Gaucher disease, Niemann Pick disease.

In this presentation, the surrogate biomarkers which have been used for diagnosis and for monitoring the response to specific treatments in clinical studies and the candidate biomarkers which are currently identified will be discussed.

According to clinical classification of inborn error of metabolism [3], peroxisomal disorders and lysosomal storage disease are found in Group.1.

Peroxisomal disorders are related to either single enzyme deficiencies (Zellweger spectrum disorders) or peroxisome biogenesis disorders. Diagnosis is confirmed by laboratory tests; plasma VLCFA (C22:0, C24:0, C26), phytanic and pristanic acids, plasma plasmalogens, pipecolic acid, and urinary bile acids [1].

After discovery of Enzyme replacement therapy for lysosomal storage diseases (LSDs), biomarkers became very important to monitor these patients. Chitotriosidase [4-6], is the most prominent biomarker, was discovered in plasma of patients with Gaucher disease [6]. Chitotriosidase which is synthesized exclusively by activated macrophages [4, 5], has been proposed as a biochemical marker of macrophage accumulation in inflammatory diseases. Recently it has been shown that chitotriosidase enzyme activity increased in patients with some other LSD such as Niemann Pick, mucopolisaccharidosis [7] (Table 1).

Cathepsin D (CTSD), Lectin galactoside-binding-soluble 3 protein (galectin-3, LGALS3) and Cathepsin D levels are high in some lysosomal disease [7] (Table 1). CTSD is a lysosomal aspartic protease,which is produced as pre-pro cathepsin than is activated in endoplasmic reticulum and lysosome [8]. Galectin-3 affects as chemoattractant in inflammation and has a role in regulation of cell adhesion and activaton [9]. Pulmonary and activation-regulated chemokine (CCL18/PARC) is chemotactic for natural resting T cells. It has been used as a marker for chronic inflammation and fibrotic scar and the plasma levels increased in Gaucher disease [10].

Apart from Table.1, there are currently few biomarkers which are available to monitor for Fabry and Pompe. Globotriaosylceramide (Gb3, Ceramide trihexoside), Galabiosylceramide (Gb2) and Globotriaosylsphingosine (lysoGb3) which are the products of glycosypingolipid metabolism, has been used as markers to determine the disease severity, as well as responses to treatment for Fabry patients [11, 12]. Urinary tetrasaccharide 6-α-D-glucopyranosyl-maltotriose (Glc4, limit dextrin of glycogen) that is product of glycogen degradation has been proposed as a marker for diagnosis and monitoring of Pompe disease. The amount of urinary excretion is correlated with the severity of disease as well as glycogen content of muscle [13].

Group2 in classification of inherited metabolic disease [3] include disorders of aminoacids, organic acidurias, urea cycle disorders and sugar intolerances. The majority of aminoacid metabolism disorders and sugar intolerances can be managed by restricting the diet of the patient, therefore there is no specific biomarker to monitor these patients.

Recently new biomarkers have been proposed to monitor treatment efficacy in a variety of aminoacid metabolism disorders [1, 14]: Plasma or dried blood spot Phenyl alanin and pterins (neopterin, primapterin, biopterin) for non-Phenylketonuria–Hyper Phenylalaninemia patients, succinylacetone and α-fetoprotein (a marker of hepatocellular carcinoma) in type I tyrosinemia disease, ceruloplasmin, neutrophil gelatinase-associated lipocalin, and vitamin D-binding protein in cystinuria, pro-inflammatory cytokines (IFN, TNF, IL1B, IL-6) for Maple Syrup Urine Disease, betaine, methylation cycle substrates/ products (e.g., creatine, phosphatidylcholine, and guanidinoacetate) in Hypermethioninemia is as a disorder due to S-adenosylhomocysteine hydrolase deficiency.

Urine organic acid testing is used for diagnostic of Organic acidemia disorders which present within 1–2 weeks after birth. Metabolic acidosis with an increased anion gap, ketosis, and hyperammonemia might be observed in acute decompensation period. Patients were treated by dietary restriction of some aminoacids and also dietary supplementation with carnitine and biotin which might be determined in blood [1].

Urea cycle disorders might be due to a defect in the urea cycle or the inhibition of N-acetylglutamate synthase (NAGS) and/or carbamoylphosphate synthetase (CPS1) by methylcitrate, propionyl-CoA or isovaleryl-CoA. The main laboratory finding is hyperammonemia, and plasma / urine amino acids, urine organic acids, and plasma acylcarnitines are used for differential diagnosis of hyperammonemia. Since Blood ammonia values varied up to 10-fold during the day, it's not a well biomarker routinely for management of treatment. Recently, urine phenylacetylglutamine (PAGN) levels and [15, 16], plasma phenylacetate (PAA): PAGN ratio proposed as useful biomarkers to monitor treatment efficacy.

α-Ketoglutaramate (KGM) which is proposed as another candidate biomarker in HE (a secondary hyperammonemia) and in urea cycle defects (primary hyperammonemias), is a product of glutaminase II pathway. In this pathway, glutamine transaminase coupled to ω-amidase and the transamination of glutamine results in formation of α-ketoglutaramate [17]. Recently it has been shown that CSF KGM levels are correlated with ammonia and glutamine levels. Urine KGM levels are also high in urea cycle disorders, lysinuric protein intolerance and citrin deficiency.

Fatty acid oxidation defects, mitochondrial disorders and glycogen storage disorders (GSD) are classified as Group 3. The most GSDs are treated by dietary regulation to maintain a normal blood glucose concentration; no biomarkers have been identified till now. The only GSD, Pompe disease (GSD Type II) is treated with Enzyme replacement therapy (ERT), and monitored by determining enzyme activity and GLc4 levels in urine [1, 13].

The clinical presentation of mitochondrial diseases may involve all organ systems especially those of which need high energy. Diseases might show various clinical findings in accordance with the age onset of disease; hypotonia, cardiomyopathy, and lactic acidosis in newborn, hearing loss and seizures in child, migraines or vision loss in adult. Diagnoses are generally based on clinical findings but not specific laboratory testing [1].

Although 35 various defects are recognized in the metabolism of purines and pyrimidines, only half of them show serious clinical consequences. Since Nucleotides cannot be directly measured, associated nucleosides and bases in urine are determined [1].

In conclusion, an ideal biomarker should be determined easily in plasma/urine samples and should predict relevant clinical outcomes, reflect prognosis and treatment efficacy. Recently, some molecules (ie. Chitotriosidase, tetrasaccharide, lysoGb3) are accepted as reliable markers to reflect disease and the response of that disease to specific treatment, for a limited number of diseases.

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Table 1. Currently used biomarkers for lysosomal storage diseases

	Chitotriosidase	CCL18/PARC	Cathepsin D	Galectin-3
Gaucher	↑↑	↑↑	↑	N
Pompe	↑	N	↑	N
Fabry	↑	N	N	N
Niemann Pick type A/B	↑↑	↑	↑	↑
MPS I	N	N	↑	↑
MPS II	N	N	N	N
MPS III	↑	N	↑	N
MPS IV	↑	N	↑	↑
MPSVI	N	N	N	↑
Krabbe	↑	N	N	N

↑ 2-9 times than normal, ↑↑ 10 and more times than normal. N. within reference range

Oral Presentations

OP-01

A Glutaric Acidemia Type II Patient With Thalasemia Minor and Novel ETF-A Gene Mutation

Neslihan Yıldırım Saral[1], Fehime Benli Aksungar[2], Çiğdem Aktuğlu Zeybek [3], Jülide Coşkun[1], Özlem Demirelce [1], Mustafa Serteser[1]

[1]Department of Metabolism, Acıbadem Labmed Clinical Laboratories, İstanbul

[2]Department of Biochemistry, Acıbadem University, School of Medicine, İstanbul

[3]Department of Pediatrics, İstanbul University, Cerrahpaşa School of Medicine, İstanbul

Objective: Glutaric acidemia type II(GA II), also known as multiple acyl-CoA dehydrogenase deficiency,is an autosomal recessive inborn error of aminoacid and fatty acid metabolism.GA II caused by a defect in electron transfer flavoprotein (ETF) or ETF dehydrogenase (ETFDH) resulting in deficiencies in multiple acyl-CoA dehydrogenases.

Materials and Methods: We report a case of GA II with novel ETF-A mutation in a 2 year girl with thalasemia minor. Patient was born at full-term to nonconsanguineous parents after an uneventful pregnancy. She was the first child of the family who had no history of metabolic diseases. First physical examination revealed a healthy infant with no dismorphic features. An episode of hypoglycemia and hypotonicity occurred at the postnatal first day.

Results: Laboratory investigations revealed elevations of multiple acylcarnitines implicating glutaric acidemia typeII in newborn screening analysis. Particularly, C4 butrylcarnitine levels were extremely high with elevated C5, C6, C8, C10, C14 and C5-DC glutaryl carnitine levels. Urinary organic acids revealed a high glutaric acid excretion. Genetic analysis revealed, 2 novel mutations in the ETF-A gene which are assessed to be compound heterozygote. Patient has been closely followed for two years with carnitine, riboflavin, koenzim Q10 and ketone supplementation in addition to high carbohydrate diet.

Conclusion: The most important goal of newborn screening for inborn errors of metabolism is to reduce morbidity and mortality. In recent years, expanded newborn screening has provided the ability to detect many inborn errors of metabolism in asymptomatic newborns. Pharmacological therapy for GAII is based on the administration of L-carnitine, Coenzyme Q10 and riboflavin. Although ketone therapy stays on the experimental side so far, sodium-3-hydroxybutyrate (NaHB) administration is a promising treatment.

OP-02

Is First Trimester Prenatal Screening Test Biochemical Parameters Related to Fetal Gender And Birth Week?

Filiz Alkan Baylan

Department of Biochemistry, Kahramanmaraş Sütçü İmam University Faculty of Medicine, Kahramanmaraş

Objective: First Trimester Prenatal Screening Test is used in the evaluation of trisomy scans at 11-13+6 weeks of gestation. The aim of this study was to investigate whether the aimed PAPP-A and Free HCG were different in girls and boys and to look at birth weight.

Materials and Methods: Between 01.01 2012 and 01.10 2017, 870 Dual Test results which came to KSU Medical Faculty Hospital Biochemistry Laboratory were examined retrospectively. From a retrospective epicritical report, the gender of the baby, the birth weight was reached. For comparison of the Group Mann Whitney U Test and for the analysis of the relationship between groups Spearman correlation coefficient was used.

Results: 428 of the babies are girls, 400 are male. PAPPA MOM were 1.08±0.73 for males and 1.01±0.64 for males and the difference was not statistically significant (p=0.304). The free BHCG MOM was 1.24±0.90 in girls and 1.07±1.08 in males, and the difference was statistically significant (p=0.00). Statistically positive correlation was found between birth weight and PAPPA MOM (R=0.175, p=0.00). There was no correlation between birth weight and free BHCG MOM (R=–0.036, p=0.304).

Conclusion: In our study, free BHCG was found higher in female babies than male babies, but we could not find any difference in PAPPA. When we could not find the relationship between birth weight and Free BHCG, we saw that PAPPA increased the leftover birth weight. This relationship between PAPP and birth weight may have been due to a correlation between PAPPA and the birth week. In our findings, Free BHCG may be useful in predicting the sex of the baby and PAPPA in predicting the birth week.

OP-03

Development and Validation of High Performance Liquid Chromatography Method for the Quantitation of Methotrexate in Plasma

Sebla Uzun Ertuğrul[1], Erdim Sertoğlu[2], Taner Özgürtaş[2]

[1]Department of Medical Biochemistry, Institute of Health Sciences, University of Health Sciences, Ankara

[2]Department of Medical Biochemistry, Gülhane School of Medicine, University of Health Sciences, Ankara

Objective: Although methotrexate (MTX) is a commonly used therapeutic agent in the treatment of cancer, its use in high doses leads to some toxic effects. Thus, we have aimed that to develop and validate sensitive, fast, inexpensive High Performance Liquid Chromatography Method-UV method for monitoring MTX concentration in plasma samples which is applicable for clinical routine analysis.

Materials and Methods: Plasma was deproteinized with acetone and the chromatographic separation was performed on C18 column (250x4.6 mmx 5µm) using mobile phases composed of 0.05 M sodium phosphate buffer/tetrahydrofuran (95:5) (pH=4.85) (mobile phase A) and 0.05 M sodium phosphate buffer/tetrahydrofuran (75:25) (pH=4.0) (mobile phase B) at a flow rate of 0.6 mL/min. Ultraviolet detection was done at 313 nm and at ambient temperature.

Results: Retention time for MTX was 7.78 minutes. The linearity is evaluated by a calibration curve in the concentration range of 1.0-50.0 µmol/L and presented a correlation coefficient of 0.9999. Precision of method within a day was 0.67-4.02% and between days was 1.16-5.19% percent. The limits of detection and quantification achieved 0.1 and 0.9 µmol/L, respectively.

Conclusion: The fast and precise method allows analyzing large number of samples by using less mobile phase that makes it to be cost-effective. Therefore, this HPLC-UV method can be used for the routine analysis. This method is suitable for quantitation of methotrexate after infusion of high doses of this drug and has good accuracy, precision and quantitation limit.

OP-04

The role of glucokınase gen (GCK, MODY 2) varıatıons in diabetes

Gülsüm Seda Güleç Yılmaz[1], Belma Haliloğlu[2]

[1]Department of Molecular Medicine, Institute of Health Sciences, Yeditepe University, İstanbul

[2]Yeditepe University Hospital, İstanbul

Objective: Adult-onset diabetes mellitus (MODY) is a common type of diabetes mellitus with a glucokinase gene (GCK) mutation. A preliminary study designed to investigate the role of four glucokinase gene variations (GCK, MODY 2), which are common in our population, in the development of diabetes.

Materials and Methods: Sample selection: In this study we included 96 subjects diagnosed with diabetes mellitus who admitted to the Yeditepe University Hospital and 89 healthy controls were included. Genotyping of 4 different regions of MODY2 GCK gene (rs2268574, rs2268576, rs758989, rs741038) was performed using Real Time PCR. LDL and HDL Subfractions analyzes were performed using the Quantimetrix Lipoprint® System. SPSS 23.0 version was used for the statistical analysis. The statistical significance level was $p<0.05$.

Results: There were no statistically significant difference between the subject and control group in genotype frequencies of the four variations of the GCK gene (rs2268574 p=0.925, rs2268576 p=0.572, rs758989 p=0.551, rs741038 p=0.199). Also, genotype frequencies were compared with clinical parameters. Variations of GCK rs2268574 and GCK rs2268576 in two intronic regions were found to be significantly higher in the wild type (GG) carriers (p=0.008 for rs2268574 and p=0.024 for rs2268576). In addition, the GCK rs2268574 carriers had high HDL levels (p=0.029). Variations in the other two intronic regions showed a negative effect of the wild type carriage; The LDL values of GCK rs741038 GG genotype were found to be higher in the significant level (p=0.045).

Conclusion: The GCK gene variations investigated were not associated with diabetes development, but they were influenced by other metabolic pathways and were shown to be effective on lipid profiles.

OP-05

Evaluation of HbA1c Levels After Extravascular Hemolysis in Glycosylated Hemoglobin (HbA1c) Measured Patients

Zeliha Cansel Özmen, Köksal Deveci, Leyla Aydoğan

Department of Biochemistry, Tokat Gaziosmanpaşa University, Medical Faculty, Tokat

Objective: Glycosylated hemoglobin (HbA1c) is considered the best indicator of metabolic control of diabetes mellitus. In this study, we aimed to evaluate the effect of extravascular hemolysis on HbA1c measurement results.

Materials and Methods: In the study, 30 whole blood samples were used that % HbA1c measured by immunoturbidimetric method at Gaziosmanpaşa University Health Research and Application Center Laboratory. The hemoglobin index (HI) of the samples was measured by spectrophotometric method. The remaining samples from the routine measurement were hemolyzed at various levels and again % HbA1c values and HI values were measured. The hemoglobin index % changing and HbA1c % changing were calculated by comparing the values after hemolysis according to the values before the hemolysis of the samples.

Results: The HbA1c % changing was above 10% in 5 (16.6%) of the 30 hemolyzed samples. There was a significant difference between group I [median (min-max): 6.2 (4.8-12.6)] and group II [median (min-max): 9.1 (8.6-13.1)] at % HbA1c levels before hemolysis ($p<0.001$). There was a significant difference between group I [median (min-max): 3.85 (0-9, 68)] and group II [median (min-max): 13.74 (10,99-15,46)] in HbA1c % changing after hemolysis (p=0.001). There was no significant difference between group I [median (min-max): 1206.7 (224.5-5354.2)] and group II [median (min-max) 1972.4 (1427.0-8125)] in hemoglobin index % changing (p=0.126).

Conclusion: The results of our study showed that extravascular hemolysis may be a preanalytical error source in patients with a particularly high % HbA1c value.

OP-06

The effect of elevated minor hemoglobin levels on HbA1c assay

Berrak Güven, Murat Can

Department of Biochemistry, Bülent Ecevit University, Zonguldak

Objective: Hemoglobin (Hb) A1c is a clinical marker used to monitor long-term glycemic control in diabetic patients. HbA2 and HbF are minor Hb components that are clinically important in the diagnosis and management of Hb disorders. The objective of our study is to compare the HbA1c values measured on high performance liquid chromatography (HPLC) and immunoassay in patients who were detected to have elevated levels of minor Hb.

Materials and Methods: HbA1c was measured by ion-exchange HPLC method (Spectra system, Thermo Scientific, Boston, USA) using commercially kit ClinRep (Recipe, Munich, Germany). HPLC variant analysis was performed on samples with abnormal patterns suggesting the presence of hemoglobin variants. Patients were identified according elevated HbA2 (>3.5%) and/or HbF (>2%). HbA1c values of the patients were measured again using the immunoturbidimetry method (Advia, Siemens Healthcare, USA).

Results: A total of 122 patients were divided into three groups: High HbF, high HbA2 and both high HbA2 and HbF. HbA1c levels in all group were significantly lower in measured by HPLC than immunoassay ($p<0.0001$). Pearson correlation coefficient between the two measurements showed a positive correlation for only high HbA2 (r=0.44, p=0.001). There were non-linear relationship between the two methods in other groups.

Conclusion: The elevation of minor Hb, especially HbF, may falsely lower HbA1c measurements. Laboratories should be aware of the limitations of their method with respect to these interferences.

OP-07

Use of Modified Poly(inulin) Micro/Nanogels in Drug Release and Blood Compatibility Tests

Dilek Ülker Çakır[1], Selin S. Suner[2], Nurettin Şahiner[2]

[1]Department of Clinical Biochemistry, University of Çanakkale Onsekiz Mart, Medicine Faculty, Çanakkale

[2]Department of Chemistry, University of Çanakkale Onsekiz Mart, Faculty of Science and Arts, Çanakkale

Objective: For the use of these obtained micro/nanoparticles in living bodies, physical and chemical properties should be wellknown and cells should not cause allergic, toxic or carcinogenic reactions.As a result, after characterization of the prepared p(inulin) particles, their use as drug-carrying system for biomedical applications and blood compatibilities were researched.

Materials and Methods: Poly(inulin) micro/nanogels were synthesized via reverse micelle microemulsion technique. The prepared p(inulin) particles are determined in spherical morphology with variance dimensions ranging from hundreds of nanometers to tens of micrometers with polydisperse size distribution. The sizes of p(inulin) particles are assessed by optic microscope and scanning electron microscope (SEM).

Results: The prepared p(inulin) micro/nanogels are modified with a cationic molecule, 2-bromoethylamine (BEA) and their potential for drug carrier/delivery applications are investigated. It is demonstrated that the p(inulin) micro/nanogels with chemical modification can release Rosmarinic Acid (RA), chosen as a model drug, up to12 h in linear release profile in phosphate saline buffer (PBS) at pH 7.4 and at 37 oC.

Conclusion: Furthermore, p (inulin) micro/nanogels are shown to be more blood compatible from hemolysis and blood clotting tests, but the modified p (inulin) micro/nanogels are found to have toxic effects depending on the concentration.

OP-08

Evaluation of preanalytical phase by sigma metrics

Ayşegül Özgenç, Nesibe Esra Yaşar, İbrahim Murat Bolayırlı, Dildar Konukoğlu

Department of Medical Biochemistry, İstanbul Univesity-Cerrahpaşa, Faculty of Medicine, Istanbul

Objective: Preanalytical errors are the major types of errors in laboratory diagnostics. The aim of this study is to evaluate the performance of the preanalytic process with six sigma and Pareto analyzes.

Materials and Methods: This retrospective study was carried out from January 2017 to January 2018, in Fikret Biyal Medical Biochemistry Laboratory of Istanbul University-Cerrahpasa Faculty of Medicine. A total of 1.130.448 samples were evaluated for preanalytical errors like improper test requisition/unsuitable barcode/improper transport/inappropriate tube/insufficient volume/inappropriate sample-anticoagulant ratio/ hemolysis/clotted specimen/lipemia. Total number of errors were calculated and converted into sigma scale (www.westgard.com/six-sigma-calculators); Pareto chart (the 80/20 rule) was drawn.

Results: Preanalytical error was detected in 0.26% of 1.130.448 samples. Sigma value of preanalytical process was determined as 4.4. When the laboratories were examined separately, the preanalytical error rates were 0.07%, 0.45% and 0.49% for the Central, Stat and Pediatric Biochemistry Laboratories and process sigma values were determined as 4.7, 4.2 and 4.1, respectively. According to the Pareto's principles, 90% of preanalytical errors in these laboratories were due to clotted specimen, insufficient volume and hemolysis.

Conclusion: While a preanalytical quality indicator with a sigma value of ≤3 is considered as poor performance, a sigma value of ≥4 is considered as well controlled process. In our study, sigma value of our laboratories was >4. However, sigma values of Stat and Pediatric Biochemistry Laboratories were found to be lower than Central Biochemistry Laboratory. This point was considered to be related to the characteristics of the patients the samples were taken from. In addition, frequent shift and inexperienced staff work in the emergency department also increases the preanalytical errors. The Pareto chart and sigma value when interpreted together could give information regarding most common type of preanalytical error and the corrective measures to be taken.

OP-09

Protective Effect of Alpha-Lipoic Acid on Cisplatin Induced Hepatotoxicity in Rats

Neslihan Pınar[1], Gökhan Çakırca[2], Sibel Hakverdi[3], Mahir Kaplan[4]

[1]Department of Medical Pharmacology, Mustafa Kemal University, School of Medicine, Hatay

[2]Department of Biochemistry, Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Şanlıurfa

[3]Department of Pathology, Mustafa Kemal University, School of Medicine, Hatay

[4]Department of Medical Pharmacology, Çukurova University, School of Medicine, Adana

Objective: The present study is designed to determine the protective effects of alpha lipoic acid (ALA) on cisplatin (CIS)-induced liver toxicity, for which histopathological findings and biochemical analyses were evaluated.

Materials and Methods: Rats were divided randomly into four equal groups and each group contained nine rats (n:9). A saline solution was administered intraperitoneally (i.p.) to group 1, as the control group; in group 2, 100 mg/kg of ALA was administered i.p. in a single dose for 10 days; in group 3, 5 mg/kg of CIS was administered i.p. as a single dose and in group 4, 5 mg/kg of CIS was administered i.p. in a single dose, followed by 100 mg/kg of ALA i.p. for 10 days. The liver tissue samples were analyzed for Bax, bcl2, caspase 3, malondialdehyde (MDA), Superoxide dismutase (SOD), Catalase (CAT), glutathione peroxidase (GPx) and myeloperoxidase (MPO) levels, and serum alanine transaminase (ALT) and aspartate transaminase (AST) levels were evaluated biochemically. The liver tissue samples were fixed in 10% formalin for the histopathological evaluation.

Results: In the CIS group, Bax, caspase 3, MDA, AST and ALT levels were found to be high, whereas bcl-2, SOD, CAT and GPx levels were found to be low. Compared to the CIS group, the Bax, caspase 3, MDA, AST and ALT levels were lower and the bcl-2, SOD, CAT and GPx levels increased in the CIS+ALA group. In the histopathologic evaluation of the CIS group, intense perivenular sinusoidal dilation, karyomegaly, pyknotic, karyolytic cells, central vein congestion, parenchymal inflammation, mild bile duct proliferation and periportal sinusoidal dilation were observed. In the CIS+ALA group, increasing hepatocyte mitosis, mild sinusoidal dilation, parenchymal inflammation, and pyknotic and karyolytic cells were observed.

Conclusion: ALA may have a therapeutic effect in the treatment of CIS-induced hepatotoxicity thanks to its antioxidant and anti-inflammatory effects.

OP-10

Serum antioxidant vitamin levels and age-related macular degeneration

Feyza Yağmur Tekeli[1], Goncagül Haklar[2], Sezen Akkaya[3], Yelda Özkurt[3]

[1]Department of Biochemistry, Antalya Training and Research Hospital, Antalya

[2]Department of Biochemistry, Marmara University of Medical Faculty, İstanbul

[3]Department of Ophthalmology, Fatih Sultan Mehmet Training and Research Hospital, İstanbul

Objective: To evaluate associations between the grades of age related macular degeneration (AMD) and serum levels of antioxidant vitamins (vitamin A, C and E) and smoking.

Materials and Methods: Fifty-three AMD patients and 31 individuals having ages matching with the patient group were enrolled the study. Colored fundus photographs of the macula were used to place participants (n=84) into one of the five groups(Grade I-V)based on the frequency and severity of the lesions associated with AMD. Serum antioxidant vitamin levels were measured using High Performance Liquid Chromatography (HPLC). Smoking status was classified as non-smoker, ex-smoker and current smoker. Total number of packs smoked per year, was defined.

Results: The distribution of vitamin A, E, and C levels were 0.874±0.326 mg/L, 10.739±4.874 mg/L, 1.737±0.447 mg/L in control group and 0.880±0.305 mg/L, 9.487±6.060 mg/L, 1.870±2.191 mg/L in AMD group, respectively. The difference between AMD and control group was not statistically significant for vitamin A, E and C levels (P>0.05). There were no significant differences between subgroups of AMD for vitamin A (P=0.881) and vitamin E (P=0.293) but there was a contradicting rise of vitamin C levels (P=0.044) with increasing levels of the disease. There were no significant differences between AMD and control group regarding smoking status, but there was a significant difference for total number of packs smoked per year (P=0.02). An increase of number of total packs smoked per year was determined along with the rising grade of AMD (P=0.007).

Conclusion: We found no relation between AMD and serum levels of vitamin A and E but vitamin C levels was increase with AMD grades unexpectedly. We found dose-response relationship between smoking and AMD.

OP-11

Determination of Vitamin B12 Reference Ranges in Elazığ

Mehmet Kalaycı, Hakan Ayyıldız

Biochemistry Laboratory, Elazığ City Hospital, Elazığ

Objective: It is aimed to calculate vitamin B12 reference intervals of 18-80-year-old male and female patients who applied for Elazığ Education and Research Hospital between the years 2017 and 2018.

Materials and Methods: 32751 vitamin B12 levels from serum samples obtained from individuals admitted to our hospital between the years 2017 and 2018 were studied using roche Cobas E602 device and roche brand commercial kits by menas of electrochemiluminescence method. The vitamin B12 levels of people aged 18-80 were taken retrospectively from the laboratory information system. The data used to determine the reference intervals were obtained using the indirect method, the Med-Calc version 18.6 programme according to the C28-A3 protocol proposed by CLSI.

Results: As a result of the removal of end values, 30756 remained from 32751vitamin B12 data. 22228 ones of these data belong to female, while 8528 ones belong to males. The reference range given by the manufacturing firm for both sexes was 156-663 (pg/ml), and the reference range obtained in our study was 128-550 (pg/ml) for both sexes; 122-549 (pg/ml) for males and 131–550 (pg/ml) for females.

Conclusion: We identified differences between the reference ranges given by the manufacturing firm and the reference ranges of our own population. We observed that reference ranges for femlaes and males did not differ for vitamin B12.

OP-12

Liquid Waste and Waste Management in Health Facilities

Selda Murat Hocaoğlu, İrfan Baştürk, Recep Partal, Mehtap Dursun, Oltan Canlı

TUBITAK MRC Environment and Cleaner Production Institute, Kocaeli

Objective: Separate collection and/or treatment of the entire liquid waste generated in health facilities is not sustainable technically and cost. Here, investigated how the liquid wastes/wastewater should be managed in health facilities via four pilot medical institutions, including 3 full-fledged hospitals and one central laboratory.

Materials and Methods: Here, whole liquid waste sources and formations were examined in pilot institutions, and it was estimated the amount of liquid waste generated if the World Health Organization (WHO) approach would be implemented. Moreover, hazardous wastes and ecologically hazardous pollutants identified and liquid wastes proposed for separate collection have been determined, considering formation of wastes. With the WHO approach, separate collection of liquid wastes and on-site treatment in cost was compared.

Results: Biochemistry laboratory produces most liquid waste, when compared to other units, analyzers generate wastewater 150-850 m^3/year in labs, according to the WHO approach (separate collection of all liquid wastes containing hazardous chemicals/wastewater) as hazardous waste disposal cost of these waste is about 350 thousand-2 million TL/year. Furthermore, on-site treatment of all liquid waste/ wastewater in healthcare facilities requires 2-10 MTL investment per hospital, depending on treatment technology and hospital size. On the other hand, it is predicted that in case of separate collection of liquid wastes which are carcinogenic, toxic, mutagenic and ecologically harmful to the reproductive system, health institutions will dispose of very low volumes of liquid waste, on average 4-15 m^3/year. Among the liquid wastes that need to be collected separately include formaldehyde, xylene, ethylbenzene, halogenated solvents, dyes and analyzer wastes.

Conclusion: The most economical and effective solution in terms of cost and applicability is collection the waste at the source and disposed. This study was supported the Ministry of Environment and Urbanization and guideline prepared, containing liquid wastes resources, collected separately (http://cygm.csb.gov.tr).

OP-13

Cell count in body fluids with manual hemacytometer and Mindray BC6800 hematology analyzer

Mustafa Şahin[1], Barış Eser[2], Ünsal Savcı[3], Hüseyin Kayadibi[4]

[1]Hitit University, Çorum Erol Olçok Education and Research Hospital, Medical Biochemistry Laboratory, Çorum

[2] Department of Nephrology, Hitit University School of Medicine, Çorum

[3]Hitit University Çorum Erol Olçok Education and Research Hospital Medical Microbiology Laboratory, Çorum

[4] Department of Medical Biochemistry, Hitit University School of Medicine, Çorum

Objective: The counting and identification of blood cells in body fluids provides important informations for diagnosis and treatment of various medical conditions. The manual hemocytometer method is accepted as the gold standard for the evaluation and classification of cells in body fluids. In this study, we aimed to compare the hemogram and body fluid modes of the BC-6800 Mindray hematology analyzer with the manual hemocytometry method in terms of cell count in body fluids.

Materials and Methods: A total of 155 samples were included in the study: 110 peritoneal fluids, 35 pleural effusion fluids, 4 cerebrospinal fluids, 4 synovial fluids, 1 pericardial effusion fluid and 1 intraabdominal aspiration fluid. Three different methods were used for cell counts: manual hemocytometric method with Neubauer slide, hemogram and body fluid modes on the Mindray BC-6800 (Mindray, Shenzhen, China) hematology analyzer. Leukocyte and erythrocyte cells in clinical samples were counted by these methods.

Results: Leukocyte counts of the samples were detected as 15(0-400) cell/mm^3 by manual hemacytometer method, 16 (2-410) cell/mm^3 by body fluid mode, 60 (30-420) cell/mm^3 by hemogram mode. Leukocyte counts were similar in body fluid mode and manual hemocytometric method, and there was no statistically significant difference between the two methods ($p=0.818$). The leukocyte count in the hemogram mode was statistically significantly different from the other two measurement methods ($p<0.001$, $p<0.001$). Statistical evaluation was not possible because the numbers of erythrocytes in most of the samples were insufficient.

Conclusion: Morphologic evaluation of cells in the manual hemocytometer method may contribute to the diagnosis. The together use of manual hemocytometer and body fluid mode to make cell counts in body fluids will increase the safety of the results. As alternative to manual hemacytometer for cell count in body fluids in clinical laboratories, we suggest using the body fluid mode instead of the hemogram mode in hematology analyzers.

OP-14

Evaluation Of Blood And Tissue Testosterone Levels In Rats Feeding With High Fructose Corn Syrup

Köksal Deveci[1], Leyla Aydoğan[1], Velid Ünsal[2], Zeliha Cansel Özmen[1]

[1]Department of Medical Biochemistry, Tokat Gaziosmanpaşa University, Faculty of Medicine, Tokat

[2]T.C. Mardin Artuklu University, Health Services Vocational School, Mardin

Objective: High fructose corn syrup (HFSC) is produced with liquefaction, fractionation and isomerization stages with chemical and enzymatic hydrolysis techniques of corn starch. It is a food additive that has the highest useage in the food sector because it is cheap and sweet. In recent epidemiological studies and experimental animal models, consumption of HFSC has been reported to increase obesity. In this study we aimed to evaluate whether blood and testicular tissue testosterone levels were affected in male rats fed HFSC.

Materials and Methods: Twelve male adult wistar albino rats randomly selected for study were divided into 2 groups. All groups were fed standard food for 12 weeks. Group 1 was fed with drinking water whereas group 2 was fed with 15% HFSC. Groups were followed for weekly weight gain for 12 weeks. At the end of 12 weeks, rats were sacrificed and blood samples and testicular tissue samples were taken. Serum and tissue cholesterol and testosterone levels were measured from the obtained samples.

Results: The weights of group 2 rats fed with HFSC were significantly increased compared to group 1 rats. Serum cholesterol levels of group 2 rats were significantly higher than group 1, while serum and tissue testosterone levels were significantly lower.

Conclusion: The results of our study makes us think that feeding with excess HFSC may cause weight gain as well as decrease in testosterone levels.

OP-15

The effects of Using Pneumatic Transportation System on Hemolysis Rate and Turnaround Time (TAT) in Emergency Services

Cemal Kazezoğlu

Central Laboratory Health Science University Kanuni Sultan Süleyman Research and Training Hospital, İstanbul

Pneumatic transport systems are used for rapid and reliable transfer of samples in many hospitals. Hemolysis-related sample rejection rates and turnaround times (TAT) were compared total 14.897 samples retrospectively during the period when the Pneumatic transport system (PTS) was malfunctioning in our hospital. It was determined that there was no significant contribution of PTS to TAT, only 2.2 minutes decreased. When hemolysis induced rejection rates in PTS Active and PTS Failure were compared, it was found that PTS had 34,75% (vs before failure) and 39.87% (vs after failure) ($p<0.005$) lower hemolysis in the absence of activity. At emergency patients, the pneumatic transport system can lead to an increase in the rate of hemolysis and the inability to make a meaningful contribution to the outcome time may be due to user errors and the type of sample used. In emergency departments, plasma can be used instead of serum to reduce PTS induced hemolysis and to make a meaningful contribution to the outcome times. Continuous trainings can be organized to prevent and correct PTS system user mistakes. Process responsibilities can be defined and traceability can be achieved or new generation single tube PTS systems should be introduced.

OP-16

Calculation of Measurement Uncertainty and Reference Change Values of Tests Operated in Autoanalyser in Emergency Biochemistry Laboratory

Alper Kütükçü[1], Fatih Özçelik[1], Halime Hanım Pençe[2]

[1]Department of Medical Biochemistry, University of Health Sciences, Haydarpaşa Numune Training Hospital, İstanbul

[2]Department of Medical Biochemistry, University of Health Sciences, İstanbul

Objective: In medical laboratories, measurement uncertainty is used to describe different results that can be detected in consecutive measurements of the same sample. In clinical diagnosis and treatment monitoring, besides the measurement uncertainty of the measurement process must be given from the reference change value including biological variations. We also aimed to improve the accuracy and reliability of our test results by calculating the measurement uncertainty of our routine biochemical parameters in our study and the reference change values that test the significance of the change in sequential results of the individual.

Materials and Methods: The original kits of the ci4100 and ci8200 Architect autoanalyzer and 23 types of routine Biochemistry tests were used in the measurement uncertainty. (Albumin, amylase, AST, ALT, direct-total bilirubin, BUN, Ca, CK, creatinine, glucose, LDH, lipas, Na, Mg, K, Cl, P, total protein, CRP, B-HCG, CK-MB, Troponin-I) calculation. The Classic Fraser and logarithmic transformation formula was used in reference change value calculation. Uncertainty results are compared with international accepted (CLIA'88 and Westgard) total error limits.

Results: The results of measurement uncertainty of all biochemical tests of both devices showed that CLIA'88 limits were met (<%TEa), but albumin, Ca, Cl, Mg, Na and total protein results failed to meet Westgard limits. (respectively >%4.07, >%2.55, >%1.5, >%4.8, >%0.73, >%3.63). When the reference change values calculated by Fraser approach of the tests are examined, Especially, the reference change value in the decreasing direction of the CRP appears to exceed 100%, so it isn't possible and therefore can be used than the logarithmic transformation formula.

Conclusion: Each laboratory should determine all tests' measurement uncertainty values and comparison with international limits. Uncertainty values should be reported with patient outcome and the reference change value, which is a sign of the changes in the test repeats, should be added to the report.

OP-17

Evaluation of Rational Use of Laboratory Tests in Emergency Laboratory

Hakan Ayyıldız, Mehmet Kalaycı, Mahmut Bozkurt

Department of Biochemistry Laboratory, Elazığ City Hospital, Elazığ

Objective: In the world, mean annual increase in the number of patients and tests are 2% and 10% respectively. The economical burden of laboratory tests to healthcare system comprises approximately 4-11% of budget allocated to healthcare system worldwide. Is this increase in the test for the diagnosis or is it unnecessary? The aim of this study is to determine test orders which may be unnecessary and evaluate cost analysis in terms of total test orders by comparing pathological result rates of Troponin test which is order by emergency of our hospital.

Materials and Methods: Statistical data of Troponin tests ordered by the emergency between the dates February 2018 and March 2018 were obtained from automation system of our hospital. Cost of pathological result rates in total tests were calculated by using Microsoft Excel programme.

Results: Positivity rate was found to be 6.7% for troponin tests ordered by the while troponin tests comprised 20% of costs among all tests. We attributed the frequency of troponin test order, which comprised one-fifth of overall laboratory costs in emergency department and was found to be negative in 93 of 100 patients, to defensive medicine practice resulting from malpractice act.

Conclusion: In conclusion, provision of consistent feedback and information to clinicians as well as regulations on reasonable test order decisions can reduce laboratory costs which comprise 5% of overall healthcare expenses.

OP-18

Comparison and Stability of Urine Results in Three Different Urine Collection Tubes

Murat Akşit, Fatma Demet Arslan, Anıl Baysoy, İnanç Karakoyun, Ayfer Çolak, Banu İşbilen Başok

Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, İzmir

Objective: Accurate collection and transport of the urine sample is necessary to obtain a qualified and reliable urine analysis result. Therefore it was aimed to compare three different urine tubes and to evaluate their stability.

Materials and Methods: Forty samples were randomly selected from the urine samples sent to the laboratory. Urine samples were transferred to urine tube without additive, Vacutainer containing chlorhexidine, Vacuette and Monovette tubes containing stabilur. It was evaluated as chemical and microscopic at 0, 3, 6, 24 and 48th hours. 0th hour value of tube without additive accepted as reference. The stability of tubes was evaluated by comparing with the 0th hour value for each tube. Kappa value ≥0.600 was accepted as good agreement.

Results: When we look at the agreement with the tube without additive, WBC, RBC, crystal, leukocyte esterase, blood, protein and bilirubin in the Vacutainer tube; WBC, RBC, bacteria, crystal, leukocyte esterase, blood, protein and bilirubin in the Vacuette tube; RBC, bacteria, blood, protein and bilirubin in the Monovette tube were found as well. pH, leukocyte esterase and protein parameters were stable until the third hour in the tube without additive while the stability continued until and after the third hour for the different parameters in all three tubes.

Conclusion: The use of preservative has been found to increase sample stability on a parameter basis. However, preservative and type of the tube use are affecting the results obtained.

OP-19

The Assessment of Clopidogrel Resistance by Using Light Transmission and Multiple Electrode Aggregometry

Zeynep Levent Çıraklı, Nilgün Işıksaçan, Yüksel Gülen Çiçek, Şehide Baz

Health Sciences University Bakırkoy Dr. Sadi Konuk Education and Research Hospital Medical Biochemistry Laboratory, İstanbul

Objective: Clopidogrel, a thienopyridine derivative is an effective antiplatelet drug and despite its proven efficacy in various clinical trials, some patients exhibit impaired response to it and have activated platelets while on usual clopidogrel treatment. In vitro evaluation of platelet aggregation is used to monitor anti-platelet treatment. The most commonly used method of evaluating the efficacy of clopidogrel adenosine diphosphate (ADP)-induced thrombocyte aggregation. It has been reported that all the tests used in laboratory diagnosis of clopidogrel resistance have different limitations and that different results can be obtained with two different tests in the same patient. We aimed to compare light transmission aggregometry (LTA) and multiple electrode aggregometry (MEA) for the measurement of clopidogrel resistance in this study.

Materials and Methods: The study comprised 23 patient samples which treated in the neuroradiology clinic of Bakirkoy Dr. Sadi Konuk education and research hospital. APACT 4004 Platelet Aggregometry (LABiTec, Germany) and Multiplate® analyzer (F. Hoffmann-La Roche ltd. Germany) instruments were used. In this study, a special protocol was applied for each instruments.

Results: The rates of clopidogrel resistance were 30% and 43% as detected by LTA and MEA, respectively. The two methods were statistically compared using correlation analysis between the methods and there was a medium positive dependence between the methods (r=0.38).

Conclusion: As supported by the results of this study, recent studies have reported that clopidogrel resistance is 5-44% and that methods of clopidogrel resistance determination are not standardized. For this reason, clinicians and laboratory specialists should work together to comment on this issue.

OP-20

Evaluation Of Bıotın Interference For hs-cTnI Test

İnanç Karakoyun

Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, İzmir

Objective: Some laboratory test manufacturers design tests that use a strong interaction between biotin and streptavidin in the detection of analytes, but preparations containing high doses of biotin used by patients may cause interference in these principled immunoassay systems. In our study, we aimed to evaluate the biotin interference for the high-sensitivity cardiac troponin I (hscTnI) test, one of the most critical tests in emergency laboratories.

Materials and Methods: Biotin (Sigma-Aldrich, USA) was added at 5 different levels (5-12.5-25-50-100 ng/mL) to serum pools containing 4 different levels of TnI (0.025-0.066-0.153-2.890 ng/mL). Serum hs-cTnI measurements were performed using a chemiluminescence immunoassay on an Advia Centaur XPT (Siemens Healthcare Diagnostics Inc, Tarrytown, NY, USA) analyzer. Following the addition of biotin, the change of the recovery value that exceed >16.32% (acceptable bias) accepted as an interference.

Results: Following addition of 25 ng/mL biotin in the serum pool containing 0.025 ng/mL TnI and addition of 50 ng/mL biotin in the serum pools containing 0.066, 0.0153 and 2.890 ng/mL TnI, interference was began.

Conclusion: The samples taken from patients using high doses of biotin can contain biotin at up to 1200 ng/mL. This situation is even more critical for patients who has hs-cTnI test result close to the upper reference limit, and it is an interference source that should be considered in patients such as acute coronary syndrome that time is important at the diagnosis and starting treatment.

OP-21

Evaluation of Neutrophil/Lymphocyte and Platelet/ Lymphocyte Ratios in Patients with Colon Cancer

Arzu Kösem, Turan Turhan

Ankara Numune Training and Research Hospital, Biochemistry Laboratory, Ankara

Objective: The neutrophil/lymphocyte ratio (NLR) is a simple index of systemic inflammatory response, and has been shown to be a prognostic indicator in some types of cancer. The aim of this study was to investigate the predictive value of neutrophil/lymphocyte (NLR), platelet/lymphocyte (PLR) in discrimination between control and colon cancers.

Materials and Methods: A total of 228 (98 with colon cancer and 130 control) selected patients admitted to our hospital between 01.01.2018 and 31.07.2018 were retrospectively analyzed through the hospital information system. We analyzed results of neutrophil, lymphocyte counts, platelet distribution width (PDW), mean platelet volume (MPV) and NLR, PLR.

Results: The neutrophil, monocyte, lymphocyte, NLR, PLR count was significantly higher in patients with cancer than in those with control (p=0.049; p=0.001; p=0.00; p=0.047; p=0.007,respectively).

Conclusion: Our study demostrated that neutrophil, lymphocyte counts, PDW, MPV, NLR, PLR levels can actually be relied on as a diagnostic factor in patients with colon cancer.

OP-22

Comparison Of Hematological Inflammation Parameters In Pediatric Patients With Acute And Chronic Otitis Media With Effusion

Ayşe Hedef[1], Filiz Alkan Baylan[1], Saime Sağıroğlu[2], Hasan Dağlı[3], Fatma İnanç Tolun[1]

[1]Department of Medical Biochemistry, Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Kahramanmaraş

[2]Department of Otorhinolaryngology, Kahramanmaraş Sütçü İmam Faculty of Medicine, Kahramanmaraş

[3]Department of Medical Biochemistry, Gazi University, Faculty of Medicine, Ankara

Objective: Otitis media with effusion is defined as the accumulation of serous fluid in the middle ear without symptoms of acute ear infection. Inflammation has an important role in the etiology of otitis media with effusion. We aimed to investigate the relationship between haematological inflammation parameters in healthy pediatric populations with otitis media with acute and chronic effusions.

Materials and Methods: The data of 365 patients diagnosed with COME and AOME recent months were analyzed retrospectively in KSU Hospital Department of Otorhinolaryngology. Eighty patients with acute serous otitis media and 285 patients with chronic serous otitis media were included in the study. Control consisting of 75 healthy children with demographic characteristics was included.WBC, neutrophil, lymphocyte, platelet and MPV parameters were studied by electrical impedance method on SYSMEX XN3000. NLO and PLO were calculated and the results were compared statistically.Nonparametric Kruskal-Wallis H test that the Kolmogorov-Smirnov test did not fit the normal distribution in the statistical evaluation of the data. Statistical significance was accepted as $p<0.05$. IBM SPSS package program version 18 was used to evaluate the data.

Results: Hemogram results of patients; control Mean values WBC=7.317, neutrophil=3.879, lymphocyte=2.692, MPV=8.260, platelet=303.342, N/L=2.013 P/L=126.936; AEOM Mean values WBC=9.484, neutrophil=4.642, lymphocyte=3.800, MPV=9.381, platelet=350.154, N/L=1.622 P/L=107.917; KEOM Mean values WBC=9.427, neutrophil=4.478, lymphocyte=3.885, MPV=9.467, platelet=350.908, N/L=1.493 P/L=105.496.

Conclusion: Comparing the hemogram results of the COME, AOME patients and control, the WBC, neutrophil, lymphocyte, platelet and MPV values were significantly higher in the COME and AOME patients than the control ($p<0.001$).

OP-23

The Value of Fractional Magnesium, Sodium and Potassium Excretion as Indicators of Early Renal Tubular Injury in Normotensive Type 2 Diabetic Patients

Şerif Kaçtaş, Fatih Özçelik, Büşra Efem Toy

Department of Medical Biochemistry, University of Health Science, Haydarpaşa Numune Training Hospital, İstanbul

Objective: Better markers are needed to predict kidney damage early, as albumin levels may not rise in the early stages of diabetic nephropathy. Electrolyte levels may be a beter predictor according album into indicate the function of tubules and reabsorption capacity to excretion in the early stage of diabetic nephropathy. We aimed investigated the use of fractional excretion of electrolytes as a marker of tubular damage in the kidneys in normotensive type-2 diabetic patients.

Materials and Methods: 49 normoalbuminuric and 42 microalbuminuric 91 normotensive type-2 diabetic patients, 40 healthy were included in the study. Sodium, creatinine, potassium and magnesium in spot urine and serum samples of all participants and microalbumin levels in spot urine samples were measured. Correlation analysis was performed to determine the relationship between EGFR and fractional excretion of electrolytes. A comparison of ROC curves was performed in the evaluation of FEMg and the diagnostic power of eGFR in microalbuminuric patients. Relative risk analysis was also performed for FEMg and eGFR associated with renal injury.

Results: Normoalbuminuric and albuminuric group FEMg values were higher ($P<0.05$). A moderately-close, proportional correlation was found between FEMg values and urinary albumin excretion($r=0,3215, P<0.05$). There was a slight but inversely correlation between FEMg and eGFR values ($r:-0.1934, P<0.05$). In the ROC analysis for eGFR and FEMg, the areas under the curve were determined to be 0.625, 0.732, respectively. Inpatients with a FEMg score greater than 3.67,the risk of microalbuminuria was 2.97-fold greater than in those with a lower (95% CI:1.91-4.61, $P<0.0001$). The risk of detecting microalbuminuria in patients with an eGFR level of less than 89.83 ml/min is 2.04 fold over the greater ones (95% CI:1.35-3.06, $P=0.0006$).

Conclusion: In renal tubular damage detected by microalbuminuria, FEMg has adequate diagnostic and prognostic value. It is also thought that patients with type-2 diabetes may be able to use the renal tubular pathology, which can not be detected by albuminuria, even at the beginning.

OP-24

Relationship Between Vitamin D and Specific IgE, Eosinophil in Children

Sibel Kulaksızoğlu

Department of Medical Biochemistry Laboratory, University of Health Sciences, Antalya Training and Research Hospital, Antalya

Objective: In recent years, the prevalence of allergic diseases has increased significantly. Although studies have suggested that vitamin D levels in the etiology of allergic diseases has a significant effect, the findings in this regard are contradictory. In particular, the relationship between vitamin D and blood eosinophil levels has not been found significantly in most studies. The aim of our study is to investigate the relationship between specific IgE, eosinophil and vitamin D with respiratory panel in children who applied to Antalya Policlinic Training and Research Hospital.

Materials and Methods: Between January 2017 and August 2018, specific IgE, eosinophil and 25 (OH) D vitamin results were assessed retrospectively in the Antalya Training and Research Hospital.

Results: A total of 1074 (66% M, 34% F) patients were found to have an average age of 5.06±4.12. The eosinophil count was 0.51±0.41 103/mm^3 in 713 children with 25 (OH) D vitamin value <30 ng/ml, while the eosinophil count was 0.36±0.31 103/mm^3 in 361 children with a 25 (OH) D vitamin level of ≥30 ng/ml (p<0.01). The mean value of 25 (OH) D vitamin in children with respiratory panel specific IgE<0.4 kU/L was 28.29±13.1, while the mean value of 25 (OH) D vitamin in children with respiratory panel specific IgE ≥0.4 kU/L was 23.09±10.4 (p<0.01).

Conclusion: In our study, children with low levels of 25 (OH) D vitamin had higher respiratory panel specific IgE positivity. At the same time, blood eosinophil levels are higher in children who have low 25 (OH) D vitamin levels. The high eosinophil level detected in the hemogram test may be a sign for the low levels of 25 (OH) D vitamin. The relationship between 25 (OH) D vitamin deficiency and allergic diseases may be clinically important.

OP-25

Serum Vitamin D Levels of Patients in Neurology Critical Care

Nilgün Işıksaçan[1], Murat Çabalar[2], Zeynep Levent Çıraklı[1], Pınar Kasapoğlu[1]

[1]Departments of Biochemistry and [2]Neurology, The University of Health Sciences, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul

Objective: Recent studies have shown that as well as vitamin D deficiency is associated with metabolic syndrome, cardiovascular disease, increased morbidity and mortality, positive effects of replacement studies on the immune system, brain and central nervous system, cell proliferation, differentiation and neurotransmission. Vitamin D levels of patients receiving critical care in neurology were evaluated, and in relation to the lenght of hospitalization and mortality was examined.

Materials and Methods: 57 (27 female/30 male) critical care patients in neurology clinic and 27 (20 females/7 males) healthy controls were included in the study. Local ethics committee approval (2016/178) was taken. Measurements of 25-OH vitamin D levels from serum samples were performed using a Cobas-e411 analyzer (Roche Diagnostics, USA). Statistical significance level was determined as 0.05.

Results: The mean age of critical care patients was 67.49±15.57 and 65.41±14.46 for healthy individuals. 25-OH vitamin D levels were measured as 12.19±9.13 ng/ml in patients and 31.54±22.29 ng/ml in control group. The vitamin D averages of healthy subjects were statistically higher than the patients group (p<0.005). There was a statistically significant difference in the distribution of age (45+/-years) according to vitamin D levels (p<0.05). 88.5% (n=23) of vitamin D levels ≤10 and 89.7% (n=26) of vitamin D levels between 11 and 29 were >45 years old. 11.5% (n=3) of vitamin D levels ≤10, 10.3% (n=3) of those with vitamin D levels of 11-29 were >45 years old. There is a difference between vitamin D levels and the lenght of hospitalization, although not statistically significant (p<0.052).

Conclusion: Vitamin D is known to play a role in the pathophysiology and progression of many diseases, furthermore vitamin D deficiency is to be common in some risk groups, especially in the elderly. This data suggests that if vitamin D replacement is not done, patients' hospitalization in critical care will extend.

OP-26

Can Lymphatic Endothelial Specific Markers Predict Secondary Lymphedema Following to Breast Cancer Treatment?

Nilhan Nurlu Ayan[1], Gül Tuğba Bulut[2]

[1]Department of Medical Biochemistry, Gaziosmanpaşa Taksim Education and Research Hospital, İstanbul

[2]Department of Physical Therapy and Rehabilitation Clinic, Gaziosmanpaşa Taksim Education and Research Hospital, İstanbul

Objective: Lymphedema (LE) is a common iatrogenic complication after axillary lymph node dissection (ALND) and radiotherapy for breast cancer treatment.It is a chronic, progressive disease and there is no definitive treatment yet. Significant progress has been made in recent years in understanding the mechanisms controlling the lymphatic system by the discovery of lenfatic endothelial cell (LEC) markers.Our aim in this study is to investigate the markers of Prox1, LVYE-1, PDPN in the LE after breast cancer treatment.

Materials and Methods: Forty-four female patients who developed lymphedema in the upper extremity to form the LE group and 44 healthy women to form the control group were included in the study.The diagnosis of LE was made by anamnesis, physical examination and arm circumference measurements.The difference between the sum of the two arm circumferences (DSOAC) of the patient was accepted as LE when the difference was 2 cm or 10%. The staging of LE was made according to the International Society of Lymphology. Serum Prox1, LVYE-1 and PDPN concentrations were measured by ELISA.

Results: In the LE group, Prox 1, LVYE-1 and PDPN levels were significantly lower than the control group (p<0.01, p=0.02, p=0.04, respectively).Prox1 levels were significantly higher in Stage 1 LE, and DSOAC and ALND were significantly higher in Stage 2 LE (p<0.001). There was a weak negative correlation between Prox1 levels and DSOAC and ALND (r=–0.417, –0.426, p<0.01), a positive and moderate correlation (r=0.533, p<0.001) between DSOAC and ALND. The ROC curve for the Prox1; AUC=0.753 (95% CI=0.699-0.808); sensitivity= 86%, specificity= 66%, cut off=477.6 pg/ml,for the LVYE-1; AUC=0.650 (95% CI=0.589-0.711), sensitivity=70%, specificity=52%, cut off=5.5 ng/ml, for the PDPN; AUC=0.631 (95% CI=0.567-0.695), sensitivity=68%, specificity=54%, cut off=1.1 ng/ml, (for all p<0.001).

Conclusion: Prox 1, LVYE-1, PDPN markers play an important role in LE pathophysiology. Further investigations of LEC markers will lead to the development of new perspectives on LE diagnosis, prognosis and treatment.

OP-27

Assessment of Vascular Calcification in Renal Transplant Recipients

Bilge Karatoy Erdem[1], Vural Taner Yılmaz[2], Gültekin Süleymanlar[2], Halide Akbaş[1]

[1]Departments of Clinical Biochemistry and [2]Nephrology, Akdeniz University Faculty of Medicine, Antalya

Objective: The progression of vascular calcification is an important cause of cardiovascular morbidity and mortality in chronic kidney diseases. The aim of this study was to assess the relationship between calcification activators and inhibitors in renal transplant recipients.

Materials and Methods: 35 recipients were included in this study. Plasma 1.25-dihydroxyvitamin D3, serum 25-hydroxyvitamin D, calcium, phosphorus, inorganic pyrophosphate (PPi), osteoprotegerin (OPG), alpha-2 heremans-schmid glycoprotein (Fetuin-A), alkaline phosphatase (ALP), bone morphogenic protein-2 (BMP-2), creatinine, parathyroid hormone (PTH) levels were analyzed before and 6 months after transplantation.

Results: 1.25 (OH) 2D3 and serum 25 (OH) D levels showed a significant increase due to the improvement of kidney function after transplantation ($p \leq 0.0001$, $p=0.0003$ respectively). Serum creatinine, phosphorus and ALP levels significantly decreased after transplantation, while calcium levels increased. We did not find any significant difference BMP-2 levels. On the other hand, significant differences were found between PPi, OPG and Fetuin A levels before and after transplantation ($p=0.03$, $p=0.007$, $p=0.006$ respectively).

Conclusion: In the present study, most important parameters of vascular calcification risk factors were assessed in renal transplant recipients. Detection of vascular calcification is difficult in renal diseases. Therefore, selected biomarkers would be valuable and clinically important in non-invasive monitoring of early signs of vascular calcification.

OP-28

Variation in Clinical Biochemistry; Biological Variation

Halil İbrahim Akbay[1], Erdem Çokluk[2], Hamit Hakan Alp[1]

[1]Department of Medical Biochemistry, Van Yüzüncü Yıl University, School of Medicine, Van

[2]Department of Medical Biochemistry, Sakarya University, School of Medicine, Sakarya

Objective: We aimed to evaluate the use of population-based-reference-intervals by calculating the individuality index and reference change value of iron, transferrin, ferritin, folate, vitamin B12 and 25-OH vitaminD parameters.

Materials and Methods: A total of 5 venous blood samples were taken from, 11 female and 10 male individuals on days 0,7,14,21,28. All tests were performed on an autoanalyzer and CVI, CVG, II, RCV values were calculated for both genders and the whole groups.

Results: CVA(%)/CVI(%)/CVG(%) for Iron, 0.67/27.3/32.3 Transferrin, 0.62/3.60/10.27 Ferritin, 2.27/6.21/105.6 Folate 4.71/10.3/28.56 Vitamin B12, 6.1/5.77/34.6, D Vitamin 3.4/8.2/54.9 respectively. RCV calculated as a 2-tailed value at level of probability of significant change set at 0.95-0.99; 74.9/98, 7-10.1/13, 3-18.3/24, 1-31.4/41, 3-23.4/30, 8-24.7/32.5 and II were 0.8-0.4-0,-0.4-0.17-0.1 respectively.

Conclusion: CVI and CVG values for Iron, Transferrin, Folate, Vitamin B12, 25-OH Vitamin D are in accordance with the literature. Ferritin were calculated differently from the values in the database. This difference might be due to the characteristics of selected individuals for study. Evaluating the suitability and utility of the use of RR with values found for II, For iron, the use of RR was considered appropriate when taken as II<0.6 and II>1.4. However, that the use of RCV is more appropriate for Transferrin, Folate, Vitamin B12, 25-OH Vitamin D.

S-29

Drug-Herb Interactions

Aslıhan Avcı

Department of Medical Biochemistry, Ankara University, Ankara

In most of the developed or developing countries, 50-70% of the population uses herbal supplements. Individuals with an illness tend to use herbal supplements more than healthy people. Particularly cancer patients, individuals with HIV infection tend to use more herbal supplements.. In one report, 66% women with breast cancers used at least one alternative therapy during the previous 12 months of the survey, and most of these patients did not inform their physicians regarding their use of alternative therapies. The reason for using such therapies was the belief that such therapy could prevent cancer recurrences and would also improve the quality of life. The contents of the most frequently used herbal supports to support the treatment of diseases in the community; echinacea, gingko-biloba, glucosamine, garlic, St. John's wort, ginseng and kava. Because the metabolism of plants and the metabolism of medical drugs coexist in the system of cytochrome P450, the plants may affect the metabolism of some drugs. This interaction sometimes leads to the outbreak of toxic levels of the medical drug, but sometimes it can lead to inadequate blood levels and inadequate efficacy. Some medicinal drugs that interact with plants include: HIV protease inhibitors, reverse transcriptase inhibitors, cyclosporine, tacrolimus warfarin, digoxin, protease inhibitors, anticoagulants, protease inhibitors, anticoagulants, cardioactive agents, Irinotecan, imatinib, benzodiazepines, anticancer agents, phenytoin, tricyclic antidepressants, cholesterol-lowering drug, synthetic opioids, oral contraceptives, proton pump inhibitors and asthma medications.

OP-30

Comparison of ISE Analysis on Mindray BS-2000M and Architect C8000 Instruments

Fatih Yeşildal, Rabia Korkmaz, Hayriye Erman, Afife Şerifoğlu, Ferruh Kemal İşman, Mustafa Baki Çekmen

Department of Medical Biochemistry, İstanbul Medeniyet University, Göztepe Education and Research Hospital, İstanbul

Objective: The aim of this study was to compare the test performance of sodium, potassium and chloride in Mindray BS-2000M (Shenzhen, China) and Abbott Architect C8000 (Illinois, USA) instruments.

Materials and Methods: Sodium, potassium and chloride analysis of 151 patient samples from our laboratory were performed twice in both devices. The results were compared with the EP Evaluator program (Vermont, USA). Regression analysis and difference plots were prepared.To assess the difference between the two devices, the allowable total error (TEa) value of the relevant test from the "desired specifications" in Westgard database was used.The external quality assessment (EQA) (KBUDEK, Turkey) results were also evaluated for the incompatible tests.

Results: Precisions of the sodium, potassium and chloride tests of both instruments were good (CV% values for Architect C8000 were 0.49, 0.77, 0.81 respectively, CV% values for Mindray BS-2000M were 0.62, 0.79, 0.73 respectively). The relation between Architect C8000 (x) and Mindray BS-2000M (y) analyzers was y=0.957x+7.718 for sodium (r=0.9543), y=0.996x+0.046 for potassium (r=0.9965) and y=0.923x+7.677 for chloride (r=0.9677). Considering the difference between the two analyzers; 51.7% of the sodium results, 99.3% of the potassium results, and 83.4% of the chloride results were within the TEa limits. In general, the sodium results were higher on Mindray BS-2000M, while the chloride results were higher on Architect C8000 platform,and the potassium results were similar. EQA results of the two analyzers for the last 3 months were examined. The standard deviation indices (SDI) for sodium, potassium and chloride were 1.002, 1.052 and 0.910 respectively on Mindray BS-2000M instrument, and 0.585, 0.719 and 1.544 respectively on Architect C8000.

Conclusion: According to these results, the difference of the sodium results between the two devices was found to be due to positive bias in Mindray BS-2000M analyzer and the difference of the chloride results was found to be due to positive bias in Architect C8000 analyzer. Potassium results were compatible.

Poster Presentations

PP-01

Comparison of Albumin Measurement Methods; Urine Strips and Immunoturbidimetric Method

Emre Yalçınkaya, Eray Kıraç, Ferruh Kemal İşman, Mustafa Baki Çekmen

Department of Medical Biochemistry, İstanbul Medeniyet University Göztepe Training and Research Hospital, İstanbul

Objective: Albuminuria may be associated with transient proteinuria and renal pathologies. Albuminuria is an independent risk factor in development of chronic kidney disease. When 24-hour urine wasn't available for detection of albuminuria, we evaluated the analytical and clinical performance of the urine strip.

Materials and Methods: Urine samples (n=51) were analyzed by strip (tetrabromfenolblue method, LabStrip U11plus, Labumad) and polyclonal immunturbidimetric method (Abbott Architect c8000) within 2 hours. Albumin results were classified semiquantitatively (negative:<30 mg/dL, 1+:30-100 mg/dL, 2+:100-500 mg/dL, 3+:≥500) and positively-negative (<30 mg/dL, ≥30 mg/dL) according to the values of the producer. The concordance between methods was determined by agreement rate and Cohen's kappa coefficient (0.00-0.20 poor, 0.20-0.40 fair, 0.40-0.60 moderate, 0.60-0.80 good, 0.80-1.00 excellent). Variability of negative-positive distribution was determined by McNemar test. Diagnostic performance of the strip [sensivity, specificity, positive predictive value(PPV), negative predictive value (NPV)] were calculated. In the statistical analysis, EP Evaluator and MedCalc were used.

Results: The results were classified as positive-negative, agreement rate and Kappa coefficient were 88.2% (76.6-94.5%) and 75.3% (56.8-93.9%); as semi-quantitatively 52.9% (39.5-65.9%) and 35.5% (16.7-54.3%), respectively. Incompatible results affected 11.7% of clinical judgment. Clinical sensitivity, specificity, PPV, NPV were 90.32%, 85.00%, 90.32% and 85%, respectively.

Conclusion: The negative-positive agreement of the strips was better than the semi-quantitative agreement. The negative results are more reliable than positive results and use of "rule out" may be more beneficial. Number of samples can be increased to obtain more accurate and precise results.

PP-02

Evaluation of the Analytical Performance of Clinical Biochemistry Tests

Kenan Güçlü, Bilal İlanbey, Rukiye Nar

Department of Medical Biochemistry Laboratory, Kırşehir Ahi Evran Education and Research Hospital, Kırşehir

Objective: In 2016 Laboratory Services Department, Standardization and Harmonization Working Group recommended that laboratory's method performances should be evaluated by determining error limits allowed for 15 biochemistry test parameters. They also suggested that corrective and preventive action should be taken for the test parameters other than the allowed total error limits. For this purpose, we calculated the Total Analytical Error (TAE) value by using our retrospective 6-month internal and external quality control data from 2018 for 15 test parameters routinely run in our laboratory. We aimed to compare our results with the total allowed error limits published by the Department of Laboratory Services and we aimed to make corrective and preventive action planning if necessary.

Materials and Methods: For this calculation, "bias" from external quality control data and "% CV " from internal quality control data were calculated. Total Analytical Error account was calculated for each parameter separately using% TAH=% Bias+1.65 *% CV formula.

Results: The 15 clinical biochemical test parameters run in our laboratory had a lower total analytical error than the allowed error limits. These results show that our method performance is appropriate for these 15 analytes. For patient safety, the Total Analytical Error must not exceed the Allowed Total Error limit.

Conclusion: Each laboratory should evaluate test performances at least once a year, even within permitted limits. In case of exceeding the allowed limits, it should be repeated once a month with corrective and preventive actions until it gets back to normal limits.

PP-03

Precision studies for amino acid measurement method with LC-Tandem MS

Rana Türkal[1], Tülay Çevlik[1], Ozan Ünlü[2], Önder Şirikçi[2], Goncagül Haklar[2]

[1]Department of Biochemistry, Marmara University Pendik Education and Research Hospital, İstanbul

[2]Department of Biochemistry, Marmara University School of Medicine, İstanbul

Objective: Amino acid profiling in biological fluids is important for the diagnosis of several diseases. Time efficient and comprehensive quantification of amino acids is challenging and needs higher technologies. Although amino acid analyzers are used widely, their long run time is a disadvantage. HPLC-tandem MS technology (LC-MS/MS) is promising with high separation efficiency and short run time. In our study, we aimed to determine the precision of amino acid determination in biological fluids of our LC-MS/MS method.

Materials and Methods: Detections and measurements were performed on a Shimadzu LCMS 8050 tandem mass spectrometer (Shimadzu, Japan) using Immuchrom reagents (ImmuChrom GmbH, Germany). Precision studies were conducted according to CLSI guide EP5-A2 "Evaluation of precision performance of quantitative measurement methods; approved guideline-second edition". Briefly, within-day and between-day variations were determined using 2 levels of control materials (ImmuChrom GmbH, Germany), and plasma and urine pools containing normal and pathological samples.

Results: From the measured 30 parameters, within-day and between day variations were below 12.5% for threonine, serine, glutamic acid, alanine, citrulline, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, 3-methyl histidine, 1-methylhistidine, tryptophan, ornithine, lysine, arginine and proline in plasma samples. In urine samples, although within-day variations were below 14.6% for all parameters except taurine, aspartic acid, GABA, and homocysteine; between day variations were below the limit for only glutamic acid, alanine, citrulline, valine, cysteine, methionine, isoleucine, leucine, tyrosine, homocysteine, and proline.

Conclusion: LC-MS/MS technology was advantageous for amino acid measurements in biological fluids but validation studies should be done in the laboratory.

PP-04

Comparison of Pyrogallol Red-Molybdate and Lowry Assay in Determination of Tissue Protein Levels

Berrak Güven

Department of Biochemistry, Bülent Ecevit University, Zonguldak

Objective: Determination of total protein content is common to use in biochemistry research and routine clinical laboratory practice. In this study, we compared protein concentrations of tissue using Lowry and Pyrogallol red-molibdat assays

Materials and Methods: Rat brain tissue (n=35) samples were used for analysis. Tissues were minced and homogenized using a Ultratrax homogenizer (4% wt/vol) in buffer containing 1.15% KCl. The homogenates were separated by centrifugation at 1000 g for 10 min. Total protein concentrations were measured by the Lowry and Pyrogallol red-molibdat spectrophotometric techniques in the soluble protein fractions of the homogenates.

Results: Mean protein values (6.66 4.59 mg/ml) assayed by pyrogallol-red molybdate method were close to mean protein values (6.67±3.21 mg/ml) assayed by Lowry method. In this study, there was a statistically significant correlation between the two methods according to the Pearson correlation analysis (r=0.99, p<0.0001). In the Bland-Altman analysis, it was seen that there was no agreement between the two method measurements.

Conclusion: The difference in measurements can occur due to reagent stability, protein stability, and interference in the products. For this reason, further studies are needed to test the Pyrogallol red-molybdate assay in tissue samples and to identify possible interferences.

PP-05

Does Extracorporeal Shockwave Lithotripsy Therapy Affect Thiol-Disulfide Homeostasis?

Aliseydi Bozkurt[1], Cuma Mertoğlu[2], Mehmet Karabakan[3], Gülşah Şiranlı[2], Emine Feyza Yurt[4], Özcan Erel[4]

[1]Departments of Urology and [2]Clinical Biochemistry, Faculty of Medicine, Erzincan University, Erzincan

[3]Department of Urology, Mersin Toros State Hospital, Mersin

[4]Department of Clinical Biochemistry, Yıldırım Beyazıt University Faculty of Medicine, Ankara

Objective: Extracorporeal shockwave lithotripsy (ESWL) is a non-invasive method that is effective at crushing stones in the upper urinary tract. Disturbance of the thiol/disulfide homeostasis, in favor of the disulfide, has been shown to be involved in the disease pathogenesis.

Materials and Methods: A total of 36 individuals that underwent ESWL had blood samples collected before ESWL (0 hrs), 6 hrs, and 1 week after the ESWL. Sera native and total as wells as disulfide amount was measured using an automated method sodium borohydrate (NaBH4) reduction. In addition, ischemia modified albumin (IMA) levels were measured using colorimetric assay method.

Results: Native thiol level was reduced at the 6th hour following ESWL compared to baseline. While the ratios of disulfide level, disulfide/total thiol (DTT), disulfide/native thiol (DNT) and IMA level were increased at the 6th hour following ESWL compared to baseline, they were found to be similar with their baseline values at the end of 1st week. Total thiol and native/total thiol did not show any significant change.

Conclusion: ESWL treatment disrupts thiol/disulfide homeostasis and the structure of albumin at the acute term. Therefore, it increases protein oxidation and leads to increased oxidative stress. However, this state is transient and returns to normal within the proceeding days.

PP-06

Determination of the Extent of Hemolysis Interference in Direct Bilirubin Measurements

Günel Bahramzada[1], Ahmet Faruk Tekin[1], Ozan Ünlü[1], Tülay Çevlik[2], Önder Şirikçi[1], Goncagül Haklar[1]

1 Department of Biochemistry, Laboratory, Marmara University School of Medicine, İstanbul

[2]Department of Biochemistry, Marmara University Pendik Education and Research Hospital, İstanbul

Objective: Free hemoglobin interferes with direct bilirubin measurements and causes lower results. Greene et al. have proposed an equation (corrected bilirubin=(0.334x hemoglobin concentration0.334)x measured bilirubin1.56xhemoglobin concentration-0.14) to correct the bilirubin levels in hemolytic samples. We aimed to assess the extent of hemolysis interference by correcting the measured bilirubin results by the Greene equation.

Materials and Methods: We retrospectively analyzed 5828 direct bilirubin and hemolysis index results. Direct bilirubin was measured by a diazo-based method (AU680, Beckman Coulter, USA). The free hemoglobin concentration was calculated spectrophotometrically at 410-480 nm and were grouped into 4 groups from +1 to +4 corresponding to 75, 150, 250, and 400 mg/dL hemoglobin (n=2576, 1878, 806, 568, respectively). The bilirubin results were corrected with the Greene equation and the difference was expressed as relative bias precentage [(RBP=corrected concentration–measured concentration)/measured concentration x100]. The RBP was compared with the reference change value (RCV), which encompasses both the analytical variation and the biological variation and determines the limits of change that can be interpreted as a "change in the clinical status".

Results: The median(min-max) RBP values for the groups were 90 (11.3-178), 182 (23.8-405), 266 (34.7-531), and 380 (53-1007)% respectively. The RCV value was 106%. 13.6% of +1, 85% of +2, 93% of +3, and 97% of +4 cases had RBP values exceeding RCV value. Hemolysis values of +2 to +4 led to decreases that can be interpreted as "change in the clinical status" in direct bilirubin measurements.

Conclusion: Hemolysis causes decreases that can be interpreted as "change in the clinical status".

PP-07

Fecal Calprotectin Levels in Irritable Bowel Syndrome and Inflammatory Bowel Disease

Özge Cindemir, Esma Sürmen Gür

Department of Clinical Biochemistry, Bursa Uludağ University Faculty of Medicine, Bursa

Objective: Irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) have similar symptoms that cause confusion in differential diagnosis. IBS is a common benign gastrointestinal functional disorder; IBD is a form of chronic inflammation with two major forms: Crohn's disease (CD) and ulcerative colitis (UC), that can cause serious complications. Although endoscopy is the gold standard to confirm IBD diagnosis, its use remains limited because the procedure is invasive, expensive and operatordependent. Therefore, need for new tests on IBD diagnosis is still essential. Calprotectin is a new marker of intestinal inflammation, especially in IBD. In this study, we evaluated fecal calprotectin (FC) levels in IBS and IBD patients.

Materials and Methods: Between 01.05.2016 and 30.06.2017, the FC level of the individuals who applied to our hospital was evaluated retrospectively. IBS patients and CD and UC patients whose diagnosis were confirmed by endoscopic imaging and/or pathological evaluation were included in the study. FC level was measured immunochromatographically. Statistical analysis was performed using SPSS 23.0. Statistical significance was set at $p<0.05$.

Results: 121 (59 female, 62 male) of the subjects were IBS, 90 (45 female, 45 male) were CD, and 182 (88 female, 94 male) were UC patients. The mean FC levels of IBS, CD and UC patients were 60.07 mg/kg, 100.78 mg/kg and 142.85 mg/kg, respectively. FC was significantly lower in IBS group compared to both UC and CD patients ($p<0.001$) and was significantly higher in UC compared to CD cases ($p<0.001$).

Conclusion: FC appears to be a reliable predictor of intestinal inflammation and may be used in discriminating IBS from IBD, preventing unnecessary endoscopy. Future studies may support FC to be a promising test for differentiating IBS, CD and UC.

PP-08

Knowledge and Attitude of Laboratory Employees Towords to Occupational Accident; A Survey Study

Erdem Çokluk, Tuba Batur

Department of Medical Biochemistry, Yüzüncü Yıl University, School of Medicine, Van

Objective: The aim was to investigate the occupational accidents and the knowledge and attitudes of laboratory employees.

Materials and Methods: A descriptive type study involving the employees of the laboratory and a questionnaire consisting of 36 questions prepared by the researchers in the light of literature was applied using face to face interview technique. Statistical significance was accepted as $p<0.05$. Descriptive statistics and Chi-square test were used.

Results: Of the 44 participants, 52.3% were female and 47.7% were male. It is stated that 45.5% of cutlery injuries, 60% of them are more than once and most frequently needle puncture. The rate of contact with body fluids is 54.5%, of which 62.5% is contacted more than once, with a maximum of 41.7% blood and urine. The rate of exposure to violence in the workplace was 25% and at least one of them was spoken orally. Exposure rates with body fluids were significantly lower ($p=0.038$) when they felt safe in the unit they were working in. The injuries of cutter tools were significantly higher in those who had high worries about work accidents ($p=0.013$). The highest exposure to violence was found in the biochemistry unit employees ($p=0.028$).

Conclusion: The most frequent occupational accidents of employees were contact with biological material and needler-stick injuries By providing adequate training on occupational accidents, we believe that employees' anxiety levels and accidents can be reduced, and more accurate attitudes towards initial intervention can be demonstrated.

PP-09

Determination of Medical Waste Awareness Status of Laboratory Employees

Erdem Çokluk[1], Tuba Batur[2], Bünyamin Uçar[2]

[1]Department of Medical Biochemistry, Sakarya University, School of Medicine, Sakarya

[2]Department of Medical Biochemistry, Van Yüzüncü Yıl University, School of Medicine, Van

Objective: The goal of medical waste management is to protect the health of people risk from the dangerous and disease-causing effects of wastes during the lifetime of waste disposal. It was aimed to determine the medical waste awareness situations of laboratory employees.

Materials and Methods: A descriptive type study, a questionnaire consisting of 26 questions prepared by the researchers in the light of literature was applied using face to face interview technique. Statistical significance was accepted as $p<0.05$. Descriptive statistics and Chi-square test were used.

Results: A total of 30 participants, 50% of them were male and 50% of them female. 63.3% of participants were laboratory technicians and 16.7% doctor. 46.7% of the participants work more than 10 years in the same unit and 30% work less than 5 years. 16.6% of the participants have high school education, 63.3% have a bachelor's degree and 20% have master's degree and above. The rate of responding correctly to the questions on the disposal of medical waste and medical waste management was significantly higher in employees worked more than 10 years ($p <0.05$). When comparing genders, the correct response rates of males were higher than the females ($p<0.05$).

Conclusion: Medical waste training practices taken by hospital employees during the collection and transportation of medical wastes are important to prevent damage from medical wastes. For this purpose, we recommend that the necessary measures be taken in line with the Medical Waste Control Regulation and that the training given should be continued.

PP-10

Evaluation and Importance of Troponin-I Interference With a Case Report

Sevim Kahraman Yaman[1], Hüseyin Yaman[2], Serap Kant[1], Hatice Bozkurt Yavuz[2], Mehmet Akif Bildirici[2]

[1]Department of Medical Biochemistry Laboratory, T. C. Ministry of Health, Health Sciences University, Ahi Evren Thoracic and Cardiovascular Surgery Training and Research Hospital, Trabzon

[2]Department of Medical Biochemistry, Faculty of Medicine, Karadeniz Technical University, Trabzon

Objective: According to the World Health Organization, the presence of two of three criteria which are specific clinical complications, specific ECG changes, and the presence of cardiac biomarker elevation are sufficient for the diagnosis of acute myocardial infarction (AMI). The use of cardiac troponins (cTnI or cTnT) as a biomarker in the AMI is accepted as gold standard. In this case, it was aimed to evaluate the false positiveness of cTnI in patient with chest pain.

Materials and Methods: A 46-year-old female patient was admitted to the emergency room with severe chest pain. When the ECG findings were normal, the patient underwent angiography due to 789 ng/L cTnI result and lack of additional evidence to explain the noncardiac elevation. Angiography was normal, repetitive cTnI values were measured as 740,772,800 ng/L and because of persistent pain, myocarditis treatment was applied. In case of the heterophile antibody positiveness, the sample was run on the same autoanalyzer (Beckman Coulter DXI-600) by using both the heterophile antibody blocking tube(HBT) (Scantibodies Laboratory) and PEG-6000 precipitation, to measure cTnI.Furthermore, the interference was assessed by studying hs-cTnT in a different autoanalyzer (Roche Cobas-e411).

Results: First result of cTnI was 896 ng/L, 660 ng/L when treated with HBT and 84 ng/L after precipitation with PEG-6000 was measured. The hs-cTnT result was 5.57 ng/L in the patient's untreated sample.

Conclusion: A modest decrease (26%) was observed when working with the sample HBT, and the presence of the heterophile antibody was not confirmed clearly. A low level of cTnI as a result of precipitation with PEG may be due to the presence of macro-cTnI or heterophile antibodies. The fact that hs-cTnT result is at normal level also supports this situation. Even if measuring with HBT does not change the result PEG precipitation method should be used for parameters with low molecular weight. This becomes even more important in tests such as cardiac troponins.

PP-11

Investigation of Analysis of Kreatin By EP 10-A3

Rabia Korkmaz, Eray Kıraç, Emre Yalçınkaya, Alperen Aksoy, Afife Şerifoğlu, Hayriye Erman, Ferruh Kemal İşman, Mustafa Baki Çekmen

Department of Medical Biochemistry, İstanbul Medeniyet University Göztepe Training and Research Hospital, İstanbul

Objective: Creatinine is used to identify the stage of renal failure and to assess glomerular filtration rate. CLSI EP10 discloses a preliminary evaluation of the protocol of clinical chemistry methods. We found that the outcome of our hospital's creatinine was fluctuating in delta check values and we intended to evaluate the performance of the creatinine test according to EP 10-A3.

Materials and Methods: Two levels, serum pool and calibrator, were selected at concentrations close to the low(DS) and high(YS) reportable range. Intermediate level (OS) was produced by mixing 1:1 ratio of these levels. DS, OS, YS were aliquoted for 6 days and stored at -20°C. All samples were run every day: 10 times as OS-YS-DS-OS-OS-DS-DS-YS-YS-OS. Except first OS, other 9 results were used in the statistical calculation.

Results: For EP10 to be valid, the bias and CV musn't exceed the allowable bias and CV: t-value musn't exceed 4.6 for slope, intercept, carry over, nonlinearity and drift. We observed calibrator values within the allowable total error; bias and CV were outside the allowable bias and CV (Ricos desirable specification). Exept for intercept, t-values for slope, carryover, nonlinearity, and drift were lower than 4.6. Serum pool values were outside the all limits. Except for slope and nonlinearity, t-values for intercept, carryover and drift were lower than 4.6.

Conclusion: We could not meet EP10 criteria for calibrator and serum pool in creatinine performance. Biochemical tests may fluctuate from time to time according to the standard conditions. Although internal and external quality results are normal, we think that the performance analysis should be repeated at different times.

PP-12

Evaluatıon of Unnecessary Testing With NT-PROBNP Test

Hatice Bozkurt Yavuz, Hüseyin Yaman, Mehmet Akif Bildirici, Süleyman Caner Karahan, Mustafa Tat, Merve Katkat, Asım Örem

Department of Medical Biochemistry, Faculty of Medicine, Karadeniz Technical University, Trabzon

Objective: Most of the errors in the total test process are in the pre-analytical period, and one of these is the unnecessary test. NT-proBNP is used as a biomarker in heart failure. If this test is in the same place as other cardiac biomarkers such as cardiac troponin in the physician test request program, it may lead to unnecessary test request during acute myocardial infarction diagnosis and follow-up. It was aimed to evaluate test numbers of NT-proBNP and high-sensitive cardiac troponinT(hs-cTnT) and the changes observed with the corrective-preventive action(CPA).

Materials and Methods: In our hospital, it was determined that NT-proBNP test was repeated same day in certain services. Between July-December2017, the total and combined number of NT-proBNP and hs-cTnT tests requested from the internal medicine, cardiology, cardiovascular surgery(CVS) and pulmonary medicine units were determined.

As part of CPA, the NTproBNP test was replaced from under the heading of 'cardiac biomarkers' to under the heading 'markers' on the physician screen, the relevant units were informed and the search button with the parameter name was active. Between January-June2018, the NTproBNP and hs-cTnT request numbers were determined.Data before and after CAF were compared with chi-square test.

Results: The mean number of hs-cTnT, NT-proBNP, and combined tests were found as 973,425,192 and 921,248,69 before and after CAF, respectively. NT-proBNP/hs-cTnT ratio 0.44 and 0.27; the number of combined tests/NT-proBNP ratio 0.45 and 0.28 before and after CAF, respectively. These differences were statistically significant ($p<0.01$).

Conclusion: It was determined that NT-proBNP requests were reduced in a short time after CAF, and this was achieved by reduction of unnecessary request with hs-cTnT. We believe that this reduction is important both economically and in terms of shortening the time of test results for other cardiac biomarkers studied in the same system. Comprehensive studies involving other systems and tests will reduce both cost and labour.

PP-13

Heterophile Antibody Interference in Thyroglobulın Test in Reference Range

Mehmet Akif Bildirici, Süleyman Caner Karahan, Mustafa Tat, Hüseyin Yaman, Hatice Bozkurt Yavuz, Yüksel Aliyazıcıoğlu, Merve Katkat

Department of Medical Biochemistry, Karadeniz Technical University, Faculty of Medicine, Trabzon

Objective: Thyroglobulin (TG) is a large glycoprotein stored in the follicular colloid of the thyroid gland. Because TG is synthesized only in the thyroid gland, it falls to an undetectable level in patients with total thyroidectomy. Therefore, it is important to analyze TG levels for the evaluation of metastases in patients with thyroid carcinoma (ca) who underwent total thyroidectomy. Heterophilic antibody is one of the common causes of interference in the immunoassay method

Materials and Methods: A 58-year-old female patient who has undergone a surgery because of the thyroid ca in an external center admitted to our endocrinology department. PET-CT imaging of the metastatic study was performed because the patient's repeated TG measurements ranged from 2.2 ng/mL to 8.34 ng/mL (Beckman Coulter DXI-800, healthy individual reference range 1.15-50 ng/mL). The laboratory was consulted. For the evaluation of the interference, it was decided to repeat the measurement using the Heterophile Antibody Blocking Tube (HBT) (Scantibodies Laboratory).

Results: The TG value of the sample treated with HBT was outside of the measurable lower limit and the result was reported as <0.1 ng/mL. Communication with the clinic was made and information was provided about the situation. Requested the laboratory to be informed of the patient's ongoing follow-up.

Conclusion: The level of TG measured by HBT indicates the presence of heterophile antibody in the patient. Heterophile antibody positivity usually comes to mind with very high or very low results. Such as in this case where the result is in healthy individual reference intervals, it should be kept in mind that the measurement can be effected by the heterophile antibody. In case of incompatible results with the clinical appearance, the laboratory should be in contact with the physician of the patient.

PP-14

Comparison of Hematological Inflammation Parameters and Liver Enzymes in Preeclampsia Patients

Ayşe Hedef[1], Güven Arslan[2], Filiz Alkan Baylan[1], Emine Araz[1], Leyla Dokumacı İşler[3], Selen Dündar[3], Hacer Arıkan[3], Fatma İnanç Tolun[1]

[1]Department of Medical Biochemistry and [2]Department of Obstetrics and Gynecology, Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Kahramanmaraş

[3]Kahramanmaraş Sütçü İmam University, Institute of Health Sciences, Kahramanmaraş

Objective: Preeclampsia characterized by proteinuria associated with hypertension that occurs after 20 weeks of gestation.CBC is a routine test in which white blood cells, neutrophils, lymphocytes, platelets,mean platelet volume (MPV) can be determined. Platelet consumption and persistent inflammation during preeclampsia may lead to changes in these parameters. We aimed to determine relationship between control and patient of these parameters.

Materials and Methods: The data of 47 patients diagnosed with preeclampsia who were admitted to KSU Hospital during the last 2 years were analyzed retrospectively. 61 healthy controls that were compatible with the patient in terms of demographic characteristics were included. Aspartate aminotransferase, alanine aminotransferase were studied enzymatically in SIEMENS ADVİA 1800. WBC, neutrophil, lymphocyte, platelet and MPV parameters were studied on SYSMEX XN3000. NLO and PLO were calculated and the results were compared. Nonparametric Kruskal-Wallis H test that the Kolmogorov-Smirnov test did not fit the normal distribution in the statistical evaluation of the data. We tested Independent Samples the variables that fit the normal distribution. Descriptive statistics were expressed as Mean. Statistical significance was accepted as $p<0.05$. IBM SPSS package program version 18 was used to evaluate the data.

Results: Hemogram results of patients; control Mean values WBC=10.05, neutrophil=7.08, lymphocyte=1.89, mpv=10.9, platelet=229.28, N/L=4.1123 P/L=123.96, ast=20.15, alt=14.94; preeclamptic patient Mean values WBC=11.1291, neutrophil 8.16, lymphocyte=2.23, mpv=10.80, platelet=236.17, N/L=4.37 P/L=111.82, ast=39.51±8.93, alt=32.53.

Conclusion: Lymphocyte, MPV, aspartate aminotransferase, alanine aminotransferase values were significantly higher in the patients than in the control group ($p<0.001$).

PP-15

Vitamine D Dependent Intact Parathyroid Hormone Reference Values Study

Fatih Özçelik[1], Büşra Efem Toy[1], Halime Hatun Pençe[2], Şerif Kaçtaş[1]

[1]Department of Medical Biochemistry, University of Health Science, Haydarpaşa Numune Training Hospital, İstanbul

[2]Department of Medical Biochemistry, University of Health Science, Faculty of Medical, İstanbul

Objective: We aimed to determine the reference range for intact-PTH relative to different levels of vitamin D for our population in order to provide more effective diagnostic and therapeutic results in accordance with IFCC standards in line with our clinical needs.

Materials and Methods: Healthy 513 subjects included in the study were divided into 3 groups according to 25-OH-VitD3 levels (25-OH-Vit-D3<20 ng/ml=Group I, 20 ng/ml ≤25-OH-VitD3<30 ng/ml=Group II, 25-OH Vit D3≥30 ng/ml=Group III). Calcium, magnesium, phosphorus, 25-OH Vit D3 and Abbott I-PTH were studied in serum samples of all participants and eGFR values were calculated. The I-PTH reference interval was calculated according to different 25-OH-Vit-D3 levels. In addition, I-PTH levels in Roche and Siemens instruments were measured in 472 of healthy populations to determine the relationship between different methods.

Results: 154 of the population were in group I, 111 were in group II, and 248 were in group III. I-PTH levels of all reference populations were found to moderately correlate with 25 OH Vit D3 levels (Spearman r=–0.568, P<0.001). The Abbott I-PTH values were highly correlated with Siemens and Roche I-PTH values (r=0.941, r=0.957, P<0.0001; respectively), the I-PTH median/mean values were statistically different from each other (56.2/62.7±26.0, 44.7/50.3±20.9, 33.6/37.1±14.8, P<0.0001; respectively). It was also found that the widest reference interval belonged to the Abbott method among all three test methods. As Abbott I-PTH levels were influenced by 25-OH Vit D3 levels, the reference interval value meeting the clinical need for Group III reference population was determined to be 17.7-90.9 pg/ml.

Conclusion: For each method that does not have absolute compliance, the laboratories should determine the reference intervals, taking into account their clinical needs, according to their populations.Furthermore, since D-vitamin P affects the parathormone level, I-PTH reference range study was also determined according to different 25-OH Vit D3 levels and the result was reported accordingly.

PP-16

Effects of Urine Containers and Sampling Methods on Microscopic Parameters Analyzed in the Urine Autoanalyzer

Mustafa Tat, Hüseyin Yaman, Hatice Bozkurt Yavuz, Süleyman Caner Karahan, Merve Katkat, Yüksel Aliyazıcıoğlu, Asım Örem

Department of Medical Biochemistry, Karadeniz Technical University, Faculty of Medicine, Trabzon

Objective: Complete urine analysis (CUA), chemical and microscopic analysis of urine, is frequently performed in clinical laboratories. With the prevalence of CUA autoanalysers, the need to a microscope for evaluation of hematuria and urinary tract infections, is diminishing day by day. The aim of our study is to compare the microscopic parameters of samples taken from different lot numbered urine containers with different methods, analyzed in urine autoanalyzer.

Materials and Methods: Urine containers of the same brand were numbered 1, 2 and 3 for three different lot numbers. Urine was collected into the urine containers 1, 2 and 3 from 30 people. Then, 3 separate samples were obtained from these containers by vacuuming to the vacutainer (V), pouring to the vacutainer (D) and pouring the nonvacuum tube (N). Thus, 9 samples were taken from 1 person. The samples were analyzed in the Iris IQ200 Elite autoanalyzer. The distribution of the parameters was assessed by the Kolmogorov-Smirnov test. The significance of the difference in erythrocyte and leukocyte values between the samples was evaluated by the Friedman test. p<0.05 was considered statistically significant.

Results: Erythrocyte and leukocyte counts were not normally distributed.The median values for erythrocytes were found as 2.5 forV1; 2 forV2; 18.5 for V3; and 1 for other tubes. The median values for leukocytes were found 4.5 for V3 and 1 for other tubes. Statistically significant differences were found when leukocyte and erythrocyte values were compared in all samples. It was determined that this difference was caused by the values in the V3 sample.

Conclusion: The leukocyte and erythrocyte values of the V3 which is vacuumed from container number 3, were statistically and clinically different from the other samples. Even if it belongs to the same brand, it should always be considered that different results can be obtained in different lot numbered containers.

PP-17

Evaluation of Analytic Performance of Ethanol by Total Error, Six Sigma Processing and Measurement Uncertaınty

Hatice Bozkurt Yavuz, Süleyman Caner Karahan, Mehmet Akif Bildirici, Hüseyin Yaman, Mustafa Tat, Yüksel Aliyazıcıoğlu, Asım Örem

Department of Medical Biochemistry, Karadeniz Technical University, Faculty of Medicine, Trabzon

Objective: Ethanol analysis, is important in ethanol intoxication, assessing legal situation in traffic accidents and forensic events. Total error, process sigma analysis, and measurement uncertainty are the criteria that assess the analytic phase. The purpose of this study is to evaluate the analytical performance of the ethanol parameter by using these criteria.

Materials and Methods: The study was carried out in Karadeniz Technical University Clinical Biochemistry Laboratory for the ethanol test, measured in Beckman Coulter AU5800 autoanalyzer in 2017. Internal quality control (IQC) and external quality control data were used to calculate analytical performances. Total error and process sigma values were calculated monthly. CLIA values were used for the total allowable error (TEa) limits. Measurement uncertainty (% UM) was calculated separately for 2 IQC levels annually according to Nordtest and AACB guidelines.

Results: The total error value of ethanol in our laboratory ranged from 5.1% to 16% per month and the annual average was calculated as 9.3%. Process sigma values ranged from 3.36 to 11.87 per month and the annual average was calculated as 7.4. %UM was found as 11.19 and 9.62 at 40 mg/dL level according to Nordtest and AACB, respectively and these values were 6.88 and 7.98 at 100 mg/dL level.

Conclusion: The ethanol test was within the limits of CLIA TEa for all year. While the process was evaluated according to six sigma values, the results were above 6 for several months, between 4-5 sigma for some

months and 3.36 sigma for just one month. The measurement uncertainty values were found to vary according to the test levels. We believe that the methods should be considered together to make a complete evaluation of the test performance. We believe that this is more important in tests involving toxicology and forensic cases, such as ethanol.

PP-18

Lipid Profile and Atherogenic Indices and Their Association with Platelet Indices in Familial Mediterranean Fever

Gökhan Çakırca[1], Muhammet Murat Çelik[2]

[1]Department of Biochemistry, Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Şanlıurfa

[2]Department of Internal Medicine, Mustafa Kemal University, Faculty of Medicine, Hatay

Objective: The aim of this study was to investigate lipid profiles and atherogenic indices and their association with platelet indices in Familial Mediterranean fever (FMF) patients.

Materials and Methods: A total of 63 FMF patients and 51 healthy individuals were included in this retrospective study. Inflammatory marker values (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP] and fibrinogen), platelet indices (mean platelet volume, plateletcrit value, platelet large cell ratio, and platelet distribution width), lipid profiles (levels of total cholesterol, triglycerides, high-density lipoprotein [HDL] cholesterol, and low-density lipoprotein cholesterol) were recorded. Atherogenic indices (atherogenic index of plasma [AIP], atherogenic coefficient [AC], Castelli's risk indices I and II [CRI I and II]) were calculated using lipid parameters.

Results: In FMF patients, while AIP, AC, and CRI I and II values were significantly higher than in the healthy control group, the HDL cholesterol level was significantly lower (all $p<0.05$). However, no significant difference was determined in terms of the other studied parameters (all $p>0.05$). In male FMF patients, whereas AIP, AC, and CRI I and II values were significantly higher than in female FMF patients, the platelet count, ESR, and HDL cholesterol levels were significantly lower (all $p<0.05$). The level of CRP was negatively correlated with HDL cholesterol ($r=-0.275$; $p=0.032$) and total cholesterol level ($r=-0.313$; $p=0.014$) in FMF patients. HDL cholesterol level was negatively correlated with disease duration ($r=-0.269$; $p=0.049$).

Conclusion: The use of atherogenic indices may be recommended to identify patients with an increased risk of atherosclerotic cardiovascular disease in FMF, especially in male patients.

PP-19

Evaluation of Gas6 and sAxl Levels During Attacks and Attack-Free Periods of Familial Mediterranean Fever

Gökhan Çakırca[1], Muhammet Murat Çelik[2]

[1]Department of Biochemistry, Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Şanlıurfa

[2]Department of Internal Medicine, Mustafa Kemal University, Faculty of Medicine, Hatay

Objective: We aimed to assess the growth arrest specific protein 6 (Gas6) and soluble Axl (sAxl) levels in the familial Mediterranean fever (FMF) patients, and to investigate the correlation between the levels of these with the inflammatory markers including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and fibrinogen.

Materials and Methods: Seventy nine FMF patients (35 in attack period and 44 in attack-free period) and 40 healthy controls were involved in the study. The levels of serum Gas6 and sAxl were measured by enzyme-linked immunosorbent assay (ELISA) method.

Results: Gas6 levels of the FMF patients with attack were significantly lower than both the attack-free patients and the healthy controls ($p=0.007$ and $p=0.003$, respectively). However, no significant difference was detected between the Gas6 levels of the attack-free patients and the healthy controls ($p>0.05$). sAxl levels of the FMF patients with attack were significantly lower than the healthy control ($p = 0.007$). A positive correlation was found between the Gas6 and CRP levels of the FMF patients with attack ($r=0.379$, $p=0.025$).

Conclusion: This study indicates that decreased serum Gas6 and sAxl levels may be associated with FMF attack period. Further studies on the role of the Gas6/Axl system in FMF are needed.

PP-20

Comparison of Analytic Performance Using Two Different Automatic Urinary Analyzer

Saniye Başak Oktay[1], İkbal Özen Küçükçetin[2], Sadıka Halide Akbaş[1], Sebahat Özdem[1], Süleyman Gültekin Yücel[1]

[1]Department of Medical Biochemistry, Faculty of Medicine, Akdeniz University, Antalya

[2]Department of Nutrition and Dietetics, Faculty of Health Science, Akdeniz University, Antalya

Objective: Urine analysis is used in diagnosis and follow-up of renal, genitourinary and many systemic diseases. Because of the clinical laboratories workload, manual urine analysis has been replaced by automated analyzers. In our study, the performances of two different automatic analyzers used in routine urine analysis were compared.

Materials and Methods: A total of 96 urine specimens, submitted for chemical and sediment analysis to our laboratory at Akdeniz University Medicine Faculty Hospital were used in this study. The samples were separated into 10 mL of equal volumes and analyzed on Iris iQ200 ELITE-iChem VELOCITY and Siemens Atellica 1500 analyzers at the same time. Microscopic and chemical analyzes of urine samples were performed on both analyzers. Erythrocyte, leukocyte, crystal, epithelium counts in microscopic analysis; bilirubin, hemoglobin, glucose, ketone, leukocyte esterase, nitrite, protein, pH and specific gravity results in chemical ana-

lyzes were evaluated. Independent Sample t-Test and Mann Whitney U test was used for statistical comparison of the results.

Results: The measurement times for both analyzers were as indicated in the catalogs. The Siemens Atellica 1500 analyzer has easy-to-use strip cassette test format to prevent contamination, providing a more reliable test result and faster workflow. There was a statistically significant difference between the specific gravity results of the two analyzers ($p<0.001$). There was no significant difference between the counts of erythrocyte ($p=0.51$), leukocyte ($p=0.87$), crystal ($p=0.32$), epithelium ($p=0.60$) and results of pH ($p=0.16$).

Conclusion: Both urine analyzers seem to be compatible in terms of delivering reliable test results and ensuring maximum productivity. It is planned to carry out comparative studies with more urine samples for some parameters with significant differences between the measurement results.

PP-21

Reference Change Values of Clinical Biochemistry Laboratory Tests

Niyazi Samet Yılmaz, Bayram Şen, Burak Arslan, Belkıs Narlı, Nigar Afandiyeva, Özlem Gülbahar, Canan Yılmaz Demirtaş, Şehri Elbeg

Department of Medical Biochemistry, Gazi University, Faculty of Medicine, Ankara

Objective: The number of samples in clinical biochemistry laboratories has reached high levels. This makes it difficult for the laboratory specialist to interpret the test results in post-analytical phase. At this point, by automatically validating a certain proportion of patient results according to algorithms previously identified by the clinical biochemist,the remaining results can be assessed more carefully. One of the steps can be used in autovalidation algorithms is the reference change value (RCV). The difference between serial measurements of an individual can be due to analytical variation (CVa), intra-individual (within-subject) variation, changes in clinical status, or the combination of the effects of these factors.The reference change value (RCV) is a numerical value that allows us to evaluate objectively whether the difference between an individual's serial measurements is significant. When assessing patient results, reference intervals (RI) are often used,particularly when unable to reach a previous result of patient. However, RI may be inadequate for clinical decision making, particularly in tests with low individuality index;in which case the use of RCV may be considered. Significant differences between the two measurements can be noticed with RCV even if the reference range is not exceeded. In this study, it is aimed to calculate the RCVs in order to be included as a query in the autovalidation algorithms and an alternative to the reference interval in the tests with low individuality index.

Materials and Methods: In the study,RCVs of 19 tests running at AU5800 (BeckmanCoulter) autoanalyzer were calculated. The formula in CLSI-EP33 is used for RCV calculation (0.95, bidirectional). The analytical CV value (CVa) was calculated using results of 20-day internal quality controls.The CVI values in Westgard website are used for intra-individual(within-subject) variation.

Results: RCVs were Creatinine=%20, BUN=%34, Calcium=%7, Inorganic phosphate=%25, Magnesium=%13, ALT=%54, AST=%35, ALP=%19, GGT=%37, LDH=%25, CK=%64, amylase=%25, lipase=%90, Glucose=%16, Uric Acid=%24, Total Protein=%9, Albumin=%13, Total Bilirubin=%61, Direct Bilirubin=%102, respectively.

Conclusion: The use of RCV provides standardization of the validation of the patient results,and enables the laboratory specialist to concentrate on significant results.In addition, the use of RCV facilitates the detection of analytical errors.

PP-22

Vitamin D status of healtly women between 40-65 years: association with Parathroid hormone, biochemical bone markers and Bone Mineral Density

Medine Alpdemir[1], Mehmet Fatih Alpdemir[1], Rukiye Yazıcı[2], Emre İşpir[1]

[1]Clinical Biochemistry Laboratory, Balıkesir State Hospital, Balıkesir

[2]Department of Physical Therapy and Rehabilitation, Balıkesir State Hospital, Balıkesir

Objective: Vitamin D is effective in calcium absorption and bone metabolism. Our aim in this study is to determine the levels of vitamin D in healthy women aged 40-65, correlate with parathyroid hormone, biochemical bone markers and bone mineral density levels.

Materials and Methods: A total of 60 female patients with ages ranging from 40 to 65 years attending to the Polyclinic of the Physical Therapy and Rehabilitation Policlinic of Balıkesir State Hospital participated in the study. Serum 25 (OH) vitamin D, parathyroid hormone (PTH), alkaline phosphatase (ALP), calcium (Ca) and phosphorus (P) levels and bone mineral densitometry were examined in all patients. Body mass indexes (BMI) were calculated (kg/m^2). Vitamin D insufficiency was considered to be below 20 ng/ml.

Results: The mean vitamin D level of the patients was 10.97±6.25 ng/ml. The mean age was 51.06±9.5. There was no correlation between vitamin D levels and age, Ca, P, ALP and VKI. 25 (OH) vitamin D and bone mineral densitometry total lumbar vertebra (L1-L4) and femur neck measurements. However, there was a negative correlation with PTH level. The prevalence of 25 (OH) vitamin D deficiency was 89.8%.

Conclusion: According to our results, very common D vitamin deficiency was seen in healthy women aged 40-65 years. D vitamin deficiency was not had a negative effect on bone mineral density.

PP-23

Serum Vitamin D Levels in Women Patients with Androgenetic Alopecia

Ebru Yorulmaz Ertuğ[1], Ruken Alp Yılmaz[2]

[1]Departments of Clinical Biochemistry and [2]Dermatology, Çerkezköy State Hospital, Tekirdağ

Objective: Androgenetic alopecia is an androgen-dependent progressive hair loss of the scalp in genetically predisposed both male and female patients.It creates serious emotional stress with aesthetic concerns. It is characterized by diffuse reduction in hair density over the crown and frontal scalp with retention of frontal hairline and characteristic pattern distribution in women. The effect of vitaminD on hair cycle has not yet been clarified.It is thought that vitaminD supports hair follicles differentiation. The aim of this study was to examine serum vitaminD levels in female patients with AGA, and to investigate its possible role in the disease pathogenesis.

Materials and Methods: This study was designed as case-control study. The study included totally 117 female patients; 62 in the AGA group and 55 in the control group who presented to Dermatology outpatient clinic of Çerkezköy Hospital who were aged between 18–45 years (mean age 29.41±8.71 years). All patients and controls were studied during the same period to avoid seasonal variations in vitaminD (2016 November-2017

March). Study exclusion criteria were history of surgical operation, pregnancy, breast-feeding, presence of systemic disease, serious weight loss, being on a low-calorie diet, receiving vitamin d and calcium supplementation, presence of menstrual irregularities, and usingdrugs that could induce hair loss. All patients were examined by the same dermatologist. AGA was diagnosed on the basis of detailed patient history and physical examination.

Results: Patients with AGA (18±11.92 ng/ml) had significantly lower serum vitamin D concentrations compared to the controls (27.38±11.69 ng/ml) (p=0.001). We performed binary multivariate logistic regression analysis to identify risk factors for hair loss, and the results indicated vitaminD is significant predictor of hair loss (OR=3.52, p=0.001).

Conclusion: The fact that vitaminD levels were significantly low in AGA patients suggests that it may also play a role in pathogenesis of disease. In patients with complaints of hair loss, elimination of deficiency may be useful in the treatment of AGA, by looking at vitaminD levels.

PP-24

Diurnal Variation of Coagulation Tests

Fatma Demet Arslan[1], Alperen Halil İhtiyar[2], Mehmet Hicri Köseoğlu[3]

[1]Department of Medical Biochemistry, Tepecik Training and Research Hospital, İzmir

[2]Department of Medical Biochemistry, Selahaddin Eyyubi State Hospital, Diyarbakır

[3]Department of Medical Biochemistry, Atatürk Training and Research Hospital, İzmir

Objective: Active partial thromboplastin time (APTT), prothrombin time (PT) and plasma fibrinogen level used in follow-up of bleeding diathesis could be evaluated at any time of day. In our study, the change of these three coagulation parameters during the day was investigated.

Materials and Methods: Blood samples were taken from 15 healthy adult volunteers (10 males, 5 females) at 09.00, 10.00, 11.00, 12.00, 15.00, 18.00 and 24.00 o'clock. The samples taken at 09.00 am were accepted as basal. The results of APTT, PT ve fibrinogenobtained at the different times of the day were statistically and clinically compared to the results obtained at 09.00 am.

Results: In our study, APTT values were highest at 09.00 a.m. and and the other APTT results were significantly higher than baseline (maximum -16.1%). PT values were lowest at 09.00 a.m. and when compared to the baseline, clinically significant differences were seen in samples taken at 10.00,11.00, 12.00 and 24.00 in for PT results (5.41%, 2.7%, 2.7% and 3.6%, respectively). In the fibrinogen values, there was a clinically and statistically significant difference between the samples taken at 10.00 and 24.00 (-5.42% and -6.44%, respectively).

Conclusion: According to our study, coagulation parameters have a significant variation within day and the results of these tests should be interpreted according to these variations.

PP-25

Diurnal Variation of Calcium, Phosphorus, Magnesium, PTH and Vitamin D Levels

Alperen Halil İhtiyar[1], Fatma Demet Arslan[2], Mehmet Hicri Köseoğlu[3]

[1]Department of Medical Biochemistry, Selahaddin Eyyubi State Hospital, Diyarbakır

[2]Department of Medical Biochemistry, Tepecik Training and Research Hospital, İzmir

[3]Department of Medical Biochemistry, Atatürk Training and Research Hospital, İzmir

Objective: Parathyroid hormone (PTH) and vitamin Dplay an important role in the regulation of calcium homeostasis. Tests related to calcium metabolism were evaluated at any time of day. There could be some variations at these different time intervals in a day. In order to make a correct and reliable decision on the diagnosis and follow-up of patients, the clinical significance of these variations should be known.

Materials and Methods: Blood samples were taken from 17 healthy adult volunteers (11 males, 6 females) at 09.00, 10.00, 11.00, 12.00, 15.00, 18.00 and 24.00 o'clock. The samples taken at 09.00 am were accepted as basal. The results of PTH, vitamin D, calcium, phosphor and magnesium obtained at the different times of the day were statistically and clinically compared to the results obtained at 09.00am.

Results: There was no clinically significant difference in vitamin D level during the day. While PTH and phosphor levels were the lowest at 10.00 o'clock. (–46.78% and –10.31%, respectively), they increased steadily until 24.00 o'clock. An increase (5.33%) for magnesium levels were observed until 24.00 o'clock. in a day. The bias for calcium was found between 1.07% and 2.15% at the other hours, except 18.00 o'clock.

Conclusion: According to our study, PTH, phosphate (phosphor), magnesium and calcium concentrations have a significant variation within day and the results of these tests should be interpreted according to these variations.

PP-26

The Results of Intervention Within Rational Use of Vitamin D Test Requests in May 2018 at ANEAH

Arzu Sakallı, Ortaç Ateş, Uğurcan Eker, Turan Turhan

Department of Medical Biochemistry, Ankara Numune Education and Research Hospital, Ankara

Objective: Particular attention is given to the control of costs through the appropriate use of scarce resources in the health care for diagnostic tests. Awareness of vitamin D deficiency, which is considered to be a pandemic of this epoch, also increases in our country. Increased number of test requests and costs add extra financial burden to our healthcare system. In our hospital in order to rational use of vitamin D test requests, a warning page was came upon the prompt screen when the clinician requested a second vitamin D test from the same patient. The aim of this study is to analyze the effect of the intervention on the test request rate.

Materials and Methods: D vitamin test request rates were analyzed retrospectively and estimated their costs. Prior to the intervention of D vitamin tests of this year, the outpatient labor process and post-intervention response rates were compared with each other and their distributions were calculated.

Results: Between August 2016 and July 2017, 71.566 D vitamin tests (3.78%) were performed in our hospital and it was costed 707172 TL. Between August 2017 and July 2018 74721 D vitamin tests (3.76%) were performed and it was costed 738348 TL. 8502 D vitamins were tested in March 2018 before the intervention. In April 4541 were tested and were only sent to external laboratories. After our intervention 5205 tests were performed during May.

Conclusion: Since the number of vitamin D tests has increased significantly in our country, it appears that despite the increasing number of patients, the intervention made allows the request rate to remain at a constant value. Due to the intervention a low increase occur in costs.

PP-27

Reject Statics of Ankara Numune of Education and Research Hospital For 4 Years: Retrospective Overview

Nebi Yılmaz, Muhammed Fevzi Kılınçkaya, Turan Turhan

UHS Ankara Training And Research Hospital, Clinic of Medical Chemistry, Ankara

Objective: The preanalytical phase is known as phase in which most mistakes are made in biochemistry laboratories. Improper samples are rejected in preanalytical analytical phase. In the case of rejected samples, there is an increase in turnaround time, standby time and cost in the test request-result. Our study aimed to examine 4-year rejection rates of the Ankara Numune Training and Research Hospital Medical Biochemistry Laboratory.

Materials and Methods: In our laboratory, the number of patient samples rejected between 2014-2017, demographic characteristics of the patients, outpatient clinics and the reasons for rejection were obtained from laboratory information system. Data were analyzed retrospectively. The total number of rejected samples, reason for rejection was calculated.

Results: Total of 42.448 tubes were rejected over a period of four years. While the samples rejected in 2014 constituted 24.5% of all samples (n=10.416), total of 11.479 tubes were rejected in 2017 (27.0%). While the most frequent reason for rejected is clotted sample (n=16.922), insufficient sample is second (n=13.898). When rejected samples are viewed from the services they receive, emergency service was the most frequent service of rejected samples (25.7%) followed by intensive care units (14.2%).

Conclusion: As can be seen from the results, large part of the preanalytical errors constitute preventable causes. In services where sample reject rates are relatively high, more effort is needed to keep the equipment in view, to inform clinician about correct testing, to take corrective-preventive actions like health care personnel and laboratory staff, to manage the process in the preanalytic stage in the best possible way. Importance of the preanalytic phase in the total test process is now better known. In this context, some qualification tests such as external quality control have begun to be applied for preanalytical phase.

PP-28

The Decision Making Levels of Urine Tetrasaccharide For Diagnosis of Pompe Disease

Erhan Canbay[1], Melisa Vural[1], Sema Kalkan Uçar[1], Ebru Demirel Sezer[2], Mahmut Çöker[1], Eser Yıldırım Sözmen[2]

[1]Departments of Medical Biochemistry and [2]Pediatric Metabolism, Ege University Faculty of Medicine, İzmir

Objective: Recently, urinary excretion of the tetrasaccharide 6-α-D-glucopyranosyl-maltotriose (Glc4) has been proposed as a marker for diagnosis and monitoring of Pompe disease. We aimed to determine reliable decision making levels of urine tetrasaccharide concentrations for diagnosis of Infantile- and Late-Onset Pompe patients.

Materials and Methods: 8 patients with Pompe disease (4 of them with Late-onset Pompe disease) and 150 healthy controls were included into this study. Urine tetrasaccharide concentrations were determined using UHPLC MS/MS method.

Results: Tetrasacharide level of Pompe patients were 42±14 mmol/mol creatinine for Infantil onset (aging 4.5±3.5) and 3.7±1.5 mmol/mol creatinine for Late-onset (aging 32±10). Our data showed that urine tetrasacharide level of healthy subjects decreased by aging. Especially it was high in first year of life compared to olders.

Conclusion: The result from this study suggests that decision levels should be defined by age especially for diagnosis of late onset Pompe disease.

PP-29

Appropriate External Quality Control Application For Blood Gas Analysers

Hacer Bilgin Topaloğlu, Ebru Yaprak , Merve Türker, Medeni Arpa

Department of Medical Biochemistry, Recep Tayyip Erdoğan University, Rize

Objective: Arterial blood gas analysis has an important role in determining the etiology and severity of diseases for evaluation of critical patients. In terms of assessment of acid-base balance and respiratory balances, partial arterial blood oxygen pressure (PaO_2), partial carbondioxide pressure ($PaCO_2$), oxygen saturation (SaO_2), measurement of pH, and bicarbonate levels are analysed by blood gas analysers (1)It is important to ensure the reliability of these tests. In some hospitals, one external quality control sample can use for multiple analysers.Its aimed in this study to exhibit how blood gas tests changed in this case.

Materials and Methods: Four blood gas analysers (ABL series, Radiometer) that placed two locations by two analysers (A, B, C, and D) were used for the study.In first study design pH, pCO_2, pO_2, K, Na, Cl, iCa, glucose, and lactate tests were performed on analysers from one location to the other location (A→D) with same external quality sample by order then reversely (D→A) with another sample on four analysers.And the second study design performed with two samples and two analysers.Each sample applied four times for same tests above to each analyser.Prior to the analyzes, proper calibration and internal quality controls performed for per analysers.Then the evaluation done according to the external quality assessment program results as percent difference from the peer group mean.

Results: In the first study there was an evident difference between different located analysers; an increase in pH measurement and a decrease in pCO_2 measurements. No unacceptable change in other tests.Also in the

second study an increase in pH and a decrease in pCO_2 between first two run and last two runs detected.No unacceptable change in other tests.

Conclusion: Laboratories that have multiple blood gas analysers are recommended to use separate external quality control samples for each analyser for appropriate external quality control application.

PP-30

Diagnostic Evaluation of Inherited Metabolic Diseases by Cases

Fatma Demet Arslan[1], Aybike Günaslan Hastürk[1], Burcu Hışmi Öztürk[2], Pınar Gençpınar[3], Nihal Olgaç Dündar[3], Fatih Durak[4], Ayşe Berna Anıl[4], Eren Soyaltın[5], Seçil Çamlar[5], Belde Kasap Demir[5], Banu İşbilen Başok[1]

[1]Departments of Medical Biochemistry and [2]Pediatric Metabolism Clinic, University of Health Sciences, Tepecik Training and Research Hospital, İzmir

[3]Departments of Pediatric Neurology, [4]Pediatric Intensive Care Clinic and [5]Pediatric Nephrology Clinic, Katip Çelebi University, İzmir

Objective: Clinical evaluation of laboratory results is important to diagnose metabolic diseases. For this reason, we aimed to evaluate the three cases that have been admitted by the pediatric clinics and whose tests were performed in our metabolism laboratory. A 8-years-old girl with microcephaly, mental-motor retardation, edema in face, feet and hands was hospitalized due to hypokalemia, hypophosphatemia, glycosuria, and proteinuria. There was epilepsy diagnosis in patient history. Family history reveals that the presence of a second-degree intermarriage and a girl sibling with the similar clinic. Pyruvate carboxylase deficiency was considered due to elevated urine lactate/pyruvate ratio and fumaric acid in organic acid analysis and the high plasma alanine in amino acid analysis. A 1.5-years-old boy was admitted to the pediatric neurology outpatient clinic with motor retardation. There was second-degree intermarriage in the family history. The peroxisomal disease diagnosis was considered due to the presence of periventricular dysmyelinated areas in imaging studies and due to the presence of elevated plasma phytanic acid in fatty acid analysis. Hypotonia, hepatomegaly, liver dysfunction and renal tubulopathy were detected in a 1-year-old girl who was hospitalized with fever, diarrhea and vomitings. Family history reveals that the presence of a second-degree intermarriage. Medium-chain acyl- CoA dehydrogenase deficiency was considered due to the increase of urine 3-OH sebacic acid, sebacic acid, adipic acid and suberic acid in organic acid analysis. It is necessary to confirm the diagnosis of a patient who has clinical findings lead to a suspicion for a metabolic disorder in collaboration between clinicians and laboratorians, including medical geneticists. Therefore, the multidisciplinary approach will be completed on rare metabolic diseases.

PP-31

The Post-Analytic Effect of Procalsitonin; Can It Be Calculated?

Gülay Ok[1], Serkan Erdal[2], Çiğdem Banu Çetin[3], Cevval Ulman[2]

[1]Departments of Anesthesiology and Reanimation, [2]Medical Biochemisty and [3]İnfectious Diseases, Manisa Celal Bayar University, Faculty of Medicine, Manisa

Objective: Procalsitonin has emerged as a biomarker for bacterial infection and sepsis.The purpose of this study is to evaluate the post analytic effect of procalsitonin internal medicine intensive care unit (ICU) of Manisa Celal Bayar University Hafsa Sultan Hospital. To assest the post analytical effect of our procalsitonin results, we calculated the laboratory turn around time (TAT) for procalsitonin and reviewed the records of consultations to Infection Diseases Department.

Materials and Methods: We reviewed the data of patients in the internal medicine ICU about procalsitonin in December 2017. 2.2 ng/ml procalcitonin result was considered the clinical suspection valuefor sepsis.In the post analytical process assesment; we calculated the TAT as the time from laboratory admission to results approval andapproval of procalcitonin result to consultation request.The data of fourty eight patients consultation was obtained.The data of patients who had consultation for antibiotics and consultation prior to procalcitonin request were excluded from the study. From the remaining twenty two; ten of these had procalsitonin level above 2.2 ng/ml. The data of eight patients whose consultation request were within 24 hours of procalsitonin approval were examined.

Results: The number of patients in ICU who had procalsitonin result above 2.2 ng/ml in December 2017 was twenty. Average TAT of our laboratory for eight patients was 59 min; 25-121 min (min-max). Average period of approval of procalcitonin result to consultation lapse is 6 hours 42 min (422 min); 106-1481 min (min-max).

Conclusion: The results of procalcitonin over 2.2 ng/ml suspecting sepsis may post analytically influence patient treatment. We believe procalcitonin could be included in the alert list where immediate communication of values stipulated by the laboratory are of critical importance.It would be wise to review the post analytical effect of tests that will enable laboratory directors to customize the process with the clinicians.

PP-32

5-Year Retrospective Analysis of Patients Whom Had Ordered Blood Ethanol Concentration

Muhammed Fevzi Kılınçkaya, Çiğdem Yücel, Turan Turhan

Department of Clinic of Medical Chemistry, UHS Ankara Training and Research Hospital, Ankara

Objective: Ethanol is the most commonly used addictive substance and the frequency of referral due to the emergencey service intake of ethanol is increasing. In the US, more than half of the adult population reported using ethanol. In addition to the above-mentioned problems, the effects of alcohol on the central nervous system lead to a decrease in the driving ability of the persons, followed by traffic accidents. Alcohol reaches peak concentration within 60 minutes following ingestion. The ethanol concentration is reduced by about 15-20 mg/dL per hour. The aim of this study is to retrospectively evaluate the demographic characteristics, ethanol concentration distributions in the Ankara Numune Training and Research Hospital (ANEAH) between 2013-2017.

Materials and Methods: Between 2013-2017 all patients with ethanol intolerance in ANEAH were included in the study. When the requested service was divided into the Emergency Service and others, two groups

were divided into ethanol concentrations of 10-49 mg/dL and ≥50 mg/dL. Etanol demand reasons were divided into two groups, the Judicial Incident and the others. A total of 6073 patients were studied over a period of 5 years.

Results: The mean blood ethanol concentration of these patients was 179.94±96.86. While 83% of the patients are male, 61.7% of the patient diagnoses are forensic reasons. 99.7% of the requests were made in emergency services, 89.5% of patients had a blood ethanol concentration of 50 mg/dL and above.

Conclusion: Our work is important for a long period of time. Accurate measurement and reporting of blood ethanol concentration is important, especially for judicial events.

PP-33

Evaluation of Patients Who Were Applied AMATEM: 3-Year Retrospective Analysis

Muhammed Fevzi Kılınçkaya, Turan Turhan

Department of Clinic of Medical Chemistry, UHS Ankara Training and Research Hospital, Ankara

The prevalence of substance use and related disorders in the world and in our country is increasing steadily. In a study conducted in our country, the rate of substance use at least once during life was 80.2% for cigarettes, 31.9% for alcohol and 3.6% for other addictive substances. In a screening study conducted in the US between 1990 and 1992, lifetime prevalence rates for substance use were 1.1% for heroin, 8.7% for hallucinogens, 11.3% for cocaine, 33.7% for marijuana, and 37.2% for any illegal substance. Alcohol and substance use disorders are frequently accompanied by other psychopathologies, and the appearance of identities of the identities affects the course and course of treatment. In this study, it was aimed to investigate the demographic characteristics and the diagnoses of patients with blood ethanol concentration of ≥10 mg/dL in a training research hospital AMATEM clinic over a period of three years. A total of 248 cases of ethanol were studied over a 3-year period. The mean age of these patients is 41.34±11.03. When the patients' diagnoses were examined, alcohol dependence was found in 60.9% of the patients, while 95.2% of the patients were male. Considering that the number of patients who meet the diagnosis of alcohol and substance use disorders is increasing in our country and that various initiatives are underway under the leadership of the Ministry of Health in order to facilitate their access to treatment, there is a need for additional research that can be evaluated by comparing the sociodemographic and clinical characteristics and treatment choices of patients with various AMATEMs in our country it can be said researchs can constitute a step in this direction.

PP-34

Helicobacter Pylori Infection in β-Thalassemia Major Patients

Ayşegül Uğur Kurtoğlu[1], Erdal Kurtoğlu[2], Volkan Karakuş[3]

[1]Departments of Biochemistry and [2]Hematology, SUAM Antalya Education and Research Hospital; Antalya

[3]Department of Hematology, Muğla Sıtkı Koçman University, Antalya

Objective: Patients with β-TM are in greater risk for infectious diseases due to multiple causative factors and infections constitute the second most common cause of mortality in thalassemia. In this study we aimed to investigate the prevalance of H.pylori infection in β-TM patients.

Materials and Methods: This study was carried out on 51 β-TM patients and 25 healthy volunteers. Samples were analysed by qualitative membrane-based immunochromatographic The analyses were carried out promptly including a complete blood count (CBC) that was performed for all patients and control subjects using a hematology analyzer (Coulter LH 780 Analyzer, Beckman Coulter). Serum ferritin levels were measured by chemoluminescence immunoassay method in Beckmann Coulter DXI instrument, as ng/ml.

Results: H.pylori infection was detected in 2 (%4) of 51 patients. Ferritin levels of two H.pylori infected patients were 530 and 2133 ng/mL. H.pylori infection was detected only in one (%4) of 25 healthy controls. There was no statistically significant difference between the patient and control groups regarding H.pylori positivity. There was no statistically significant difference between the patient and control groups regarding H.pylori positivity.

Conclusion: H.pylori infection is seen in similar ratio in both β-TM patients and healthy population.

PP-35

The Role and the Importance of Early Diagnosis with Upper Gastrointestinal Bleedings

Tuncay Seyrekel

Department of Medical Biochemistry, Yozgat City Hospital, Yozgat

Objective: Upper Gastrointestinal system (UGS) bleedings appear as a serious, common problem. When UGS bleeding happens, it means the illness that has caused the bleeding is advanced and the treatment is uneasy. In this study we tried to discover if there are any other early stage symptoms of a probable bleeding other than commonly known parameters such as; coagulation factors, bleeding diathesis tests.

Materials and Methods: Amongst the 2026 patients whose samples are sent to our laboratory from gastroenterology departmant between 01.04.2018 and 30.05.2018, 28 of them are diagnosed with UGS Hemorrhage and their all laboratory studies are examined retrospectively. (oldest result dated back to 02.09.2005 and there were 728 samples).

Results: The most rapidly spoiling parameter was urea(each rate was %25 higher than the previous one). Albumin was observed to decrease 50 percent. The last parameter that we declared as spoiled was calcium and the decrease was %20 with it. Findings like anemia, clotting disorders were present with all advanced type of patients.

Conclusion: Urea increase and calcium decrease should especially be watched with the patients whose clinical chart is unsettled. As much as urea increase may seem more likely to be the result of a kidney disease, UGS Hemorrhage probability should not be ignored.

PP-36

The Serum Levels of Klotho, Fibroblast Growth Factor-23 and Vitamin D in Multiple Sclerosis Patients

Esin Eren[1], Hamit Yaşar Ellidağ[1], Necat Yılmaz[1], Fatma Kurtuluş[2], Özgür Aydın[1], Ayça İnci[3], Süleyman Dolu[3], Aylin Yaman[2]

[1]Departments of Biochemistry, [2]Neurology and [3]Nephrology, Antalya Education and Research Hospital, Antalya

Objective: The klotho (Klt)-fibroblast growth factor-23 (FGF-23)-vitamin D axis is the main component of calcium (Ca) and phosphorus (P) metabolisms; on the contrary, it is also secreted from the choroid plexus (CP). This study is aimed at evaluating serum soluble Klt (sKlt), FGF-23, and 25-(OH)-vitamin D levels in multiple sclerosis (MS) patients.

Materials and Methods: Methods: Thirty-two relapsing-remitting MS patients (11 males and 21 females; mean age 38.3 years) and 31 age-sex matched healthy controls (12 males and 19 females; median age 38.5 years) were included in this study. All patients were diagnosed with MS according to the criteria of McDonald.

Results: Serum sKlt, FGF-23, and P levels were significantly higher in MS patients compared to the control group ($p<0.01$, $p<0.01$, and $p=0.02$, respectively). Serum 25-(OH)-vitamin D and Ca levels were significantly lower in MS patients ($p<0.01$ and $p=0.04$, respectively).

Conclusion: Klt, which is secreted from CP, could be a response to the inflammatory condition in MS. Elevated FGF-23 levels suppress 1α-hydroxylase and upregulates 24α-hydroxylase, which results in a decrease in 1.25-(OH)2D3 levels. Thus, the neuroprotective and immunomodulatory effects of vitamin D might not be seen in MS patients.

PP-37

Thyoredoxine System in Coronary Artery Disease and Type 2 Diabetes Mellitus

Esin Eren[1], Necat Yılmaz[1], Hamit Yaşar Ellidağ[1], Cihan Demir[1], Selçuk Küçükseymen[2]

[1]Departments of Biochemistry and [2]Cardiology, Antalya Education and Research Hospital, Antalya

Objective: In this study, the relation between Thioredoxin System (Thioredoxin and Thioredoxin Reductase and Thioredoxin-Interacting Protein levels) and serum lipid levels are investigated in patients diagnosed with type 2 DM and Coronary Artery Disease (CAD) by coronary angiography and compared with those who have no CAD.

Materials and Methods: Eighty-nine participants undergoing elective coronary angiography (CAG) were divided into DM+CAD, CAD alone and control groups. Demographic and clinical profiles, serum thioredoxin system protein concentrations, lipid profiles, some biochemical and hormonal parameters were compared in three groups.

Results: There was no difference between the groups in terms of thioredoxin system. Lipid profile, insulin resistance were not different between the groups. Serum uric acid and creatinine levels in the diabetic group were higher than the other groups ($p=0.011$ and $p=0.029$). There was a significant positive correlation between thioredoxin system proteins and TXNIP ($p<0.001$).

Conclusion: No significant differences between the groups in terms of proteins and TXNIP concentrations and lipid profiles of the thioredoxin system were found to be incompatible with previous findings of lipid oxidation and oxidative stress markers in atherosclerotic pathogenesis.

PP-38

Thioredoxin and Thioredoxin-Binding Proteins in Patients with Gestational Diabetes Mellitus

Necat Yılmaz[1], Esin Eren[1], Hamit Yaşar Ellidağ[1], Onur Erol[2]

[1]Department of Biochemistry and [2]Obstetric and Gynecology, Antalya Education and Research Hospital, Antalya

Objective: This study examined the clinical and biological significance of thioredoxin (Trx) and thioredoxin-binding protein (TrxBP), which are redox-active proteins that control multiple biological functions, in gestational diabetes.

Materials and Methods: We measured serum concentrations of Trx, TrxBP, insulin and other blood parameters, as well as insulin resistance and glucose tolerance in pregnant women with or without gestational dieabetes mellitus (GDM) (34/34) at the early second trimester.

Results: Serum TrxBP levels were lower in women with GDM than healthy pregnant controls. The serum insulin concentrations were higher in GDM, but the difference was not statistically significant. Serum redox potential ratio (Trx/TrxBP) of GDM patients was higher than that of the control group.

Conclusion: Our results suggest that the Trx/TrxBP system may mediate a compensating mechanism in GDM. Reduced TrxBP levels and consequent enhanced Trx activity may alleviate oxidative stress and may protect the foetus from oxidative stress.

PP-39

Effects on Coagulation Tests of Blood Volume Level and Waiting Period

Selin Onur, Fatma Demet Arslan, Banu İşbilen Başok

University of Health Sciences, Tepecik Training and Research Hospital, İzmir

Objective: To be able to report correct and reliable results, it's necessary to determine and to minimize the preanalytical errors. We aimed to evaluate the effects of two most common preanalytical errors, missing volume and prolonged waiting time on coagulation analysis according to bias, significant change limit(SCL) and reference change value(RCV).

Materials and Methods: Blood samples of 6 healthy volunteers collected into a blood tube (Becton-Dickinson, USA) containing 3.2% sodium citrate and a 10 mL injector. Prothrombin time(PTZ), activated partial thromboplastin time(aPTT) and fibrinogen were measured in 90.(basal), 120., 150., 180. and 210. minutes. These tests were also analyzed at 90 minutes after transferring and filling at the portions of 100%(basal), %90, %80, %70, %60 and %50 into sodium citrate tubes. Each measurement was compared with the basal level according to bias, SCL, and RCV.

Results: PTZ was not influenced by tube filling rate. In the waiting period, it started to affect from 180th minute according to bias and 210th minute according to SCL. aPTT was beginning to be affected from the 80% tube filling rate according to the bias, 70% tube filling rate according to SCL and from the 60% tube filling rate according to RCV. In the waiting period, 150th minute for bias and 210th minute for SCL started to be affected. Fibrinogen has begun to be affected by 90% tube filling rate according to bias and SCL and was not influenced by tube filling rate according to RCV. aPTT and PTZ for RCV and fibrinogen in all three calculations was not affected by waiting time up to 210 minutes.

Conclusion: When the results were compared, it was seen that bias was first, then SCL and last RCV were exceeded. PTZ in terms of sample volume and fibrinogen in terms of stability did not change in 3 methods.

PP-40

Sample Matrix Effect on Biochemical Test Parameters

Zeynep Levent Çıraklı, Soner Erdin, Nilgün Işıksaçan, Şebnem Tekin Neijmann, Alev Kural

Department of Medical Biochemistry, Laboratory of Health Sciences University Bakırkoy Dr. Sadi Konuk Education and Research Hospital, İstanbul

Objective: Recently, plasma matrix is widely used for providing rapid turnaround times (TAT) for clinical biochemistry tests in emergency laboratories. The aim of this study is to compare the biochemical test results of serum samples with plasma samples which obtained from two blood collection tubes one of them containing a mechanical separator and another containing a gel separator.

Materials and Methods: After informed consent, three additional blood specimens were collected from 29 adult patients visiting the outpatient clinics of Bakirkoy Dr. Sadi Konuk Training and Research Hospital. [1. Clot-activator included tube with gel (Z serum sep clot activator, Greiner Bio-one) (control group), 2. Lithium heparinized tube with gel (Greiner Bio-one) (group 1) 3. Lithium heparinized tube with a mechanical barrier (Becton Dickenson) (group 2)]. The tubes clot-activator with gel were centrifuged after 60 minutes at 19ºC for 10 minutes at 3500xg. Other tubes were instantly centrifuged under same condition for 5 minutes. The serum and lithium-heparinized plasma samples were assayed for 18 clinical chemistry tests using Beckman Coulter AU 5800 autoanalyzer. Test results in different tubes were compared with the control tubes. The results were evaluated within a 95% CI and the intraclass correlation coefficient of the biochemical parameters was between 0.77 and 0.99. The bias % was determined with the formula.

Results: In this study, glucose, creatinin, aspartate aminotransferase, lactate dehydrogenase, total protein, gamma glutamyl transferase, iron, calcium, phosphorus, sodium, potassium had a significant bias in both group 1 and group 2, urea in group 1, bilirubin, direct and amylase in group 2.

Conclusion: In recent years many healthcare institutions for the short turnaround service performance have converted to the use of plasma instead of to use of serum. It is important for each laboratory to verify the appropriate test reference range for the blood collection tube used.

PP-41

The Investigation of the Relationship Between the Activity of Juvenile İdiopathic Arthritis Disease and Adiponectin Levels

Oktay Çalışkan[1], Kenan Barut[2], Sezgin Şahin[2], Almira Adroviç[2], Özgür Kasapçopur[2], Mine Kucur[1]

[1]Departments of Medical Biochemistry and [2]Pediatrics, İstanbul University, Cerrahpaşa, Cerrahpaşa Medical Faculty, İstanbul

Objective: Juvenile idiopathic arthritis (JIA) consists of a group of heterogeneous disorders of chronic arthritis in childhoodwith no apparent cause. In the current study, we aimed to investigate the possible association of serum adiponectin levels with rutin laboratory parameters (hemogram, erythrocyte sedimentation rate-ESR and C reactive protein-CRP) which are frequently used to monitorize the disease activity.

Materials and Methods: In this study 87 children (male: 37, female: 50, mean ages: 9.26±3.98 years) with JIA that were monitorized at rheumatology clinic of Cerrahpasa Medical Faculty Children's Hospital, between March 2015 and November 2016, were included. Control group (n=50) was selected from healthy child clinic (male: 27, female: 23, mean ages: 9.28±4.62 years) Serum adiponectin levels were measured by ELISA method. Complete blood count (Beckman Coulter LH780), ESH (Therma NE Linear) and CRP (Roche Cobas C 501) were also analyzed. Neutrophil/Lymphocyte ratio (NLO) was calculated by dividing the number of neutrophils by the number of lymphocytes. ANOVA, Student's t test, Pearson's Correlation test were calculated in SPSS20.0 for comparison of groups.

Results: There were statistically significant differences between the active, remission and control groups; respectively leukocyte count (p=0.002), neutrophil count (p<0.0001), percentage of neutrophils (p=0.006), percentage of lymphocytes (p=0.008), platelets (p<0.0001), NLO (p=0.003), ESR (p<0.0001), CRP (p<0.0001) and adiponectin (p=0.015) levels.

Conclusion: Serum levels of adiponectin establish a positive correlation between lenfocyte count, ESR and CRP which were used during the monitorisation of the therapy in both remission and active form of JIA. We can assume that adiponectin can be used as a prognostically valuable parameter in children with JIA.

PP-42

The Rational Test Ordering From Stat Laboratory

Mutlu Adıgüzel, İbrahim Murat Bolayırlı, Nesibe Esra Yaşar, Dildar Konukoğlu

Department of Medical Biochemistry, İstanbul University Cerrahpaşa, Cerrahpaşa Medical Faculty, İstanbul

Objective: Emergency biochemistry laboratories are established to present accurate and reliable test results as soon as possible to the patients and physicians in all the health institutions. In this study, s aimed to compare the test numbers ordered from Stat and Central Biochemistry Laboratories of Cerrahpaşa Medical Faculty, and to determine the distribution of test orders from stat laboratory according to the departments which makes test ordering.

Materials and Methods: We compared the test numbers ordered from Stat and Central Biochemistry Laboratories of I.U. Cerrahpaşa Medical Faculty in the first 6 months of 2017. The distribution of test ordering from stat laboratory according to the departments which makes test ordering was determined.

Results: In the first 6 months of 2017, 1029131 test were ordered from the stat laboratory and 1156040 tests were ordered from the central biochemistry laboratory. When we look at the distribution of some tests, glucose: 48921 (44%), urea: 55663 (37%), creatinine: 56772 (36%), total bilirubin: 44079 (57%), blood count: 55.017, prothrombin time: 26.314 (57%) parameter were ordered from the stat laboratory.Total, glucose:64430 (%56), urea: 98934 (%63), creatinine:102721 (%64), total bilirubin:33582 (%43), blood count: 74.437 (%57) were ordered from the central biochemistry laboratory. 370487 (36%) of the total 1029131 tests ordered from stat laboratory were requested from the emergency department and 658644 (64%) tests were ordered from the other inpatient and outpatient clinics.

Conclusion: When we look at our results, stat laboratory serves for inpatient and outpatient clinics more than the emergency unit. Our findings are compatible with the literatures. For improving the rational test ordering from stat laboratory, the dialogue between clinicians and laboratory specialists and the number of training programs for the rational test ordering should be increased.

PP-43

Point-of-Care (POC) and Central Laboratory Instrumentatıon: Four System Comparison in INR Monitoring

Asuman Gedikbaşı[1], Yıldız Okuturlar[2], Yüksel Gülen Çiçek[1], Nilgün Işıksaçan[1], Semih Korkut[3]

[1]Departments of Biochemistry and [2]Internal Medicine, Unıversity of Health Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, İstanbul

[3]T.C. Ministry of Health İstanbul Provincial Health Directorate Emergency Health Services, İstanbul

Objective: Anticoagulation therapy requires routine monitoring using the international normalized ratio (INR). Pointof-care testing (POCT) coagulometers are increasingly being used in the anticoagulation management centres. In this study, we compared two different POC devices with the two clinical laboratory method of determining prothrombin times (PT) and the associated INR.

Materials and Methods: We included 55 patients deemed eligible for POC monitoring according to the local protocol. All 55 patients were tested in capillary blood using the POC device (Xprecia Stride™, Siemens Healthcare and qLabs PT/INR Monitoring System, Micropoint Bioscience) and compared with that of venous plasma samples determined by the conventional methods with a photooptical system (Diagon CoagXL) and optomechanical clot detection system (Thrombolyzer XRC, Behnk Elektronik).

Results: We compared the INR values generated by the two sets of POC instruments with values obtained from the central laboratory coagulation analyzer. The mean INR measured with the Diagon CoagXL central laboratory coagulation analyzer was 3.08, with a standard deviation of 2,07 and a range from 0.97 to 14.3.The Diagon CoagXL instrument had higher mean INR values than the other central laboratory coagulation analyzer (mean 2.5 for the Thrombolyzer XRC instrument with a higher SD (of 1.3). Also, the range of INR values for Diagon CoagXL was greater for the POC instruments:from 1 to 7.9 (2.6+1.3) for the Xprecia and from 1 to 6.8 (2.5+1.1) for the Micropoint. The correlation coefficients for the POC instruments compared with the central laboratory Thrombolyzer XRC instrument were comparable for the two manufacturers' instruments: 0947, p 0.0001 for the Xprecia instruments and 0.940, p 0.001 for the Micropoint instruments.

Conclusion: POC INR testing may be helpful for patients in rural or remote settings or those who may be isolated for other reasons particularly if laboratory services are not easily accessible or INR results cannot be obtained in a timely manner.

PP-44

Evaluation of Test Quality According to Six Sigma Methodology

Nesibe Esra Yaşar, Ayşegül Özgenç, İbrahim Murat Bolayırlı, Dildar Konukoğlu

Department of Medical Biochemistry, İstanbul University-Cerrahpaşa Medical Faculty, İstanbul

Objective: The aim of this study is to evaluate the analytical process performance of the parameters by six sigma methodology.

Materials and Methods: In our study, the sigma values of 15 biochemical tests obtained from 2017 data of Fikret Biyal Medical Biochemistry Laboratory of Istanbul University-Cerrahpasa Faculty of Medicine were calculated. Bias was obtained from external quality control samples (KBUDEK); %CV were calculated with internal quality control (IQC) samples (PreciControl ClinChem) of level 1-2 (Roche Cobas c702, Module 1-2). TEa ratios determined by the TC.Ministry of Health were used.

Results: Module-1: For level 1 and 2, sigma value of total cholesterol was between 3-3.99. For level 1, sigma values of albumin, ALT, AST, chloride, creatinine, glucose, potassium, sodium, triglyceride, and urea were between 4-5.99; sigma values of ALP, HDL cholesterol, LDH and total protein were ≥6. For level 2, sigma values of chloride, creatinine, potassium, sodium, triglycerides, and urea were between 4-5.99; sigma values of albumin, ALP, ALT, AST, HDL cholesterol, glucose, LDH and total protein were ≥6. Module-2: For level 1, sigma values of chloride, potassium and total cholesterol were between 3-3.99; sigma values of albumin, ALT, AST, creatinine, sodium, and triglyceride were between 4-5.99; sigma values of ALP, HDL cholesterol, LDH, glucose and total protein were ≥6. For level 2, sigma values of chloride, creatinine, potassium, sodium, urea and total cholesterol were between 4-5.99; sigma values of albumin, ALP, ALT, AST, HDL cholesterol, glucose, LDH, triglyceride and total protein were ≥6. Sigma values of total cholesterol, triglyceride for level 1; chloride, potassium and glucose for level 2 varied between the modules.

Conclusion: As a result of this study, the analytical performances of both biochemistry modules were satisfactory according to the six sigma method. Sigma-based assessments can enable separate IQC and performance improvements for each analyzer and test.

PP-45

Association Between Monocyte, Neutrophil, Eosinophil, Lymphocyte Volume Levels and Rheumatoıd Arthritis

Abdullah Sivrikaya[1], Fikret Akyürek[1], Sedat Abuşoğlu[1], Süeda Uçar[2], Ali Ünlü[2]

[1]Department of Biochemistry, Selcuk University Faculty of Medicine, Konya

[2]Department of Biochemistry, Selcuk University Faculty of Medicine Alaaddin Keykubat Campus, Selçuklu, Konya

Objective: Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease characterized by joint inflammation and destruction. RA also can damage a wide variety of body systems, including the skin, eyes, lungs, heart and blood vessels. Volume values of different types of cells of the immune system, such as lymphocyte, eosinophil, neutrophil and monocytes, can be related with autoimmune disorders including rheumatoid arthritis. Therefore, the aim of the present study was to evaluate the association of monocyte, neutrophil, eosinophil and lymphocyte volume values, which are widely available hematological marker, with disease in patients with rheumatoid arthritis as retrospective data.

Materials and Methods: 206 patients with active RA patient aged 64.7±7.4 and 102 healthy patient in remission RA aged 64.1±9.8 years who were admitted to the polyclinic of rheumatology in faculty of Medicine of the Selcuk University have been included in the study. Volume units are expressed as fL.

Results: The lymphocyte volume levels were significantly lower in active RA patient 87.85±5.63 compared with patient in remission RA group 89.71±4.89 (p=0.003). The eosinophil, monocyte and neutrophil volume levels were as respectively 157.95±14.55, 170.57±10±79, 147.28±11.38 respectively in patients group and 160.31±7.78, 170.36±7.89, 148.06±7.89 respectively in control group. There was no statistically significant difference between the two groups with respect to eosinophil, monocyte and neutrophil volume levels.

Conclusion: According to this study's results, decreased lymphocyte volume values may be a potentially useful biomarker in patients with rheumatoid arthritis.