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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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Fax: +90 212 550 61 12
e-mail: info@karepb.com
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INTERNATIONAL CONGRESS & LAB EXPO 2019

2ND NATIONAL HEREDITARY METABOLIC DISEASES LABORATORY SYMPOSIUM

02 - 05 October 2019

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INTERNATIONAL CONGRESS & LAB EXPO 2019
2ND NATIONAL HEREDITARY METABOLIC DISEASES LABORATORY SYMPOSIUM

Dear Colleagues,

As Association of Clinical Biochemistry Experts, we are pround to be with you at KBUD International Congress & Lab Expo 2019.

We prepared a program in which we will follow scientific and technological developments in the field of biochemistry and clinical biochemistry and share our experiences. With the courses, conferences, panels and satellite symposiums in our program, we will have the opportunity to benefit from the knowledge and experience of very valuable national and international speakers.

We believe that our congress and symposium will make significant contributions the world of science. We would like to thank to all participants, all speakers, researchers and the diagnostic companies for their their participation.

Professor Dr. Dildar Konukoğlu

President

Association of Clinical Biochemistry Specialists

Conference

C-01

Immunofixation Electrophoresis

I. Murat Bolayirli

Department of Medical Biochemistry, Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Istanbul, Turkey

Immunofixation electrophoresis (IFE); is a combination of serum protein electrophoresis and immunoprecipitation techniques. It was especially used in the diagnosis of monoclonal gammopathies at the end of the 1970s. In addition to agarose gel in barbital buffer as support medium; human IgG, IgA, IgM, kappa and lambda light chain anti-sera are also used in IFE applications. Some factors like antigen excess, just heavy or light chain reactions, high titres of rheumatoid factor, heterophilic antibodies, C-reactive protein and fibrinogen make IFE difficult to interpret. Capillary electrophoresis which is used primarily for serum protein electrophoresis, is based on the separation of charged particles at different speeds in the electrical field. The application of immune typing to capillary electrophoresis systems has made the that technique become widespread. Capillary electrophoresis is a rapid method, suitable for automation, requires small sample volumes for analysis, has a lower detection limit and able to separate many molecules as small, large, charged and uncharged. Initially, the protein electrophoresis of the patient is analyzed in the capillary immune typing process. Subsequently, serum sample reacts to human IgG, IgA, IgM, kappa and lambda light chain anti-sera. In the antisera patterns, decreasing or disappearing fractions are detected according to the reference serum protein electrophoresis pattern. Excess amount of antigen, just heavy or light chain reactions, dilution problems and biclonal gammopathy are common difficulties for the interpretation of immune subtracticting technique.

As typing and quantification of monoclonal immunoglobulins is very important for the diagnosis, treatment and follow-up of diseases; IFE and capillary immunosubtracting assays are increasingly preferred laboratory order rather than others. They are frequently preferred by hematology, oncology, neurology, nephrology and rheumatology departments. Collaboration of the laboratory specialist and clinician is very important for the effective and widespread use and interpretation of these tests. Evidence of new interferences for the current methods (imaging agents, new agents entering treatment schemes) arises necessity of the medical laboratory for the development of new approaches.

C-02

Innovative Biochemistry (Biochemistry 4.0)

Ozcan Erel

Department of Biochemistry, AYBÜ & Ankara City Hospital, Ankara, Turkey

Innovation is the novelty of products, services and processes that provide economic or social benefits. Innovation is a mandatory way for institutions and governments to succeed, develop, increase their welfare, increase quality, increase productivity, improve employment and achieve sustainable economic growth. It is not enough to do what everyone else does or the like for sustainable success. In order to increase competitiveness in organizations, it is important to establish an innovation culture that will improve product, service, technology, quality, process and organization.

The innovation performance of our country is far behind compared to both western and East Asian countries. One of the most important reasons for this is the weakness of innovation culture in the state and social life.

We need innovative individuals for our future. This can only be achieved through training. A classical, repressive, rote, imitator and accepting education cannot be successful in the innovation process. There is a need for innovative, collaborative, productive and entrepreneurial biochemists who are able to see and analyze and critique the developments in the world, confident, questioning, investigating, taking risks, tolerating failure and communicating.

In medical biochemistry, the priority should also be given to innovation (Biochemistry 4.0) beside of routine services (Biochemistry 1.0), education (Biochemistry 2.0) and research activities (Biochemistry 3.0).

C-03

Nutrigenomic, Chronic Diseases and Cancer

Gultekin Yucel

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

Nutrigenomics deals with the relationship between nutrition and human genome. Nutrigenomic introduces the concept that nutrition affects the human genome, which means substances in foods that affect the genome. Diseases such as cancer formation, atherosclerosis and diabetes are the worse conditions those originate from the affected genomes. Cytocrom p 450 substances are very important in nutrigenomic point of view because a number of food, drug and chemicals are metabolized by cytochromes and a lot of metabolites are produced by cytochrome p 450 those interact with genome. Cytochrom polimorfizm is especially important in explaining the difference among people who smoke and use alchool may develop lung cancer and liver chyrosis or not. Nutrigenomic science must be evaluated together with epigenetic changes and microbiata. Epigenetics refers to hereditary changes in gene expression without alterations in the DNA sequence, resulting from changes between active and inactive genes. DNA methylation, histone modification, gene silencing with non coding RNA are the main mechanisms of epigenetics. Intestinal system contains the microbial mass called microbiata which affects metabolic response, defense mechanisms of the immune system and the general health status of the body. A lot of metabolites is produced by the action of microbiata from the foods taken, affecting susceptibility to diseases and health status. These metabolites act through epigenetic mechanisms. A healthy microbiata is created only with a healthy diet. Decreased calori intake and formation of healthy microbiata are very important for the protection of cancer and chronic disease. Further research based on evidence, is needed to investigate the carsinogenic or beneficial effect of foods, we are just in the beginning.

C-04

External Quality Assessment of HbA1c; Lessons Learnt and Future Prospects for Quality Targets

Cas Weykamp

Department of MCA Laboratory, IFCC Network Coordinator, Queen Beatrix Hospital, Winterswijk, the Netherlands

Due to economic growth life style has changed dramatically: people eat more and exercise less. In many persons this results in obesites, followed by diabetes. Numbers illustrate that there is a diabetes epidemic: by now there are worldwide about 400 million diabetic patients, this number will increase to about 650 million in twenty years. Prevalence in Turkey is about 12%. There is a need to diagnose diabetes soon and in an early stage. Therapy prevents or delays complications, treatment reduces com-

plications significantly. By now it is estimated that there is a gap of 7 years between onset and diagnosis and 25–30% of patients do already have irreversible complications at the time of diagnosis. Half of patients are undiagnosed.

Therapy is to keep glucose within limits and to achieve that physicians and patients rely on laboratory tests of which HbA1c is a very important one. Given the key position of HbA1c, good quality should be warranted by the laboratory. Standardisation is the starting point as this allows uniform clinical decision limits, uniform clinical guidelines and optimum patient care. Also, important: a standardised test promotes laboratory medicine and is as such beneficial for clinical chemists and manufacturers.

The IFCC achieved standardisation: a reference network and network of reference laboratories is in place. IFCC also developed a model for Quality Targets to set quality criteria for HbA1c. In this model the two important sources of error in the laboratory – bias and imprecision – are included. The model can be applied in a single laboratory but also in groups of laboratories e.g. countries or users of a specific method. The model is also used in another IFCC activity, the EurA1c Trial. Once a year national EQA/PT organiser use the same two samples. In 2018 25 national EQA/PT organisers, covering about 4000 laboratories participated. Among them Tubitak UME/Pamukkale University from Turkey. Results are evaluated overall, per country, per method and per method per country. In this way good performing tests can be distinguished from poor performing tests. The comparison of methods urges manufacturers to improve their test.

Due to the success of standardisation HbA1c has become the gold standard in diabetes managements. That is true for monitoring but HbA1c is also more and more used for screening and diagnosis. Although there is still discussion on the use for diagnosis. The major reason is that there is only a small difference between normal and diabetic HbA1c concentrations. A small error does already have a high impact on interpretation. In the daily practice of the author 25% of results is interpreted as normal. If the lab would have had a positive or negative bias of 3 mmol/mol (0.3% in NGSP units), 36 and 12% of the results would have been interpreted as normal. In the opinion of the author, total error of HbA1c should be limited to 3 mmol/mol (0.3%) when HbA1c is used for screening and diagnosis.

Another hot topic is the use of point of care instruments for diagnosis. From the EurA1c trial it can be seen that some POCT instruments perform as well as laboratory instruments when used professionally. Therefor it can be concluded that POCT can conditionally be used for diagnosis. This implies professional handling, a system of internal and external quality control in place, good batch management taking into account a minimum throughput and expiry date, and an instrument that is IFCC- and NGSP certified.

C-05

Inherited Disorders of Autophagy: A New Category of Inborn Error of Metabolism

Carlo Dionisi-Vici

Division of Metabolism, Bambino Gesù Children's Hosptial IRCCS, Rome, Italy

Autophagy is a tightly regulated and highly conserved lysosomal degradative pathway, with important roles in cellular homeostasis including removal of apoptotic cells and unwanted or damaged proteins and organelles, metabolic adaptation and immune defense. The term autophagy derived from the Greek word αύτόφαγος [autóphagos], that means to 'self-devouring' or 'self-eating'. The autophagy pathway includes several steps, evolving from the initial formation of isolation membranes (or phagophores) to autophagosomes, which fuse with lysosomes resulting in the final structures of degradation, autolysosomes. Autophagy plays a fundamental role in cellular and tissue homeostasis and its function is mediated by evolutionarily conserved autophagy-related (ATG) genes. Autophagy-related molecules/proteins play important roles in cell metabolism including translocation and processing of endocytosed microorganisms, modulation of immune responses, membrane trafficking and signaling pathways. Three major forms of autophagy, that differ with respect to their mechanisms, physiological functions and cargo specificity, exists: chaperone mediated autophagy, microautophagy, and macroautophagy. Deficiencies in these processes may lead to disease in humans such as cancer, neurodegenerative disorders, immune/inflammatory disorders and even aging. Over the last years, over 20 genetic disorders, primarily affecting the autophagy pathway, have been discovered. This novel disease category of inborn errors of metabolism has a prominent involvement of central nervous system, causing developmental disabilities, epilepsy, neurodegeneration, CNS malformation, but can also cause multi-system manifestations affecting visceral organs, immune system, with storage disease phenotypes in some syndromes.

C-06

Adaptation of Reference Intervals to Routine Laboratories

Yesim Ozarda

Department of Clinical Biochemistry, Uludag Universitesi, School of Medicine, Bursa, Turkey
The IFCC Committee on Reference Intervals and Decision Limits

Reference intervals (RIs) are the most frequently used diagnostic tools presented by laboratories and used in the evaluation of laboratory tests. RIs are most commonly defined as the central 95% of laboratory test results expected in a healthy reference population. According to the International Organization for Standardization (ISO) 15189 standard for clinical laboratory accreditation states that each laboratory should periodically reevaluate its own RIs. Despite these requirements, RIs in most clinical laboratories generally couldn't find enough time, money and energy for their establishment. Therefore, instead of developing RIs directly from an apparently healthy population, most laboratories receive RIs for clinical use from various sources (e.g. manufacturers' package inserts, publications, textbooks, multicenter studies, published national or international expert panel recommendations, guidelines, local expert groups or data mining of existing data). However, several differences can exist between the sample collection procedures and laboratory operations of the laboratory originated RI study and the local laboratory receiving the RI. Therefore, it is of critical importance for a local laboratory to address the following question prior to receiving RIs from an external source: "Is this RI suitable for my laboratory's collection processes, method, and population?". The Clinical and Laboratory Standards Institute (CLSI), EP28-A3c guideline for "Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory"provides recommendations for transferring and verifying RIs established by external sources for a local laboratory. One of the most important of these is conducting a method comparison analysis in the laboratory that transfers RIs and making measurements from a relatively small number of healthy reference individuals (n=20) from the local population. Indirect methods are recommended in challenging groups, such as children and the elderly, where sampling is difficult. The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), Committee on Reference Intervals and Decision Limits has been working in recent years to obtain common RAs from multicentre studies, transfer and verify them to local laboratories.

C-07

CSF Biomarkers in Neurodegenerative Diseases

Nevin Ilhan

Department of Medical Biochemistry, Firat University Faculty of Medicine, Elazig, Turkey

Degenerative diseases of the central nervous system are very common and contribute significantly to morbidity and mortality. Neurodegenerative (ND) diseases are a broad class of complex diseases including Alzheimer's disease (AD), Parkinson's disease (PD), Amyotrophic lateral sclerosis (ALS), and Huntington's disease (HD). These diseases share a key neuropathological feature: the accumulation of fibril tangles of proteins resulting from the misfolding of proteins. At present, accumulation of misfolded proteins is considered a key event in the pathogenesis and progression of these neurodegenerative diseases. Proteins prone to misfolding include AD-associated amyloid-beta (Aβ); Tau associated with AD and frontotemporal dementia (FTD); α-synuclein associated with PH; and polyglutamine-containing proteins associated with HD.

Neurodegenerative diseases are chronic, progressively weakening and incurable. This disability of individuals with ND can persist for years, or even decades.

The prevalence of neurodegenerative diseases is increasing significantly in global aging populations and is expected to triple over the next 40 years and put a heavy burden on society and health systems in terms of both economic and human impacts. Therefore, there is an urgent need for early and reliable detection of ND diseases in order to improve the quality of life of patients and provide the necessary health and social care. Numerous quantitative, highly efficient technologies have recently been added to the search for liquid biomarkers. Reliable biomarkers can also facilitate the development of therapeutic agents to slow the progression of ND diseases.

Biomarkers are essential for early diagnosis, monitoring neurodegenerative disease progression, measuring responses to treatments, and classifying neurodegenerative diseases into different subtypes. In addition to imaging, a wide variety of molecular markers in tissues and bio-fluids are being investigated; moreover, they are prominent proteins found in most cerebrospinal fluid (CSF). CSF is produced by interstitial fluid originating partly from the choroid plexus and partly from the brain parenchyma. CSF is in direct contact with the brain and therefore many changes in brain metabolism are reflected in CSF. It is used as a promising, ideal source for biomarkers of different neurological and pathophysiological processes that characterize the early stages of the disease in cases where clinical diagnosis is difficult, because changes in the brain and central nervous system homeostasis are reflected in the CSF composition. Therefore, the use of CSF biomarkers to facilitate the diagnosis of these neurodegenerative diseases (ideally at an early stage), monitor disease progression, ensure the differential diagnosis between diseases, and evaluate response to current and future treatments. Determination of brain chemical function indices measured in body fluids such as CSF, as well as brain imaging techniques that assess the brain's regional structure, function and biochemistry in neurodegenerative disease biomarkers research, more specifically, the evaluation of a combination of several metabolites, may be an indicator of the onset and progression of the disease. It is anticipated that untargeted metabolic profiling will provide great potential for biomarker discovery in this field and methods such as the combination of multiple CSF biomarkers will emerge as a definitive/early diagnosis and prognostic model. Unfortunately, CSF collection from the lumbar puncture is an invasive procedure and although the risk is low, there is a possibility of complications. Lumbar puncture requires a well-trained provider and brings discomfort and health risk to the patient. This makes it difficult to use for routine screening and regular follow-up sampling. Compared to blood and many other body fluids, CSF has low protein and RNA concentrations; therefore, sample pre-processing is much easier for plasma. However, this also creates a unique problem for CSF since any blood contamination during the sample collection will have a significant effect on the protein and RNA composition in CSF.

Despite extensive studies of a large number of candidate biomarkers in each of the major ND diseases (eg levels of CSF tau or Aβ proteins for AD), no biofluid biomarker has been fully confirmed. Since biopsy specimens are not available for the diagnosis of ND, the current diagnosis is based on a combination of genetic testing, cognitive assessment, psychiatric assessment, and imaging analysis. Final approval for some diseases comes only by post-mortem pathological or molecular analysis of brain tissue. The combination of biofluid biomarkers with functional and structural imaging is expected to improve diagnostic accuracy beyond individual analyzes. To date, only a few studies have explored this strategy. In one study, based on neuropsychological tests and other clinical data, the rate of misclassification of MCI was 41.3%. Combining MRI and PET imaging with CSF biomarkers reduced this error rate to 28%. One difficulty for the diagnosis of ND diseases is their complexity. Generally, there is no clear distinction between different ND diseases in clinical presentations. For example, it is difficult to distinguish some patients with AD or PD from patients with Lewy body dementia (32, 33). This difficulty limits the ability of phenotype-based diagnostic approaches, such as cognitive assessment, to provide an accurate or detailed classification. Furthermore, it

Table 1. Notable fluid protein biomarkers

Disease	Biomarker	Category	Change	Comments
AD	CSF Aβ42	Aggregation	Down	Also down in PD
	CSF Aβ42/Aβ40	Aggregation	Down	
	CSF tau	Aggregation	Up	
	CSF APP isoforms	Aggregation	Weak up	
	CSF BACE1		Up	
	CSF MCP-1, CD14	Inflammation	Weak up	
	CSF SOD1	Oxidative stress	Unchanged	Possible pharmacodynamic marker
PD	CSF α-synuclein	Aggregation	Down	Also up in CJD
	CSF DJ-1	Oxidative stress	Up	
HD	CSF clusterin	Inflammation	Up	
	CSF mutant huntingtin (mtHTT)	Aggregation	Up	manifest HD
ALS	CSF phosphorylated neurofilament heavy chain (pNFH)	Inflammation	Up	Early symptomatic phases of ALS
	CSF glutamate			

is difficult to obtain well-characterized human samples for biomarker discovery and to conduct meaningful clinical experiments during drug development. However, the development of new high-throughput technologies has led to the discovery of a number of new biomarker candidates for each ND disease.

CSF is an important source of biomarkers since AD pathology is limited to the brain. The biological markers for assessing neuronal degeneration are proteins in senile plaques (SP) and neurofibrillary tangles (NFT). The basic content of amyloid plaques consists of 42 amino acid forms (Aβ1-42) of Amyloid-β protein, a peptide of the Amyloid Precursor Protein (APP). The key proteins involved in Aβ production, APP and β-site APP clearance enzyme 1 (BACE1) are also of great interest as CSF biomarkers. Cleavage of APP with BACE1 produces an amyloidogenic C-terminal fragment (C99) and secretes soluble APPβ. C99 is then cleaved with γ-secretase to produce the Aβ peptide. Although reports vary for soluble APP levels, BACE1 levels are associated with Aβ in AD. Interestingly, CSF BACE1 levels are higher in patients with amnestive MCI than AH. The most likely CSF markers of this pathogenetic process are the levels of total and phosphorylated Tau proteins, which are the characteristic components of Aβ1-42 and neurofibrillary ting formation. The normal function of Tau is to bind and stabilize tubulin multimers in neuronal axons. Abnormally phosphorylated and truncated tau proteins are the main components of the neurofibrillary ball in AD. One feature of abnormal hyperphosphorylated tau (p-tau) is high resistance to proteolysis in enzymes, which causes it to accumulate in neurons. Since tau hyperphosphorylation can occur early in the development of the disease, even before the first clinical symptoms appear (Braak stage 1), CSF p-tau is not only a useful diagnostic and carrier marker in the advanced stages of the disease, but also in the earliest stages, even before the onset of the disease. that is, it may be a prognostic marker in MCI. This possibility was supported by recent research showing that increased CSF t tau and p-tau in early AD are comparable to those in advanced AD. In particular, long-term and persistently elevated CSF t-tau and p-tau levels are required in the course of the disease to predict progression of MCI to AD and to distinguish AD from other tau opaties, traumatic brain injury, multiple sclerosis, or axonal damage in other ND diseases. In many studies of Alzheimer's Disease, it was shown that Aβ42 decreased in CSF and total Tau and p-Tau levels were significantly higher. These values have been reported to have a sensitivity> 90% and a specificity of 79% to differentiate AD from vascular dementia.

Emerging biomarkers

Recent studies have focused on the clinical applications of CSF biomarkers that are associated with the classic AD triad (Aβ42, total Tau and p-Tau). Leading examples of these biomarkers are YKL-40 (also known as CHI3L, an indicator of glial inflammation), VILIP-1 (an indicator of neuronal damage, known as VLP-1), and NFL (non-specific neurodegeneration marker). High CSF YKL 40 is the most successful as a predictor of progression from MCI to clinical AD. High CSF YKL-40 has also been associated with pathological processes that are or are supposed to be associated with AD. The same can be said for CSF VILIP-1 - in AH, VILIP-1 yields increased or unchanged levels. The specificity of these markers for AD requires evaluation. CSF neurofilament light chain protein (NFL) is another sensitive marker of neuronal damage in various neurodegenerative conditions such as axonal degeneration. CSF NFL concentration increased in AD, especially in patients with rapid disease progression. However, increased NFL concentrations in CSF, dementia other than AD, FTD and vascular dementia are detected. The synaptic protein neurogranin is also a candidate CSF diagnostic biomarker. High CSF neurogranin is found in AD and prodromal AD, which reflects synaptic dysfunction or degeneration. Increased CSF neurogranin concentration in AD is not observed in other neurodegenerative diseases. It has also been shown that there is a quantitative relationship between the magnitude of neurogenesis increase and the severity of future cognitive decline and brain atrophy, and it appears to be a more specific biomarker for t-tau than AD-associated synapse loss or dysfunction. CSF UCH-L1 (neuron-specific cell cycle enzyme) was found to be increased in patients with AD, other dementias, and MCI compared to the control group. UCH-L1 has also been shown (although not specific) as a component of neurofibrillary balloon in the pathophysiology of AD; CSF UCH-L1 was positively correlated with CSF p-tau and neuronspecific enolase (NSE). Several potential CSF biomarkers have been investigated in AD (eg, NSE, MCP-1, CSF/serum albumin ratios, vascular growth factors, and various forms of sAPP), but the findings are not strong enough.

The discovery of genetic linkage between AD and variants of the trigger receptor (TREM2; TREML2) expressed in the myeloid cells 2 gene has increased interest in the identification of glial activation biomarkers. Increased CSF TREM2 concentrations in AD have been reported to be disease-specific and correlate with CSF t-tau and p-tau. These findings are supported by numerous studies reporting increased CSF concentrations of certain astrocytes, microglia and/or macrophage-derived proteins, including chitotriosidase, CD14 and YKL-40 (CHI3LI). α-Synuclein (α Syn) is an important component of Lewy bodies and Lewy neurites (prominent protein inclusions in PD, Lewy body dementia and multiple system atrophy) and has been an important field of research for PD treatments and biomarker discovery. Although α Syn has been accepted as an intracellular protein, recent studies have confirmed the presence of α Syn both PD and normal individuals in body fluids such as CSF and blood. In recent years, extracellular α-synuclein oligomers/fibrils that may arise from dying neurons have been observed to cause neurotoxic and neuroinflammatory effects in various neuronal and microglial cell culture studies. Recent studies have identified sensitive experiments that detect amplified biochemical signals in CS (not in healthy controls) that CSF α-synuclein may be a core agent in the initiation and progression of neurodegeneration.

Inflammation biomarkers; Neuroinflammation is a key process in neurodegenerative diseases. Active microglia regularly find plaques around them and secrete proinflammatory cytokines. It is assumed to have both neuroprotective and neurotoxic effects, but shifts the balance from beneficial to harm in chronic inflammation. Therefore, biomarkers of CNS inflammation will be necessary to observe this change, explore pathogenic mechanisms, and develop treatments involving microglial activation. Numerous potential markers have been investigated. Proteins produced by activated macrophages (chitotriosidase, YKL-40, MCP-1 and CD14) are elevated in CSF of AD patients. Microglial Toll-like receptors (TLRs) and CD14 participate in the inflammatory reaction surrounding Aβ residues. In addition, soluble CD14 levels were increased in CSF in AH and PH patients. These microglial markers alone are probably insufficient for the diagnosis of AD. However, these markers may be useful in combination with other types of biomarkers or subdividing patients.

Oxidative Stress Biomarkers; Decreased levels of copper zinc superoxide dismutase 1 (SOD1) were observed in the brain tissue of AD. Reduced levels of an antioxidant, such as SOD1, can alter the response to oxidative stress and contribute to neuronal cell loss.

Lipid and Metabolite Biomarkers; Lipid peroxidation is a common condition in ND diseases. In the CSF of AD or HD patients, numerous oxidized product levels have been increased, such as isoprostanes and isofurans derived from arachidonic acid and neuroprostanes derived from docosahexaenoic acid. However, the amounts of isoprostanes in plasma and urine of AD patients gave inconsistent results compared to their amounts in CSF.

In addition to miRNAs in the blood, CSFs have also been studied as potential biomarkers in AD patients. Cogswell et al. using a qPCR panel, controls (unspecified, Braak stage 1) and AD patients (dementia, Braak stage 5) reported 60 differently expressed miRNAs among CSF samples. Alexandrov et al. [38] described four miRNAs (miR-146a, miR-155, miR-9 and miR 125b) with higher levels in CSF than AH patients compared to the control group.

The clinical diagnosis of Parkinson's disease can be difficult in the early stages of the disease course. Biomarkers identified for the diagnosis and prognosis of the disease are currently not available. CSF levels of

α-synuclein, DJ 1, Aβ1-42, tau and lysosomal enzymes are identified as promising candidates for PD biomarkers. However, biomarkers have low specificity and sensitivity for PD when used individually. A combination of various biomarkers reflecting different pathogenic pathways is required.

Several studies have shown that concentrations of CSF α-synuclein and DJ-1 in PD, correspond well with brain alterations during disease progression. α-Syn is a 140 amino acid member of a highly conserved family of proteins, which localize predominantly at presynaptic neuronal terminals. The precise function of α syn is not known, but its localization and ability to interact with membranes and lipids suggests a role in synaptic plasticity, brain lipid metabolism, and regulation of vesicle dynamics and trafficking at presynaptic terminals. α Syn is the main component of Lewy bodies, which are a hallmark of synucleinopathies. Lewy bodies primarily consist of amyloid-like fibrils composed of post-translationally modified forms of α syn. α syn and tau interact dynamically and synergistically to promote mutual aggregation. A reasonable strategy in the context of detecting CSF markers of PD, therefore, is simultaneous measurement of these misfolded proteins. In one study, CSF t α-syn and t tau levels were measured in 721 patients with the synucleinopathies PD, DLB and MSA, and the tauopathies AD and PSP. Combination of CSF t α-syn and t tau values provided the most accurate discrimination of synucleinopathies from the other neurological disorders (P<0.0001). In the other study, lower t tau:t α- syn and p tau:t α-syn ratios discriminated PD from DLB, FTD and AD.

DJ-1 was a novel oncogene that works in association with ras in cellular transformation. DJ 1 is the product of PARK7-a gene that is linked to familial PD-and has a protective role in oxidative stress during neurodegeneration. The level of DJ 1 in the CSF has recently been proposed as a potential PD biomarker, although the data are conflicting. CSF DJ 1 levels (measured with quantitative immunoblotting) were considerably higher in individuals with early-stage PD compared with age-matched controls. CSF DJ-1 and a-synuclein levels are dependent on age and influenced by the extent of blood contamination in the CSF. Both DJ-1 and a-synuclein levels were decreased in PD cases compared to non-PD controls and AD cases after elimination of the effect of blood contamination. However, there was no association between DJ-1 or a-synuclein and the severity of PD. These findings led to the conclusion that total DJ-1 and α Syn in human CSF are helpful diagnostic markers for PD, if variables such as blood contamination and age are taken into consideration. It is worth noting that Ooe et al. developed specific antibodies that recognize C106-oxidized DJ-1. Examination of the oxidized DJ-1 levels could be more meaningful because abnormal oxidized DJ-1 has been specifically increased in patients with PD and AD [32, 37] and measurement of oxidized DJ-1 in the CSF or blood using these specific DJ-1 antibodies with Western blot and ELISA system could be useful.

When evaluating the possible relationship between PD phenotypes (in particular, tremor dominant and non-tremor dominant PD) and classic CSF biomarkers of PD, decreased Aβ42 levels or increased t tau: Aβ42 ratio were not reported in non-tremor dominant PD compared with tremor dominant PD. When other CSF biomarkers associated with PH pathology were investigated in patients with PD, it was found that CSF neprilis, a membrane-bound presynaptic protein contained in Aβ clearance, did not change in PD and controls but was significantly reduced in DLB and PDD. Levels of the inflammatory chemokine fractalkine have also been assessed in the CSF of patients with PD. The fractalkine:Aβ42 ratio was closely associated with disease severity. Similarly, increased CSF levels of complement C3 or factor H, together with decreased CSF levels of Aβ42, have been found to correlate with PD motor severity and cognitive impairment, suggesting that both neuroinflammation and altered Aβ42 metabolism has been involved in PD progression. CSF α syn species-including t α-syn, o α-syn, p129 α-syn and/or truncated forms-in combination with classical AD CSF biomarkers, such as Aβ42, t tau and p tau, are promising PD biomarkers because these species have various, interacting roles in pathogenesis.

Amyotrophic lateral sclerosis (ALS) is a motor neuron degenerative disease that affects upper and lower motor neurons, leading to perceptibly severe muscle atrophy. sporadic form of ALS (SALS) accounts for 90% of cases. Evidence showing that neurofilaments (Nfs) are found at elevated concentrations in cerebrospinal fluid (CSF) and blood of patients affected by ALS, has prompted the scientific research to explore their role as diagnostic and prognostic biomarkers in ALS. Nfs are present in cell bodies and axons and are involved in growth, stabilization and polarization of neural cells, enabling effective axonal conduction. According to the molecular mass of their subunits, Nfs are classified in light (NfL), medium (NfM) and heavy chain (NfH). Post-translational modifications like phosphorylation and O-glycosylation are crucial for neurofilaments aggregation, especially in NfM and NfH. Several studies have shown that both phosphorylated-NfH (p-NfH) and NfL are found at higher levels in CSF and blood of ALS patients, not only as compared to controls, but also to disease-mimics (DM), suggesting their potential utility in differential diagnosis. Furthermore, it has been investigated their role in distinguishing among different ALS phenotypes. p-NfH in CSF have shown to be a good prognostic biomarker not only in sporadic ALS, but also in ALS affected patients harboring mutation in the C9Orf72 gene. Gendron and colleagues identified a cut-off value of 176 pg/mL for p-NfH in CSF, able to discriminate with elevated sensitivity and specificity (98.8% and 96.4% respectively) between symptomatic and asymptomatic C9Orf72 mutation carriers. Transactive response-DNA-binding protein (TDP-43) is identified as the main pathological finding (approximately 95% of ALS cases) in most sporadic and familial cases of both ALS. TDP-43 is a protein with multiple functions, but is primarily involved in alternative splicing and transcriptional regulation. In ALS, TDP-43 becomes ubiquinated, hyperphosphorylated and C-terminally truncated, increasing its aggregation propensity and causing widespread neurotoxicity and cell death. Given the high burden of TDP-43 accumulation in the central nervous system of the majority of patients with FTD-ALS spectrum disorder, TDP-43 has been postulated as a biomarker in this disease. Characteristic proteinaceous inclusions of the DNA and RNA binding protein TDP-43 are found in more than 95% of cases postmortem.

Huntington's disease (HD) is an autosomal dominant neurodegenerative disease caused by CAG repeat expansions in HTT encoding mutant huntingtin protein. The cellular and molecular processes underlying the natural history of the disease have been well characterized. A CAG trinucleotide repeat expansion leads to a mutant HTT protein (mHTT) which aggregates and is toxic to neuronal cells, particularly to vulnerable striatal cells. This gives rise to neuronal dysfunction and death and ultimately the signs and symptoms of HD. Despite our certainty of the cause of the disease, the field of CSF biomarkers for HD lags behind the more common neurodegenerative diseases. Studying CSF is not a novel idea in HD research. Mutant huntingtin, the pathogenic agent in Huntington's disease, discriminated perfectly between healthy controls and mutation carriers, as the researchers had expected. CSF and plasma levels of NfL also discriminated well between healthy controls and mutation carriers. These biomarkers had areas under the ROC curve greater than 0.9. NfL in plasma and CSF also distinguished well between patients with premanifest Huntington's disease and those with manifest Huntington's disease, with areas under the curve greater than 0.9. Their discriminative ability in this regard was significantly better than that of mutant huntingtin. When investigating the relationship between the three biomarkers, the researchers found that CSF levels of NfL were strongly correlated in a linear fashion with plasma levels of NfL, and the CSF levels of mutant huntingtin were moderately associated with CSF levels of NfL. Levels of all three biomarkers increased significantly as the disease progressed and were associated with all clinical scales and imaging measures. CSF and plasma levels of NfL had superior predictive ability for clinical and imaging measures, compared with mutant huntingtin. CSF and plasma NfL were associated with brain volume, but mutant huntingtin was not.

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C-08

Procalcitonin and C-Reactive Protein in Sepsis

Fatma Ceyla Eraldemir

Department of Medical Biochemistry, Kocaeli University, Faculty of Medicine, Kocaeli, Turkey

Sepsis is a clinical condition characterized by life-threatening organ dysfunction and impaired response to systemic infection. Although it is frequently encountered in the clinics, its diagnosis still remains a serious problem. Procalcitonin and C-reactive protein tests are among the laboratory parameters commonly used by clinicians in the clinical decision process of sepsis in order to aid diagnosis, evaluate prognosis and manage treatment.

In recent years, procalcitonin appears to be prominent in the early diagnosis of sepsis and in the decision to initiate and terminate the antibiotherapy, because of its earlier increase and its shorter half-life. Although procalcitonin is especially shown as a reliable marker in the decision to terminate antibiotherapy, it does not appear to have a high diagnostic value in sepsis alone due to difficulties in interpretation and algorithm creation, the need for repeated measurements, and high test costs.

The aim of this presentation is to investigate the factors that should be considered when interpreting the results of procalcitonin and C-reactive protein tests used in the management of sepsis and to compare the usability of the tests.

C-09

Proficiency Testing (PT) schemes-External Quality Assurance (EQA) programs in Molecular Tests

Alexander Haliassos

Scientific Director of ESEAP (Proficiency Testing Scheme for Clinical Laboratories), Chair IFCC C-PT (Committee on Proficiency Testing)

Liquid biopsy, based mainly on the analysis of Circulating Tumor Cells (CTCs) and circulating tumor DNA (ctDNA), is providing the potential of real time monitoring of tumor evolution over time and a unique tool to follow-up cancer patients through simple and minimally invasive blood tests. External quality assessment (EQA) or Proficiency Testing (PT) schemes are essential tools for improving lab testing performance and successful participation in EQA-PT schemes is an absolute necessity for a clinical lab to be accredited according to ISO1589 standard. EGFR (Epidermal Growth Factor Receptor) mutation testing is an established critical parameter in NSCLC (Non-small cell lung carcinoma) tissues for therapeutic decisions according to the new era of Personalized Medicine.

ESEAP, the Greek Proficiency Testing Scheme for Medical Laboratories, under the auspices of the "Analysis of Circulating Tumor Cells Laboratory" (ACTC lab) in the University of Athens, organized an external quality assessment of the cobas® EGFR Mutation Test v2 in plasma-ctDNA in Greece, which was based on the distribution of 10 plasma samples (synthetic reference materials) with a volume of exactly 2mL per sample, which include mutations of EGFR (T790M, E746-A750del, L858R) in different allelic frequencies at eight Greek laboratories. After receiving their batch of samples, the participating laboratories had two weeks to analyze them and send the report of their results to the ESEAP using the report form they use routinely for their patients.

In 5 out of 8 laboratories, EGFR mutations were successfully identified in all samples, while 3 out of 8 laboratories presented with discrepancies. According to related literature for EQAs in Molecular Pathology, the performance was judged as excellent for 5 labs, adequate for 2 labs and poor (non-compliant) for 1 laboratory. Laboratories were also commented for both essential and formal characteristics of result reports (without score marking) as, according to ISO 15189, the results shall be reported "accurately, clearly, unambiguously, in accordance with any specific instruction", sample quality/suitability/adequacy shall be commented and interpretive comments shall be included.

In conclusion, we performed for the first time a successful pilot plasma-ctDNA EQA-PT ring trial for the cobas® EGFR mutation test v2 in clinical diagnostic laboratories using identical plasma samples certified as reference materials. Genotyping results were satisfactory; the periodic use of positive plasma controls with very low concentrations of EGFR mutations was suggested to all labs in order to check for sensitivity and specificity. New findings regarding report attributes in our study have been described in detail and certainly, supplement previous efforts from larger cohorts.

The observed inter-laboratory differences underline the urgent need for compliance to good clinical practice and conforming to specific requirements and guidelines, especially in the field of liquid biopsy applications, where standardization of the pre-analytical variants is significantly important. EQA-PT is an essential tool for improving lab testing performance. The laboratories of this pilot study could take advantage of this participation in order to require accreditation for this parameter according to ISO 15189 standard.

Our EQA effort in plasma EGFR mutation detection should expand in the future and include other platforms and techniques as well.

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Panels

PO1-Informatics and Laboratory Workshop

PO1-01

Welcome to the Health 4.0 Era!

Banu Isbilen Basok

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

The use of innovative technologies to increase the efficiency and quality of industrial processes has enabled digitalization to launch the fourth industrial revolution known as "Industry 4.0". The concept which developed in Germany in 2013, has rapidly spread all over the world, causing radical changes in many sectors including health and it called "Health 4.0". Digitalization is utmost important because it allows the interaction between people and technology in Health 4.0. The digital data produced in the health increases by approximately 48% every year and it is becoming more difficult to transform this data into "meaningful and useful" knowledge. Therefore, "artificial intelligence" (AI), which can process big data, develops processes, to make suggestions and direct decisions highly needed. Although Health 4.0 is not only consisted of the AI concept, it is one of the important and essential technologies. In the panel, other speakers will further discuss AI in detail.

Notable benefits of the health transformation might summarize as ease of access to healthcare, individualized patient care, improved preventive medicine, better follow-up of chronic diseases, increased cost-effectiveness, etc. Still, there are concerns regarding data safety, the possible ethical problems, and legal issues. For this reason, it is urgent that national even universal regulations closely follow these high-speed transformations. There is no doubt that AI and digitalization cannot operate alone and in spite of human, even as often encountered in science fiction scenarios. The Health 4.0, which emphasizes technology, in particular, evolves its place in "Health 5.0" which highlights human-technology partnership for people and society' wellness. Soon, we will feel more of the impact of Health 5.0 through the increase in human-machine interaction and the widespread use of intelligent technologies. For this reason, we need to increase our awareness of the new era for the future of medical biochemists' training and laboratory practice.

PO1-02

Digitalization and Artificial Intelligence in Laboratory Medicine

Ali Riza Sisman

Department of Medical Biochemistry, Dokuz Eylül University, Faculty of Medicine, Izmir, Turkey

The digital revolution is rapidly changing our lives in every field. We can predict the effects of these changes in medicine, especially in laboratory medicine. "Disruptive Technologies" will fundamentally change the demand, conduct, and interpretation of laboratory tests in the future and enable the collection of test results from various sources. Wearable devices and body-implanted sensors will measure a large number of laboratory parameters and data will be stored in cloud services. These will allow Laboratory Medicine to evolve into a higher level of visibility that redefines the patient-doctor-laboratory relationship as the center of diagnostics, rather than being the "secret champion of Big Data. For example, accessing digital health data will enable Laboratory Medicine to contribute more effectively to medical communication as it is today. In this respect, the way we conduct our profession will require great readings, as well as new educational concepts and continuing professional development.

Because of the increasing and multidimensional nature of medical data, it reveals the necessity of evaluating the data from a new perspective, that is, artificial intelligence (AI) and machine learning (ML) methods. In recent years AI and ML have been increasing rapidly in medical laboratories, ie it sounds like a flood; however, there are a number of defenses against AI. In the classical scientific method, while the cause-effect relationship is established, AI uses only statistics such as correlation, so it is seen as a "black box". Difficulties in the implementation of AI in the field of medicine; Inadequate estimation performance, lack of clinical approval of algorithms applied, transparency and reproducibility, lack of data quality, lack of education of patients and physicians, ethical and legal problems.

If we are not at the "breaking point" after a destructive technology, we can imagine that the clinical laboratories will preserve much of the classic role of laboratory medicine, even in the Digital Age of Health. Laboratories will be focused on total quality management, value of the tests, effective diagnostic management, consolidation of traditional tests, quality control, reduction of laboratory errors, reduction of inappropriate test requirements, global standardization of tests, finding new tests, management of near- patient testing, and consultancy services. That is, Laboratory Medicine will evolve from the "Silo model" stuck into laboratories to "the entegrated model with patient and clinic".

PO2-Illicit Drugs Workshop

PO2-01

Urine Drug Testing: With General Aspects

Cigdem Karakukcu

Department of Medical Biochemistry, Kayseri Sehir Training and Research Hospital, Kayseri, Turkey

Introduction

In this presentation, frequently asked questions and basic issues related to the analysis of illegal substances in urine will be evaluated from an overview point of view.

What should be the test panel content that I need to create while preparing the technical specifications for the screening of illegal substances in urine in my institution?

According to December 29, 2013 date, 28866 number Substance Dependence Treatment Centers Regulation and Turkey Drugs and Drug Addiction Monitoring Center (TUBİM) report, those notifying the most commonly used materials in Turkey, the suggested minimum screening test panel should contain the following ingredients and metabolites: Amphetamines, Benzodiazepines, Cannabis, Cocaine and Opiates. This panel can be expanded according to the method studied, the demand of the physicians and the regional needs.

What is 'chain of custody'? Is it necessary to provide a chain of custody when taking urine samples?

Not direct observed urine sampling is open to intervention and can easily be tricked at the sampling stage. For this reason, the sample must be monitored and protected at all stages from the start of collection to the analysis and reporting process. This is called a chain of custody.

Is the chain of custody mandatory for all samples?

Depending on the decision of the physician requesting the test, standard sampling may be carried out without supervision, especially in the medi-

cal claims. In these cases, unobserved sampling should be indicated in the report.

How long can it be stored after urine sampling?

Urine samples should be delivered to the laboratory within 24 hours if possible. In case of storage longer than 24 hours, it should be kept in locked refrigerator at 2-8 °C for a maximum of 5 days. Long-term storage should be done at temperatures <-15 °C.

What is a witness sample?

Samples that are accepted to the laboratory for screening analysis should have positive screening test results and should be stored in 2 separate portions (tubes) for confirmation analysis when necessary. Witness samples should be stored for at least 6 months in a deep-freezer (-15°C and below) in unauthorized access is restricted laboratories, where screening analyzes were performed. One is the tube in which the screening test is portioned and the other is the spare tube separated from the same sample for confirmation analysis.

What is the detection window?

It is the period in which the toxic substances and their metabolites can be detected in the sample. This time varies according to the dose of the toxic substance, frequency of use (acute-chronic), amount taken, chemical properties, metabolism and excretion rate of the individual, route of intake, test method and threshold concentration of the substance. In urine samples, the detection window may vary from several hours to several weeks.

What are urine integrity tests and why?

Since there is a high probability of tampering with urine samples, integrity testing can be questioned to determine whether the integrity of the sample is structurally deteriorated. Integrity tests should be performed on all urine samples prior to analysis. Urine temperature, creatinine, pH, density, nitrite and oxidant analysis are tests that show urine integrity and structure. If creatinine is greater than 20 mg/dL, the density is in the range of 1003-1035, pH: 3-11 and the sample is suitable for analysis if nitrite is negative. Creatinine is 4.5-20 mg/dL, pH: 1001-1003 and the sample is diluted. The dilution may be due to excessive water consumption, diuretic use or to add water to the external urine. In this case, screening analysis is performed. However, the information that the sample is diluted must be given in the report. If the test result is positive, the result is considered positive. If negative and if the person is in probation program, the result is reported as positive by the clinician by deducting the dilution sample description. Creatinine is generally in the range of 20-200 mg/dL in healthy people, but can sometimes exceed 200 mg /dL under physiological conditions or due to dehydration. This does not indicate that urine integrity is impaired.

Should a sample rejection be performed if any of the urine integrity tests is abnormal?

Integrity tests should be evaluated together, a single test out of range alone is not sufficient for sample rejection. If creatinine is below 4.5 mg/dL and density is below 1001, the sample is considered non-urine and rejected.

What methods can be used for screening and verification analysis?

Immunochemical or chromatographic (Gas Chromatography-Mass Spectrometry (GC-MS), Liquid Chromatography-Mass Spectrometry (LC-MS/MS)) techniques can be used for screening analysis, LC-MS/MS and/or GC-MS tests should be used for confirmation analyzes.

Why immunochemical methods are preferred more frequently in screening analyzes?

They have a high sensitivity, and they can easily differentiate negative samples from positives by cross-reacting with similar compounds. Rapid results can be obtained in automated devices as their applications are suitable. They require small sample volume and low reagent consumption.

What are the amphetamine group substances, which immunological methods measure?

In immunological methods, the test is generally positive in the presence of either Amphetamine, Methamphetamine, 3,4-Methylenedioxymethamphetamine (MDMA), Methylenedioxyethylamphetamine (MDEA) or Methylenedioxyamphetamine (MDA). Some manufacturers have produced separate kits for MDMA (ecstasy). In this case it is necessary to use an additional specific kit for MDMA screening.

How can I distinguish between heroin or codeine use in a patient with positive opiate screening test result?

In order to make this distinction, morphine, codeine and heroin measurements should be done separately by chromatographic technique. In addition to the opiate group, heroin-specific immunoassay kits (where other opiate metabolites do not cross-react) are available. Heroin (diacetyl morphine) is metabolized to 6-monoacetylmorphine (6-MAM) and morphine. Codeine is metabolized to morphine. When codeine-containing drug is used, morphine and codeine may co-exist in the urine, but

Table 1. Detection windows of substances in urine

Substance	Urine
Amphetamines (except methamphetamine)	1-3 days
Methamphetamine	3-5 days
MDMA (Ecstasy)	3 or 4 days
Barbiturates (except phenobarbital)	1 day
Phenobarbital	2-3 weeks
Benzodiazepines	Up to 7 days in therapeutic use. Chronic use (over 1 year): 4-6 weeks
Cannabis	Rare users: 7-10 days Chronic users: up to 30 days.
Cocaine	2-5 days (may extend to 7-10 days for chronic users and those with significant renal dysfunction).
Codeine	2 or 3 days
Morphine	2-4 days
Tricyclic antidepressants	7-10 days
Methadone	7-10 days

6-MAM is absent. 6-MAM is not excreted after codeine use. The presence of 6-MAM is evidence of heroin use. In order to reduce false positivity rates due to the use of prescription drugs (codeine and morphine derivatives), the screening threshold concentration for opiates in the USA was increased from 300 ng/mL to 2000 ng/mL in 1998 and the new screening cut-off values are also used in our country.

In which cases confirmation analysis is requested?

- In cases where there is a discrepancy between the anamnesis and physical examination findings and screening analysis results.
- Optionally in differential diagnosis of intoxication
- In case of objection to test result
- It is recommended that all positive screening test results be verified in forensic and workplace screening. Because screening test results are not evidence.
- Verification of values close to cut-off is recommended.
- In some cases, negative results may be confirmed.

Conclusions

Urine sample is the most preferred sample type in clinics for illegal substance analysis. The two-step analysis strategy in the form of screening and confirmation is applied in our country as in all countries of the world. Knowing analytical techniques, pre-analysis factors, metabolism of substances and metabolites, cross-reactions and interferences is very important in determining the strategy related to the sample.

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PO2-02

Drug Testing In Oral Fluid

Alain G. Verstraete

Department of Laboratory Medicine, Department of diagnostic sciences, Ghent University Hospital, Ghent University, Belgium

Introduction

After many years of research and development, drug testing in oral fluid is becoming mainstream for several applications. It has strengths and weaknesses, that will be explained in this contribution.

Oral fluid (OF) testing

In drug testing, one uses the term 'oral fluid' instead of 'saliva'. Oral fluid contains saliva and crevicular fluid, cellular debris and remainders of food. We produce between 0.5 and 1.5 L/day of OF, and swallow most of it. OF contains water (99%), enzymes like amylase, mucins, IgA and ions (Na^+, K^+, Cl^-, $HCO3^-$). Drugs get into oral fluid by passive contamination after oral intake, passive diffusion through the membranes, active secretion (against concentration gradient) and ultrafiltration. Basic drugs will be present in higher concentrations than in plasma, because they are 'trapped' in OF due to a pH effect. Once they reach the OF, they become ionised at lower pH, and can't diffuse back into the blood. Oral fluid testing is becoming increasingly popular because it allows supervised sampling, that can be performed by a lay person and the risk of adulteration is lower. OF can be collected by expectoration or with a specific collection device. Drug concentrations are often higher, but more variable, with expectoration. The recovery of drugs, particularly the very lipophilic tetrahydrocannabinol (THC), from collection devices can be difficult. These collection devices contain buffers to stabilise the drugs and avoid adsorption to the collection pad. This introduces a dilution, that needs to be corrected when calculating the drug concentration in the original OF. For some drugs, passive contamination is an issue. Concentrations of THC in passive smokers can reach up to 6 µg/L. Similar to testing in other biological samples, drug testing in OF is often performed in two steps, a screening by immunoassay followed by confirmation by a chromatographic technique coupled to mass spectrometry. For screening, in addition to point-of-collection devices, heterogenous immunoassays (ELISA) and some homogenous immunoassays (CEDIA) are available. For confirmation, multi-analyte LC-MS/MS methods are used. In theory, the concentrations in OF are expected to be in the same order of magnitude as the unbound blood concentrations and after the end of oral contamination, a good correlation between OF and B concentrations is expected. But in practice one observes much higher concentrations in OF, mainly because of the trapping explained above. Many studies have shown very poor correlation (e.g. r^2 of 0.03 for THC) between OF and blood concentrations for basic drugs. The correlation is somewhat better for acidic or neutral drugs like benzodiazepines. Hence OF/blood ratios have a wide range. Examples are a median OF/B ratio of 19 for amphetamine (range 3.3–78), 14 for THC (1.0–190) and 17 for cocaine (1.2–63. Several organisations have proposed screening and confirmation cut-offs for the different drugs, e.g. for workplace drug testing or for detecting drugged drivers. The detection times of drugs in OF is 24–48 hours, shorter for some drugs like THC (typically 6 h in occasional users, but 26 h in some individuals).

Conclusion

A lot of progress has been made in the last 15 years, and OF testing has become mainstream in detecting drugged drivers at the roadside and for workplace drug testing. The main disadvantage of OF testing is that the sample collection is more variable and that the correlation between OF and blood concentrations is poor. Hence, the drug concentrations are more variable in OF, and extrapolations to blood concentrations are not possible.

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PO2-3

Reviewing Legislative Regulations in Urine Drug Testing

Huseyin Kurku

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

In Turkey, drug abuse testing laboratories have been licensed under the title of medical biochemistry. Drug abuse testing laboratories should provide all quality requirements in the medical laboratories regulation and also fulfill additional responsibilities that are designated specific to them. Within this framework, the Ministry of Health has issued 3 main documents including 2 circular letters and one operating principles and notes explaining these documents here. In medical laboratories, drug abuse testing can be performed for medical (diagnosis and treatment), forensic or social (administrative) purposes. Safety procedures to be applied can be changed according to the purpose of drug abuse testing. However, by the nature of the drug searched in drug abuse testing, it is considered a crime to produce, transport, use and merchandise these drugs according to our legislation. Thus, it is impossible to separate the purposes of drug testing with hard edges. In urinary drug testing, it is required to provide criteria under the topic titles of test panel, sampling rules, chain of custody, minimum sample integrity tests, threshold concentration selection, screening/verification decision and test method selection, minimum duration of sample storage, procedures to follow for test verification and report format. In order to provide all the criteria, it is required for the institution, medical personnel and laboratory experts to have a common effort and cooperation. However, the responsibility of following and recording the process mainly belongs to the laboratory expert. Healthcare professionals have a tendency to primarily take care of the health of individuals due to the nature of their training and the characteristics of the job. Medical tasks should always be a priority. However, employees in drug abuse testing laboratories have to deal with judicial problems and fulfill administrative procedures, besides health work load. Thus, both administrative changes and scientific developments should be followed closely. Laboratory operations and procedures should be observed frequently and all the works and operations should definitely be recorded. The experts should compare the current administrative regulations in Turkey with relevant examples in the world (for instance: The Substance Abuse and Mental Health Services Administration (SAMHSA)), discuss them, propose the administration to replace them if necessary and apply them fully in a standard way until they are amended.

P03-Endocrinology Workshop

PO3-01

Rational Laboratory Approaches in The Evaluation of Thyroid Function Testing

Dildar Konukoglu

Department of Medical Biochemistry, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey

Introduction

Nowadays, there is an increasing tendency to reduce unnecessary or incorrect test demand. Due to the lack of knowledge of test performances, and errors in interpretation of test results, unnecessary and inappropriate test demands reach 25-40 %. Thyroid function tests are the most requested endocrine test group by the physician. One reason for the high number of test requests is that thyroid diseases are among the common endocrine diseases in the population. However, another important reason is that unnecessary test requests are made, or that test request intervals are not suitable.

A request for thyroid function tests

Thyroid function tests are used to screen for thyroid dysfunction, to evaluate the efficacy of levothyroxine treatment in hypothyroid patients and to monitor the treatment of hyperthyroidism. Failure to interpret the tests correctly may lead to delay in treatment and may lead to incorrect treatment. Therefore, it is necessary to ask the right patient at the right time, to have the right tests, to run the test correctly and to report the results correctly and to evaluate them correctly.

On the other hand, the contribution of thyroid function tests to the diagnosis and follow-up of subclinical thyroid diseases is very important.

1. The first test for screening thyroid function is pituitary thyrotropin (TSH). Because;

- Small changes in thyroid function lead to a marked increase in TSH secretion. TSH may increase even in very mild thyroid dysfunction.
- Tests to assess TSH levels are reliable. The most advanced (third-generation) chemiluminescence TSH analyzes can now detect both elevations and decreases of TSH levels.
- In most cases, a normal TSH level does not require additional testing.

Only when TSH is performed; Diagnosis of non-thyroid disease, TSH analytical interference, central hypothyroidism (hypothalamic/pituitary disorders), pituitary adenoma secreting TSH (TSHoma), thyroid hormone resistance and thyroid hormone transport or metabolism disorders may be missed. Therefore, some guidelines recommend that free thyroxine (FT4) with TSH be requested.

The conditions/persons at risk for thyroid disease are given below;

- All newborns (newborn screening)
- History of thyroid disease
- Family history of thyroid disease
- An autoimmune disease such as Type 1 Diabetes
- Some genetic diseases (eg Down, Turner syndromes)
- Radiation therapy on the neck region
- Taking medications such as lithium and amiodarone
- Women over 35
- Elderly patients
- Pregnant women in the first trimester
- 6 weeks to 6 months after birth in women
- Hyperlipidemia

American Association of Clinical Endocrinologists (AACE), American Academy of Family Physicians (AAFP), The American College of Physician (ACP) and the American Thyroid Association (ATA) vary greatly in their recommendations. ATA recommending routine screening at age 35 then every five years.

2. Despite normal TSH results, serum T4 is ordered if the patient has convincing signs of hyperthyroidism or hypothyroidism. Unless there is a systemic disease, the predictive value of normal TSH in excluding primary hypothyroidism and hyperthyroidism is 99%.
3. If pituitary or hypothalamic disease is suspected, the measurement of both serum TSH and FT4 is appropriate.
4. In patients with secondary hypothyroidism due to pituitary or hypothalamic disease without or lacking TSH release, serum FT4 value is important in monitoring thyroid hormone therapy.
5. Primary hypothyroid patients receiving levothyroxine replacement therapy can be monitored by evaluating serum TSH. If serum TSH is high, the dose should be increased; If it is low, the dose should be reduced.
6. During the treatment of hyperthyroidism, serum TSH may remain subnormal for several weeks and rarely for several months. Therefore,

it is necessary to rely on FT4 and FT3 measurements when evaluating the efficacy of an antithyroid drug, radioiodine, or surgery. Once stable condition conditions are met, serum TSH measurement is appropriate to assess the efficacy of treatment.

7. Serum T3 measurements are appropriate in the case of hyperthyroidism. It is important in the diagnosis of T3 thyrotoxicosis and to differentiate Graves' disease from subacute thyroiditis.
8. The evaluation of thyroid function during pregnancy should be done with TSH and total T4 measurements. The normal values of free T4 and T3 during pregnancy are not clear. Therefore FT4 and T3 should not be used. An increase in the level of T4 and consequently a decrease in the level of TSH occurs in pregnant women. TSH in the first trimester should be <2.5, and TSH should be checked every 6 weeks. 1.5 times the total T4 concentration during pregnancy is considered to be the upper limit in pregnancy.
9. Thyrotoxicosis" is the term for all disorders with increased levels of circulating thyroid hormones. "Hyperthyroidism" refers to disorders in which the thyroid gland secretes too much hormone. Radioactive iodine uptake test (RAUI) distinguishes hyperthyroidism from other forms of thyrotoxicosis.

Analytical interferences affecting thyroid function tests: TSH analysis methods have fewer disadvantages than free hormone measurements. Free hormone levels are influenced by the affinity of the carrier protein and hormone and are susceptible to multiple interferences. An inappropriate thyroid function test identifies clinical incompatible tests or tests that are incompatible with each other. In cases where the hypothalamic-pituitary-thyroid axis is not affected, the increase in TSH is associated with decreased FT4 levels; or TSH decrease is associated with increased FT4 increase. In the evaluation of subclinical conditions or incompatible thyroid function tests, interferences due to heterophilic antibody, human anti-animal antibody (HAMA), antithyroid antibody and biotin should be considered. Interferences are positive or negative and method-dependent. Another analytical interference factor is macro TSH. In this case, TSH combines with an immunoglobulin present in the blood and forms a large complex that cannot be excreted from the kidneys. This complex, which increases in serum, is not bioactive but immunoreactive. In this case, a clinically euthyroid person may be diagnosed with subclinical hypothyroidism due to high TSH.

In the case of interference, the first option, if possible, maybe to repeat the test by a different method. Methods such as dilution tests, PEG precipitation, antithyroid antibody analysis, HAMA analysis and blocking use may be used to eliminate or expose interference. Positive and negative interference in immunoassays may occur. In special cases, it is recommended to use “equilibrium dialysis” and/or liquid chromatography-mass spectrometry which is the standard of FT4 measurement. On the other hand, the effect of drugs, one of the preanalytical factors, must be taken into consideration in the evaluation of the test results. Drugs may affect thyroid tests in vivo or in vitro. Drugs can affect thyroid hormone synthesis, secretion, conversion of T4 to triiodothyronine (T3) as well as the binding properties of thyroid hormones to the carrier protein or the concentration of the carrier protein. For example, FT4 levels are found to be high in patients treated with heparin. Heparin activates lipoprotein lipase and leads to an increase in free fatty acid levels in plasma. Increased free fatty acids reduce the binding of T4 to the carrier protein (thyroxine-binding globulin).

The range of reference values for TSH varies according to age and clinical condition and has a diurnal rhythm. These features must be taken into account in the evaluation of TSH test results. The lower limit of the reference range of TSH is the same for all ages, but the upper limit is different for age. Furthermore, there are different views in terms of the accepted upper limit value of the TSH reference value. This is especially important in the evaluation of patients in terms of subclinical hypothyroidism.

Conclusion

The evaluation of thyroid diseases is made by anamnesis, physical examination, and endocrine and biochemical tests. ST4 may be added to screening tests to avoid fewer common conditions such as secondary hypothyroidism. Thyroid function tests have very heterogeneous results depending on the method. The laboratory specialist should be aware of the limitations of analytical interferences and should cooperate with the clinician. Based on the patient's complaints and physical examination findings, thyroid function tests should be evaluated. To decide the function of the thyroid gland, the selection and repetition of the tests should be performed according to certain algorithms in differential diagnosis and follow-up.

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PO3-02

Insulin Resistance and Problems of Insulin Analysis

Ozlem Gulbahar

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

Introduction

The condition of having enough insulin in the circulation but not seeing the effects of it is called Insulin Resistance (IR). It can also be defined as glucose response below normal rates to insulin concentrations. IR affects many systems such as musculoskeletal system, adipose tissue, reproduction system, immune system and SSS etc. IR has many accompanying conditions: obesity, type 2 DM, HT, hyperlipidemia, metabolic syndrome etc. Human insulin is a peptide type hormone that is formed

by 51 aminoacids. Insulin of many animals resemble the human insulin immunologically and biologically; and, while pig or cattle insulin were used in the treatment before, today the most commonly used form is recombinant human insulin. Insulin attaches to the receptors in cell membrane and shows its effects with different intracellular pathways. Insulin measurement can be used in clinic laboratories to evaluate IR. Insulin measurements are especially affected by hemolysis and some pre-analytical factors but the main problem is about the analytical method. Even though the insulin has been measured for more than 50 years, a precise and reliable procedure could not be reached! In the reports of ADA study group, the quality of the CV's in and inter studies are underlined. There is an effort to create accountability in standardization studies. For this reason, many institutions (ADA, CDC, IFCC etc) established insulin standardization study groups. On the other hand, factors such as insulin release pattern reduce the reliability of evaluating insulin analysis results. In addition to this, antibody interferences resulting from the nature of immune analysis are another factor that affects the test results. There are many methods in which insulin level is evaluated alone or in combination with glucose in the diagnosis of IR. Hyperinsulinemic-Euglycemic Clamp Technique is accepted as a reference method for IR. Although each test has an advantage and a disadvantage, one of the most commonly used tests in clinical laboratories is IR evaluation with HOMA score. Aside from that, there is not a validated test for IR. It is also stated in the guides of the clinical departments that these tests are not suitable for directing diagnosis and treatment.

PO3-3

Adrenal Gland and Endocrine Dynamic Function Tests

Yuksel Aliyazicioglu

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

The adrenal glands consist of two different functional parts: the adrenal cortex and the medulla. The adrenal cortex can be divided into three regions that produce different steroidal hormones. The outermost layer is zona glomerulosa which produces mainly aldosterone (mineralocorticoid) under the control of the renin-angiotensin system. The zona fasciculata is the second and the zona reticularis is the innermost part of adrenal cortex. Androgens are also produced in zona fasciculata and reticularis. The adrenal medulla produces catecholamines, dopamine, epinephrine and norepinephrine.

Assessment of adrenal function begins with the measurement of levels of adrenal hormones and metabolites, and sometimes secretory hormones. However, the determination of basal hormone secretion does not confirm the diagnosis in adrenal gland diseases. Therefore, in adrenal gland diseases, diagnosis is made by dynamic tests rather than basal hormonal tests. The dynamic tests used for this purpose are either adrenal gland stimulation or suppression (dexamethasone suppression test, bilateral inferior petrosal sinus sample test, saline suppression test, fludrocortisone suppression test, adrenal venous sample test, clonidine suppression test, synacthen test, insulin tolerance test, metyrapone test). Changes in the amount of hormone (analyte) in body fluids that occur at certain times of the day, week, month, or year are known as cyclic variations. Factors such as posture, activity, nutrition, stress, daylight and darkness, sleep and wakeness that may cause cyclic biological variations of the individual as well as preanalytical and analytical variations should be considered in the evaluation of HHA axis and adrenal functions. The interpretation of these tests should be evaluated in the light of the patient's history and physical examination and clinical information. The circulating forms of hormones, their carriers, if any, and their characteristics should be considered. In addition, basal levels and peripheral effects of hormones should be interpreted in the light of hormone secretion and control mechanisms.

PO4-Education of Specialists on Clinical Biochemistry and Their Experiences on the Field Workshop

PO4-01

Ministry of Health Experience in Biochemistry Education

Elif Merve Girgin

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

Biochemistry expertise consists of medical basic education, postgraduate specialist education and, in fact, lifelong professional development. The experience and equipment to be gained during the training process (specification preparation process, monitoring quality and license inspections, etc.) will make the difficulties to be experienced after the expertise less traumatic. In this context, it is unthinkable that in residency training, the assistants should not have to be active in the field and graduated without facing the problems. Expertise training should be revised to include the techniques for producing solutions to the problems that will be experienced on the basis of limited opportunities. Finally, it is essential for the continuous professional development that specialist physicians acquire the notion of following up the current publications and conducting research in order to keep them away from the developments in medicine.

PO4-02

From the Eyes of a Biochemistry Expert, First Ramps in the Expertising

Mehtap Esen

Department of Biochemistry, Bayburt State Hospital, Bayburt, Turkey

Medical Biochemistry is a medical and clinic-specific laboratory science and medical laboratory specialty that includes selection and application of tests, interpretation of laboratory findings, medical consultation and laboratory diagnosis in the examination of human biological samples by means of various laboratory methods for evaluation of health in humans (diagnosis, follow-up,prognosis,preventation…). Today, the medical biochemistry specialist is primarily responsible for maintaining a large test panel in hospital laboratories, most of which work with high test density. However, the responsibilities and roles of clinical laboratory managers are not only managing analytical processes; management of diagnostic service, technology acquisition, budget management and laboratory business management are covered by the modern role of the medical biochemistry specialist. The speciality of medical biochemistry recognized in 1928 in Turkey and with the Law of Tababet and Şuabatı Tarzı İcrası own the 11/04/1928 date and 1219 number, training started in university hospitals as well as in training hospitals. More recently, The Medical Expert Board has established and published the core curriculum for standardization of specialist training.

Although it is aimed to create knowledge and skills related to the relevant specialties by establishing a core curriculum, I think it is inevitable that experts, especially new experts, will experience some difficulties. As a 2.5-year medical biochemistry specialist trained in the university hospital's laboratory by taking the knowledge, skills and responsibilities related to area of expertise, I had some difficulties especially in the purchase process. I would like to add that, although they have the theoretical equipment, some of my colleagues who completed their training by staying away from the laboratory responsibility and even from the laboratory itself, have more difficulty in adapting to the laboratory, laboratory and process management, problem solving, quality control skills, technical specification preparation and purchasing processes; so new specialists will not have similar difficulties.

PO4-03

Routine Workflow of Biochemistry Specialists in a Public Health Laboratory

Muhammed Fevzi Kilinckaya

Department of Biochemistry, Mardin Public Health Laboratory, Mardin, Turkey

Principles of Public Health Laboratories are regulated with, "Regulation on the Working Procedures and Principles of Laboratories for Public Health Services" for non-clinical laboratories and "Medical Laboratories Regulation " in terms of clinical laboratory working procedures and principles. Laboratories are classified into 4 groups according to service type: National Public Health Reference Laboratory, L2 and L1 Service Type Public Health Laboratory and Reference Authorized Laboratory.

Each laboratory consists of two sub-units: Clinical Laboratory Unit and Non-Clinical Laboratory. In the clinical laboratory unit, diagnostic tests are performed within the scope of family medicine services and primary level diagnostic/screening tests. Medical biochemistry and microbiology laboratory units were established in the clinical laboratory unit. In the non-clinical laboratory unit, non-clinical samples are determined for non-clinical samples, non-clinical analysis of factors arising from physical/biological/environmental reasons and affecting human health. The non-clinical laboratory consists of non-clinical microbiology and chemical analysis laboratory units.

Laboratory staff are basically divided into 5 groups

1. Laboratory Responsible
2. Laboratory Unit Responsible
3. Quality Management Representative
4. Laboratory Technical Staff
5. Laboratory Support Services

Following this basic information, I will tell you about my experience in Mardin Public Health Laboratory, where I work.

PO4-04

Clinical Biochemistry and Molecular Tests: Past, Present, Future

Uzay Gormus Dégrigo

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

The presentation is about the historical process of the scientific-technological advances until current definition of 'Clinical Biochemistry' and their effects on our profession. We will disscuss about how to be prepared for the future. By focusing on contemporary concepts such as translational medicine, telepatology, system biology, proteomics, metabolomics and similar 'omic' concepts together. Shortly, our profession has direct relationship with physics, chemistry and biology and so leads to innovations and developments and it is also affected reciprocally.

In general, the following changes are expected to lead the health care in the near future, so we as clinical biochemistry experts, will discuss our roles in the following points:

- Longer life span and chronic diseases → early diagnosis and prediction
- Technological advances facilitating personalized medicine → 'patient-specific' applications
- Evidence-based medicine → differential diagnosis, algorithms and clinical guidelines
- Environmental changes → novel parameters and methods
- Global pandemics → prevention and early intervention
- Monitorization of healthy individuals → prevention medicine
- Novel parameters and increasing demand → non-medical trained professionals
- Medical tourism → increasing demand and diversity of analyses
- Demanding and 'conscious' patients → continuous learning
- Increased costs and inadequate health budgets → cost-effectiveness

PO4-05

Clinical Biochemistry Laboratory in Cellular Therapies- Cellular Therapies in the Treatment of Autoimmune Diseases

Alper Tunga Ozdemir

Department of Medical Biochemistry, Merkezefendi State Hospital, Manisa, Turkey

The main task of the immune system is to protect the body from invading and foreign organisms and structures. However, in some cases, this system can activate against the self-antigenic structures and leads to damage. In this case, autoimmune diseases occur that can be defined in a wide range from mild to life-threatening. Today, about 100 autoimmune diseases have been identified. These diseases may be organ-specific such as type I diabetes or may be pathologies with multiple organ and tissue involvement, such as systemic lupus erythematosus. Currently, there is no curative treatment for these diseases, and the treatments are usually palliative and used drugs that suppress the immune system. Recently, cellular therapy approaches have used as an alternative in severe autoimmune diseases. Mesenchymal stem cells are the most widely used adult cells in the clinic and they suppress all immune cells non-specific and non-selectively. Because of these properties, they are used in fatal pathologies such as steroid resistant graft versus host. Tolerogenic dendritic cells and regulatory T cells are isolated from the patient's own monocytes and T lymphocytes. Isolated cells are transformed into specific immunosuppressive phenotypes by using cytokine cocktails. These cellular products are more costly but more specific. There are very strict and various quality control tests to be performed before the application of cellular therapy products. For example, the phenotypic changes of cells are validated by flow-cytometry devices that available in many clinical biochemistry laboratories. The paracrine activities of the cells are measured by Luminex and ELISA methods. All these tests are services that we will encounter in the not-so-distant future as laboratory experts. The medical biochemistry specialists will get important roles in determining the specific tests to be used not only during the production phase but also in the treatment follow-up and to provide good guidance to the clinicians.

PO5-Blood Gases Workshop

PO5-01

Blood Gases: Preanalytical and Analytical Phases

Fehime Benli Aksungar

Department of Medical Biochemistry, Acibadem University, Faculty of Medicine, Acibadem Labmed Clinical Laboratories, Clinical Biochemistry Coordinator, Istanbul, Turkey

In the assessment of acid-base balance and respiratory function, arterial blood oxygen (PaO_2) and carbon dioxide partial pressures (PaCO2), oxygen saturation (SaO_2), pH and bicarbonate values are analysed by arterial blood gas analysis.

Two main functions of respiration are investigated in blood gas measurements: Ventilation and Oxygenation. In addition, blood, glucose, electrolytes, renal functions, bilirubin and hemoglobin levels can be monitored in arterial blood gas analysis and information about the patient's metabolic status can be obtained with the latest technology.

In addition to our classical knowledge, it has been shown that blood gases can be monitored in venous blood in recent years. However, the reference ranges of the values in venous blood can naturally differ from arterial blood, and the sample type should be known on the assessment of the results.

Blood gas analysis is used in;

• Diagnosis of metabolic/respiratory acidosis and alkalosis,

• Investigating the cause of respiratory failure,

• Treatment monitoring.

In this presentation, pre-analytical processes and their effects on measurements and analytical processes and their effects on measurements will be explained technically and with patient samples.

PO5-02

The Evaluation of Arterial Blood Gases and Metabolism

Isil Ozkocak Turan

Department of Anesthesiology and Reanimation, Health Sciences University, Ankara Numune Education and Research Hospital, Ankara City Hospital Critical Care Clinic, Ankara, Turkey

Arterial blood gas analysis (AKGA) took its place as a definitive method in the diagnose, categorization and quantification of respiratory and metabolic failures following the development of pH electrodes by Cremer et al. in the early 20th century. The indications for AKGA are as follows: After endotracheal intubation and /or mechanical ventilation period, acute respiratory distress syndrome (ARDS), hypoxemic and/or hypercapnic respiratory failure, acute circulatory failure, complex acid-base disorders. During blood sampling an intraarterial catheter is used or direct arterial puncture is performed. The factors as heparine amount in the syringe and the time of blood sampling, time before laboratory, hyperventilation, leukocytosis, hypothermia may affect the results. Volatile acid (CO_2) is produced by carbohydrate metabolism and nonvolatile acid (hydrogen ion, H^+) by protein metabolism. Homeostatic system tries to maintain pH within a narrow range with lungs, kidneys and blood buffers. Steward; with the concepts of strong ion difference (SID) and weak acid concentration (especially albümin) minimized the role of HCO_3^- as an acid-base indicator. The difference of SID from anion gap is lactate content and approaching of SID to zero tilts the balance towards asidemia. Systemic alkalosis due to hypoalbuminemia and hyperchloremic asidosis are better understood with this model. However, practically HCO_3^- centered approach defined with Henderson-Hasselbach equation is used more frequently. When this equation is simplified to $pH \approx HCO_3^-/PaCO_2$, the lungs are seen regulating $PaCO_2$ and kidneys HCO_3^- as the strongest buffer systems. Following detailed history and physical examination, AKGA has to be obtained concomitantly with biochemistry profile, as well as considering control of consistency and validity of the results, primary disturbance definition, calculation of expected compensation, osmolar and anion gaps in asid-base disorders. Mostly seen asid-base disorders are metabolic asidosis, metabolic alkalosis, respiratory asidosis and respiratory alkalosis. As there is a correlation between arterial and venous blood pH's and HCO_3^- levels, without hypercapnia, only pulse oximetry and venous blood gas analysis can be used if the patient is hemodynamically stabil. In conclusion, AKGA is accepted as a gold standard in defining oxygenation, ventilation and asid-base situation when evaluated with the clinical findings.

P06-Laboratory Safety and Communication in the Lab Workshop

PO6-01

Phlebotomy in Preanalytical Process

Pınar Eker

Department of Central Laboratory-2, Istanbul Provincial Health Directorate Chairman of Public Hospital Services-2, Istanbul, Turkey

The Medical Laboratory Professionals and Phelobotomy Society has started its activities in May 2018 as an association where different laboratory specialities meet with the main purpose of making safer phelobotomy in our country. After briefly talking about the reasons for establishment, the latest current safe phlebotomy steps of venous blood collection guide which had been prepared by the joint proposal of the European Clinical Chemistry and Laboratory Medicine (EFLM) Preanalytic Phase Working Group (WG-PRE) and the Preanalytic Phase Working Groups of the Latin American Confederation of Clinical Biochemistry (COLABIOCLI) (WG-PRE-LATAM) will be discussed.

The guideline has been designed to include patient safety requirements and error prevention and recommendation of implementation. The health personnel responsible for blood collection are the target group of the guide.The procedure, the details of which will be described in steps, is based on the best available evidence-based methods. The recommendation consists of four basic sections: 1) Pre-sampling procedures, 2) Sampling procedure, 3) Procedures after sampling and 4) Implementation. Each step is graded in a systematic way based on evidence. The proposal, which has been prepared in accordance with the WHO and CLSI guidelines, contains recommendations on implementation in addition to the existing guidelines. Representatives of 16 EFLM member countries; medical and scientific laboratory specialists, as well as representatives of nurses, phlebotomists and manufacturers of venous blood collection products worked together in the group.

PO6-02

"General Evaluation of Present and Future of Non-Specialist Medical Laboratory Workers", Survey Results Presentation

Feyza Genc Satir

Department of Biochemistry, Istanbul Provincial Health Directorate Chairman Of Public Hospital Services-2 Central Laboratory-2, Istanbul, Turkey

In this presentation, non-specialist personnel which are working in the field of Medical Laboratory; were asked to answer the questionnaire about the following topics: Demographic information, working area and job finding process, job orientation and in-service training, job satisfaction, career planning, communication, venous blood collection work (phlebotomy). The survey was evaluated by answering 35 questions. Determining the current situation of non-specialist personnel working in the field of Medical Laboratory, are aimed to lead the improvement and development activities.

PO6-03

Effective Communication Management in Medical Laboratory

Gulen Feyzan Aydogdu

Department of Biochemistry, Istanbul Provincial Health Directorate Chairman of Public Hospital Services-2 Central Laboratory-2, Istanbul, Turkey

Medical Laboratory is an organizational structure where employees from various occupational groups, managers and mid-level managers work together to produce outputs. The client is a clinician and indirectly a patient. Communication skills are very important tool when constructing this organizational structure to produce non-risky results for patient safety. In the presentation; it will be discussed about communication channels, types of communication, formal communication, informal communication, face to face communication, telephone communication, written communication, power point presentation, electronic communication, visual communication, nonverbal communication, communication barriers and elements of effective communication. Active listening as the most important part of the communication in the presentation and what features are needed to develop this skill will be realized interactively in the context of how and why the laboratory manager should give importance to continuous improvement and improvement within the framework of leadership quality. In addition, correct and incorrect communication models will be supported by the visual materials and samples will be discussed from our daily laboratory life practice.

PO6-04

Diary of A Laboratory Technician

Gulsah Ataker

Department of Biochemistry, Istanbul Provincial Health Directorate Chairman of Public Hospital Services-2 Central Laboratory-2, Istanbul, Turkey

What do we do as a laboratory technician/technician?

In this presentation, within the framework of the professional experience of a laboratory technician who has been working in a public institution for 19 years, information about what the laboratory technician does in one day and their expectations will be given under the following headings.

- Collection and preparation of samples
- Working of samples with manually/analyzer
- Communication management with patients and other health professionals
- Writing, reviewing and converting results into reports
- To follow relevant scientific and technical developments
- Directing the work of the personnel (supervision)
- Risk management
- Stock and resource management
- Conducting, planning, supporting and carrying out scientific research and experiments
- Management of all kinds of laboratory information
- Demonstration of procedures
- Knowledge about quality control processes and implementation
- Expectations and responsibilities in the relationship between laboratory technician and laboratory specialist

P07-Ask the Expert Workshop

PO7-01

Ethanol Analyses: Our Responsibilities and Our Problems

Turan Turhan

Department of Medical Biochemistry, TC Ministry of Health Ankara City Hospital, Ankara, Turkey

Alcohol has been used as a delighting, tranquilizing, sedative substance and also as a drug since ancient history. Alcohol is one of the oldest most well known psychoactive substances and it is the most consumed one after coffee. Reports of World Health Organisation (WHO) declare that two billion people use alcohol world wide and 76 million of them have alcohol abuse disorders. Alcohol abuse related problems are one of the most important problems of our era. Alcohol is the causative factor of more than 60 disorders and injuries. The direct or indirect cost of alcohol related disorders to USA society is mor ethan 166 billion dollars annually.

Alcohol reports are generally requested after trafic accidents or from individuals who act to ruin the order of the society. That's why, ethanol analysis is very important and it is among the most problematic tests that biochemistry specialists have to work with. To minimize the problems encountered in ethanol analyses, preanalytical, analytical and post-analytical variables are need to be weel known. In the Clinical laboratories Guide Line published by Ministry of Health in 09/10/2013 date and 28790 numbered official gazette; The working Essentials of clinical laboratories statement 12 declares that: 'The ministry of health determines the working principles of the laboratories analysing illegal and abused drugs and substances and also the laboratories serving in alcohol and substance abuse treatment centers'. Under the directions of this guideline, work flow and obligations for laboratories doing blood ethanol analysis was determined and published in 11.07.2017 with the number 95966346. Ethanol analyses are carried out in clinical biochemsitry laboratories for legal, social and health relate dissues. However, formany problems caused by analysis technique or legal procedures are expected to be solved by biochemistry specialists, and that's why the evaluation of ethanol results need sexperience and certain accumulation of knowledge.

PO7-02

Cardiac Troponins: Current Approach From Laboratory to Clinic

Asım Orem[1], Cihan Orem[2]

Department of Medical Biochemistry[1] and Cardiology[2], Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey

Abstract

Cardiac biomarkers should be capable of objectively evaluating the physiological status of the cardiomyocytes, the pathological process and the pharmacological response to a therapeutic agent. A good cardiac biomarker should have high specificity and sensitivity, early diagnosis, reflecting the area of myocardial infarction, reperfusion, and showing reinfarction. Cardiac troponins are now accepted as the gold standard due to their high sensitivity and specificity. Studies have shown that high-sensitivity cardiac troponin (hs-cTn) produced by improving the analytical performance of conventional cTns can also be detected in the circulation up to the first two hours following the AMI. Conventional cTn measurements can measure the upper limit value (URL) of 99% only with sensitivity (CV) above 20%, whereas with hs-cTn, these values can measure with CVs of 10% or less. The use of ng/L (or pg/mL) is recommended for cardiac troponins. Serial cardiac troponin measurements are important in distinguishing acute cardiac events from chronic and inflammatory events. Significant changes in ACS are observed, while changes in other events remain absent or limited. There are many studies showing that Hs-cTn contributes positively to the risk assessment of patients. High cTn levels are associated with poor prognosis and risk of death.

Introduction

Cardiac biomarkers should be capable of objectively evaluating the physiological status of the cardiomyocytes, the pathological process and the pharmacological response to a therapeutic agent.

A good cardiac biomarker should have high specificity and sensitivity, early diagnosis, reflecting the area of myocardial infarction, reperfusion, and showing reinfarction. Acute coronary syndrome (ACS) is a set of symptoms and signs that are clinically manifested by unstable angina to acute myocardial infarction (AMI). The aim of approach to patients with suspected ACS;

1. Early diagnosis
2. To rule out non-cardiac chest pain,
3. Identify high-risk patients through stratification and prevent the development of AMI

Akut coronary sendrom

Time is very important in approaching patients with ACS. Studies have shown that revascularization by angioplasty or thrombolytic therapy within the first two hours following chest pain minimizes the development of cardiac damage and positively affects prognosis. Primary interventional procedures are not recommended for events exceeding 12 hours. This is associated with poor prognosis such as cardiac necrosis, post-MI complications and cardiac failure. The discovery of cardiac biomarkers began with aspartate transaminase in the 1954s, followed by creatine kinase (CK) and its isoform, CK-MB. In 1999, the National Academy of Clinical Biochemistry (NACB) described cTn as a standard biomarker for MI. In the following years; it was also confirmed by the Joint Committee of the European Society of Cardiology and the American College of Cardiology. Cardiac troponins are now accepted as the gold standard because of their high sensitivity and specificity. Since troponins I and T have different chemical structures than skeletal muscle, they are called cardiac troponins (cTn I and T). Myoglobin is the earliest known biomarker due to its low molecular weight and the presence of a cytoplasmic protein. Since it is present in both the heart and skeletal muscle, it has no specificity to the heart. The first cardiac troponins produced for routine laboratories (1st Generation) give cross reactions with skeletal muscle, whereas this unwanted feature was eliminated in 2nd and 3rd generations. In addition, studies have shown that high-sensitivity cardiac troponin (hs-cTn) produced by improving the analytical performance of these conventional cTns can be detected in the circulation up to the first two hours following AMI. Therefore, the clinical use of MB, which has no specificity, is almost negligible. CK-MB (mass) is an alternative to cTn, but it is a preferred marker before cTn in the follow-up of reinfarcts. Since cTn T is only available for use by a company, there is no standardization problem. cTn I has not yet been standardized due to the fact that many firms, especially the protein structure, are unstable, make complexes in different forms, and produce antibodies against different regions. Studies in these subjects are being carried out by IFCC working group. cTn I analysis with different company reagents of the same type can reveal quite different results. Expectance of cardiac troponin measurements are to determine 100% of the normal population within normal reference limits and do so with a measurement accuracy of less than 10%. However, these features are provided by very few conventional cTn T and I measurement systems. High sensitivity troponins (hs-cTnT and I) measuring much higher accuracy and sensisvity have been produced with the intensive efforts of the manufacturers in this field. Conventional cTn measurements can measure the upper limit value (URL) of 99% only with sensitivity (CV) above 20%, whereas with hs-cTn, these values can measure with CVs of 10% or less. In hs-cTns where cardiac troponin analytical performance is improved, the measurement lower limit sensitivity is increased by at least 10 compared to the conventional system. Thus, reliable measurements can be made up to levels of approximately 100% of very low and normal healthy individuals, such as 1 to 20 ng/L. Due to the unit (µg/L) used for cardiac troponins, the use of at least two fractional digits (such as 0.005 µg/L) in the reports after the comma causes confusion. The use of at least two fractional digits (such as 0.005 µg/L) after the comma in reports for cardiac troponins causes confusion. Experts recommend using ng/L (or pg/mL) to eliminate this confusion in reports. Thus, a normal value that should be 0.005 µg/L is reported to be 5 ng/L and a pathological value of 5 µg/L is now reported as 5000 ng/L. cTn T shows biphasic secretion kinetics in ACS. The initial secretion to plasma occurs when the stoplasmic cTn Ts of about 7% show a short peak with membrane damage due to ischemia. The second secretion is the result of proteolytic degradation and cellular necrosis due to ischemic damage of cTn Ts due to muscle myofibrils and peaks at 12-24 hours. The secretion kinetics of cTn I is monophasic. The plasma half-life of cTn T is 120 min, whereas that of cTn I is not fully known. Due to the high analytical sensitivity of Hs-cTn, there is a 99th percentile higher value difference depending on the sex and age, and this situation should be redefined. The upper values in the 99th percentile in women lower than in men should be taken into account in the clinical diagnosis of ACS. It is also necessary to take into account the difference in reference range due to age (>70 years). Each method and society should determine these values according to their own. The type of sample used to determine these values is important. While no differences were observed in some methods, for example Architect cTnI was found to be 12 ng/L in the 99th percentile for plasma and 25 ng/mL for serum. Determining the normal reference range for cardiac troponins is a very laborious and costly process. It is recommended that the minimum person to be taken is 300 for men and women. In addition, it should be determined that people are normal in cardiac terms with many laboratory and clinical findings. It is known that false positive results observed in cTns can occur through heterophile antibodies, human anti-mouse antibodies, autoantibodies, rheumatoid factor, hemolysis, fibrin clot and immune complex formation. With the developed hs-cTn methods, some of these interference effects were eliminated.For example, the hs-cTnT method eliminated the interference effect of heterophilic antibodies using chimeric antibodies in the

new system. The problem of specificity of hs-cTn, whose analytical sensitivity was maximized, was tried to be solved by serial measurements of this test. Several recommendations for patients who are slightly under and over 99 percentile have been proposed for a clinical approach. It was emphasized that absolute and quantitative changes in troponin levels with 3-hour cTn follow-up "delta change" were important in the diagnosis of AMI. Delta variation level must be greater than both the biological variation of the test and the measurement variation of that test. Again, in terms of relative values, it was emphasized that delta change over 30% for cTn I and above 20% for cTn T was important in the diagnosis of ACS. Furthermore, studies have shown that 3-hour serial measurements are less diagnostic in comparison to 6-hour serial measurements in the exclusion of AMI. Studies with Troponin T have shown that the 7 ng/L absolute change observed over the 2-hour period is superior to the relative (percentage) change. Serial cardiac troponin measurements are important in distinguishing acute cardiac events from chronic and inflammatory events. Significant changes in ACS are observed, while changes in other events remain absent or limited. There are many studies showing that Hs-cTn contributes positively to the risk assessment of patients. High cTn levels are associated with poor prognosis and risk of death. In the assessment of cardiac troponin elevation, chronic kidney disease, heart failure, cerebrovascular events, pulmonary embolism, myopericarditis and sepsis should be distinguished from ACS. In most of these clinical pictures, low levels of troponin release not exceeding 50 ng/L are observed and usually delta changes are negative. Approximately 53% of chronic kidney patients have cTn T and 17% have high cTn I levels without clinical acute myocardial necrosis. Here, impaired renal excretion of troponins is the most important mechanism. Plasma half-life of troponins is increased due to glycosylated cTn T, especially in chronic kidney patients with diabetes. The lability of cTn I and its rapid disintegration distinguish it from cTn T. Approximately 45% of deaths in chronic kidney disease is due to cardiovascular diseases. 20% of cardiac deaths in these patients are due to AMI. Studies in patients with chronic kidney disease have shown that cTn T increases the risk of death by 2 to 4 times and cTn I increases approximately 2-fold. The increase in cardiac troponins is closely related to the increase in the risk of death.

Conclusions

High sensitive cardiac troponins are now accepted as the gold standard for rule in/rule out of AMI because of their high sensitivity and specificity. In addition, hs-cTn contributes positively to the risk assessment of patients. Serial cardiac troponin measurements are important in distinguishing acute cardiac events from chronic and inflammatory events.

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2nd National Hereditary Metabolic Diseases Laboratory Symposium

Plenary Section

PL-01

Inborn Errors of Metabolism: Clinical and Laboratory Approach

Turgay Coskun

Department of Pediatrics Division of Pediatric Nutrition and Metabolism, Hacettepe University, Faculty of Medicine, Ankara, Turkey

Inborn errors of metabolism (IEM) are rare genetic (inherited) disorders in which the body cannot properly break down a food product into energy, subsequently intermediary substrates accumulate in the body and cause a wide range of symptoms. IEMs generally result from a defect in an enzyme or transport protein which results in a block in a metabolic pathway. Effects are due to toxic accumulations of substrates before the block, intermediates from alternative metabolic pathways, defects in energy production and use caused by a deficiency of products beyond the block, or a combination of these metabolic deviations. When considered collectively, the incidence of IEMs is high. According to the generally accepted classification system IEMs can be divided into three categories; namely, [1] intoxication type, [2] energy-deficiency type, and [3] mixed type.

Diagnosis of IEMs does not require extensive knowledge of biochemical pathways or individual metabolic diseases. An understanding of the major clinical manifestations of inborn errors of metabolism provides the basis for knowing when to consider the diagnosis. A high index of suspicion is most important in making the diagnosis. A metabolic specialist may be helpful in directing the evaluation of patients with suspected or known inborn errors of metabolism. Diagnosis and treatment of IEM require a prompt and an energetic approach in order to prevent the development irreversible organ (particularly CNS) damage. Patient with a suspected diagnosis of IEM can be evaluated in five steps: [1] taking a thorough medical and family history, [2] physical examination, [3] doing initial laboratory tests, [4] doing advanced laboratory tests, and [5] using the means of definitive tests.

PL-02

Laboratory of Inborn Errors of Metabolism-Test Portfolio with Examples

Incilay Lay

Department of Medical Biochemistry, Hacettepe University, Faculty of Medicine, Hacettepe University Hospital, Clinical Laboratory, Ankara, Turkey

Inborn errors of metabolism are emerged from a genetic defect in the pathways of catabolism or synthesis of proteins, fats, carbohydrates and nucleotides. As a result of the mutations, an enzyme/carrier/activator protein involved in the maintenance of the metabolic pathway cannot function and diseases of inborn errors of metabolism with a wide clinical spectrum are seen. By the interruption of the metabolic pathway, the substrate can accumulate and/or toxic metabolites can be formed by the alternative pathways and/or the final product cannot be produced. Clinical manifestations of intoxication and/or lack of energy and/or metabolism of complex molecules are encountered [1, 2]. They are common in populations with consanguineous marriages because the majority show autosomal recessive inheritance (incidence 1/1500-3000) [3-5]. Laboratory of inborn errors of metabolism has gained more importance with the development of new treatment strategies and advancement in laboratory technologies in those diseases where clinical diagnosis is difficult.

Nowadays, screening and diagnostic tests for inborn errors of metabolism are carried out in a specialized clinical laboratory unit under the name of biochemical genetics laboratory. The biochemical genetics laboratory is an interdisciplinary organization involving biochemistry, genetics and pediatric metabolism specialists where special knowledge, experience and interpretation are required. A comprehensive biochemical genetics laboratory consists of 3 functional units: 1) Metabolite laboratory: Analyses of accumulated or toxic metabolites are performed. 2) Enzymology laboratory: Activity analyses of enzymes that cannot function are performed. 3) Molecular genetics laboratory: Mutation analyses are performed in the genes of the proteins which cannot function.

Basic tests of clinical biochemistry are usefull in approaching of a suspected patient of inborn errors of metabolism. In situtations of unexplained acid-base imbalance (metabolic acidosis, lactic acidosis, etc.), hypoglycemia, hyperamonemia, hematological abnormalities, liver dysfunction, sepsis blood gases, complete blood count, urine analysis, electrolytes, glucose, lactate, pyruvate, ammonia, liver and kidney function tests give insight into inborn errors of metabolism. Simple metabolic screening [FEC13, reducing agent, dinitrophenyl hydrazine (2-oxo acids), ketone, nitroprusside analyzes], sugar and amino acid chromatography, quantitative amino acid (tandem-MS and HPLC), free carnitine and acylcarnitines (tandem-MS), organic acids and very long chain fatty acids (GC-MS) analyses and screening for lysosomal storage diseases (liquid chromatography-tandem mass spectrometry, LC-MS/MS) are the first-line laboratory tests for inborn errors of metabolism [6]. Quantitative amino acid analysis in dry blood, urine, blood and CSF samples should be evaluated together with urine organic acid analysis. Characteristic amino acid patterns are important. For example; Elevated levels of leucine, isoleucine, valine in maple syrup urine disease; glycine in organic acidemias; methionine in tyrosinemias are observed. Elevated levels of citrulline provides a distinction in urea cycle defects. Urine amino acid analysis is valuable in amino acid transport disorders. The profile of free carnitine and acylcarnite in the dry blood sample is important in the diagnosis of over 20 inborn errors of metabolism, especially for fatty acid oxidation defects and organic aciduria. For example; Elevated level of isovalerylcarnitine isobserved in isovaleric acidemia. C14, C14: 1, C16, C18 acylcarnitins are high in very long chain acyl-CoA dehydrogenase deficiency or carnitine palmitoyl transferase 2 deficiency. Urine organic acid analysis is important in the evaluation of organic aciduria, aminoacidopathies, urea cycle disorders and congenital lactic acidemia. Characteristic organic acid patterns are observed. For example; includes Elevated levels of methylmalonate, 3-hydroxy propionate, methylcitrate and elevated levels of dicarboxylic acids (adipic ≥ suneric ≥ sebacic) are observed, respectively in methylmalonic acidemia and fatty acid oxidation defects. Variations appear in acute, asymptomatic, anabolic/catabolic disease states Drug usage is important. Peroxisomal and peroxisomal biogenesis diseases, X-linked adrenoleukodystrophy, Refsum disease are evaluated by very long chain fatty acid analysis in the blood sample. Enzyme activity analyses in dry blood spots can be used to screen for 6 different lysosomal storage diseases. Simultaneous enzyme activity measurements for Pompe, Niemann-Pick A/B, Gaucher, Krabbe, Fabry, MPS I are performed nowadays. Enzyme activity analyses for MPS II, MPS IV and MPS VI are also added to the panel in recent years. Other metabolite analyses that are specific to diseases are performed with different techniques in the metabolite laboratory. For example; urine porphyrin analysis (Porphyria), quantification and determination of the types of glycosaminoglycans in urine (types of Mucopolysaccharidoses), leukocyte cystine analysis (Cystinosis), dry blood and urine succinylacetone analysis (Tyrosinemia type I), blood and urine methylmalonic acid analysis (Methylmalonic acid and cobalamin deficiencies), urine orotic acid analysis (Urea cycle disorders, hereditary orotic aciduria), blood gycolysated transferrin analysis (Congenital glycosylation disorders) and so on. Specific enzyme activity analyses in leukocytes and fibroblasts are second-line laboratory tests and are diagnostic tests for inborn errors of metabolism [7]. Inborn erros of metabolism in

Table 1. Inborn errors of metabolism in which specific enzyme activities are performed in leukocyte and/or fibroblast cultures

Lysosomal Storage Diseases **Mucopolysaccharidoses**	**Alternative names**	**Enzyme**
MPS Type I	Hurler, Hurler-Scheie, Scheie	α-L-Iduronidase
MPS Type II	Hunter	Iduronate 2-sulfatase
MPS Type IIIA	Sanfilippo A	Heparan N-sulfatase
MPS Type IIIB	Sanfilippo B	α -N- acetylglucosaminidase
MPS Type IIIC	Sanfilippo C	α -Glucosaminide -N-acetyltransferase
MPS Type IIID	Sanfilippo D	N- Acetylglucosamine -6-sulfatase
MPS Type IVA	Morquio A	N-Acetylglucosamine-6-sulfate sulfatase
MPS Type IVB	Morquio B	ß- Galactosidase
MPS Type VI (arylsulfatase B)	Maroteaux-Lamy syndrome	N- Acetylglucosamine -4-sulfatase
MPS Type VII	Sly syndrome	ß- Glucuronidase
MPS Type VII	Natowicz syndrome	Hyaluronidase
Sphingolipidoses	Alternative names	Enzyme
Fabry	Anderson-Fabry	α- Galactosidase
Farber	Farber lipogranulomatosis	N- Acylsingosine amidohydrolase
Gaucher		Acid ß- glucosidase
GM1 Gangliosidosis		ß- Galactosidase
Krabbe	Globoid cell leucodystrophy	Galactosylceramidase
Metachromatic leukodystrophy		Arylsulfatase A
Multiple sulfatase deficiency	Austin	Measurements of multiple sulfatases
Niemann-Pick Type A/B		Acid sphingomyelinase
Sandhoff	GM2 Gangliosidosis	ß- Hexosaminidase
Tay-Sachs	GM2 Gangliosidosis	α- Hexosaminidase
Pompe	Glycogen storage type II	α- Glucosidase
Other Diseases	Enzyme	
Aspartylglucosaminuria	Aspartyl glucosaminidase	
Sialidosis	N-Acetyl α- neuraminidase	
Fucosidosis	α- fucosidase	
α-Mannosidosis	α-mannosidase	
β-Mannosidosis	β-mannosidase	
Biomarker for Gaucher	Chitotriosidase	
Schindler disease	N-Acetyl α- galactosaminidase	
Wolman disease/Cholesterol ester storage disease	Acid lipase	
X-linked ichthyosis	Aryl sulfatase C	
Biotinidase deficiency	Biotinidase	
Galactosemia	Galactose-1-phosphate uridyl transferase	

which specific enzyme activity analyses can be performed are shown in Table 1.

As the 3rd- line laboratory tests in biochemical genetics laboratory, known or unknown mutations are investigated by molecular genetic analyses. It is important in confirming the enzymatic diagnosis, in cases where pseudodeficiency exists and enzymatic analyzes cannot be performed, in determining the carrier status, and in prenatal diagnosis. If the familial mutation is known, that region is sequenced principally. However, if no DNA analysis has been performed before, the sequence of all encoded regions or the entire genome analysis is performed. If common mutations specific to the population are known, different techniques can be performed for those known mutations without performing whole genome analysis. In some inborn errors of metabolism, mutations can be heterogeneous and multiple. This situation gives rise to diffuculties in interpretation. When an unknown gene variation is detected, it should be confirmed as a mutation that causes disease, by biochemical methods or functional analyses.

For the accuracy and reliability of the results, each biochemical genetic laboratory should be a member of ERNDIM (European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inherited disorders of Metabolism) and CDC (Centers for Disease Control and Prevention) 'Newborn Screening Quality Assurance Program [8, 9].

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PL-03

Genetic Methods and Tools for the Diagnosis of Inborn Errors of Metabolism

Asli Inci

Departments of Pediatric Inborn Errors and Pediatric Genetic Disorders, Gazi University, Faculty of Medicine, Ankara, Turkey

Rapid and definite diagnosis in inborn errors of metabolism is the most important factor to initiate early treatment and to prevent morbidity and mortality. A significant number of inborn metabolic disorders show overlap in clinical and biochemical features and the definite diagnosis can only be achieved by enzyme assay or molecular genetic testing. During the recent years molecular genetic methods have gained significant attention for the diagnosis as molecular methods have some advantages over the biochemical techniques. For molecular tests, analysis for many different disorders can be carried out from a single sample and the results obtained from molecular tests are definite and objective. Also the phenotype can be predicted from the genotype for some disorders. The accuracy of DNA-based diagnostic methods is generally not affected from environmental factors and non-invasive sampling is possible for molecular methods. Molecular results are also very helpful for the prenatal/preimplantation genetic diagnosis. In general, Electronic DNA Microarray, DNA Sequencing by Capillary Electrophoresis and Next Generation DNA Sequencing are used for the detection of point mutations; High Resolution Melting Analysis is used for mutation scanning, Multiplex Ligation-Dependent Probe Amplification is used to detect deletions and duplications and Comparative Genomic Hybridization is used to detect larger deletions and duplications. Especially Next Generation DNA Sequencing enabled the investigation of many genes, even the whole exome or genome at the same time in a relatively short period of time. The recent diagnostic molecular methods have significantly enhanced our diagnostic capability for inborn errors of metabolism with notable accuracy and speed.

PL-04

Biomarkers in Laboratory of Inherited Metabolism Disease

Eser Yildirim Sozmen

Department of Medical Biochemistry, Ege University, Faculty of Medicine, Izmir, Turkey

Inborn errors of metabolism (IEM) that are genetic disorders (more than 400 human diseases), are diagnosed by determination of accumulated molecules and/or deficient protein levels especially 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 molecules which can be determined in blood or body fluids and they reflect the presence of a given disease (diagnostic biomarkers), the prognosis or response to therapeutic intervention or risk of complications or survival (surrogate biomarkers). 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. Primer (direct) biomarkers which are determined in plasma and/or urine (e.g. glycosaminoglycan in urine of patients with mucopolysaccharidosis) are the metabolites accumulated in tissue due to enzyme deficiency. The secondary (indirect) biomarkers which are found as elevated in serum/urine, non-specific, resulted from damaging of other tissues due to a disease (e.g. biomarkers of liver damage and renal damage).

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.

PL-05

Current Trends in Inherited Metabolic Disease Laboratory

Ali Unlu

Department of Medical Biochemistry, Selçuk University, Konya, Turkey

In 1963, Robert Guthrie developed a simple and effective test to detect phenylalanine based on bacterial inhibition in blood samples. Since the understanding of some metabolic disease such phenylketonuria an congenital hypotroidsm complications can be prevented by early diagnosis and intervention. Congenital hypothyroidism, congenital adrenal hyperplasia, biotinidase deficiency and galactosemias were added to screening program by the development of immunassay methods in 1970s. Fluorescence enzyme immunassay is still the most widely used method in screening. The cross-reaction inherent in the immunoassay methods affect the analysis of similar molecules and may yield false positive results. One of main goals in clinical laboratories is to develop and use sensitive, specific, practical and economic methods. Since mass spectrometers (MS) has high sensitivity and specifity, by using MS, routine biochemistry laboratories can reach more accurate results. Multiplex analysis and proportions of analytes help to diagnose inherited metabolic disease. The most practical solution to avoid cross-reaction problem is to use MS method. With the evolving automation of MS, a reference method has become available in intensive laboratories.

The introduction of tandem MS (LC-MS/MS) into newborn screening laboratories has dramatically expanded number of detectable disorders in a single blood spot since 1990. There has been a significant increase in the number of diagnoses of aminoacids, fattyacid metabolism diseases and organic acidemias with the use of LC-MS/MS and gas chromatography MS. 40 aminoacids and acylcarnitines can be determined in a single analysis. LC-MS/MS can also detect heterozygote carriers in addition metabolic disorders. With the development of MS, hemoglobinA2 analyzes can be performed and used for hemoglobinopathy screening. In developed countries, neonatal screening is carried out for nearly 40 diseases and in their newborn screening methods are replaced by MS. Despite the problem of standardization, automated MS are placed in our routine laboratories in addition to newborn screening.

Courses

Course-01

Hemoglobınopathies

Abdullah Arpaci[1], Sibel Elmacioglu[2], Bahar Unlu[1]

Department of Medical Biochemistry[1], Central laboratory[2], HMKU Faculty of Medicine, Hatay, Turkey

Hereditary hemoglobin disorders with thalassemia and sickle-cell anemia are the most common monogenic diseases in the world. It is estimated that about 1-5% of the global population is the carriers of a genetic thalassemia mutation. Hemoglobinopathies are among the most common hereditary blood diseases also in Turkey and are an important health problem especially in the southern and western part of Turkey. The beta thalassemia carrier frequency in Turkey is 2.1% and there are about 1.3 million carriers and around 4.500 patients. When the frequency of carriers is considered, 300-400 sick children are estimated to be born each year, which causes financial and emotional harm to the families and society. Even though Cooley and Lee described the pathophysiology of thalassemia syndromes 90 years ago, the management of these diseases is still complex and requires a gradual process. The high frequency of hereditary hemoglobin variants in some regions may reflect the heterozygous resistance to malaria and with further studies, the resistance was determined to be in alpha, beta thalassemia and hemoglobin E diseases.

Patients with β-thalassemia were typically categorized as minor, major or intermedia based on α-globin or β-globin chain disorders, severity of anemia, and the clinical presentation. Over 400 mutations in the β-globin gene causing the disease ranged from the silent (silent β) ones to the mild mutations leading to a relative reduction in β-globin chain production (β +) and severe mutations. The complete absence of β-globin chain synthesis (β 0), deletion of the gene is rare. β-Thalassemia minor (trait or carrier) represents the heterozygous inheritance of a β-thalassemia mutation. Patients usually have (asymptomatic) microcytic anemia clinically, but it can be stated that the others (silent carriers) have the unidentified hematological abnormalities. Whereas the patients with β-thalassemia major usually present with severe anemia in infancy and can be dependent on transfusion for life, the patients with β-thalassemia intermediate may develop with mild-moderate anemia later and require variable transfusion. Both β-thalassemia major and the intermedia may result from the homozygous or compound-heterozygous inheritance of the mutations in the β-globin gene.

There are two main forms of α-Thalassemia: α + -thalassaemia and α0-thalassemia. Their classifications depend on, by mutation, the deletion of one or both of the α-globin genes and whether its activity diminishes or not. Two common α + -thalassemia forms are called –α 3 · 7 and –α 4 · 2 to define the lengths of the underlying deletions. α + - Thalassemia has various forms caused by point mutations. The most common one is α- CS α which is caused by the chain-termination mutation hemoglobin Constant Spring.

Abnormal hemoglobin variants are also an important health problem for Turkey. Sickle cell anemia (Hemoglobin S) is caused by the replacement of glutamic acid at the 6th position in the beta globin chain with valine (β6 Glu→Val). While the frequency was between 0.37% and 0.6% across Turkey, this frequency was determined to be between 3% and 44% in some regions especially in Cukurova. The term "sickle cell anemia" is used for the patients who carry the sickle cell hemoglobin in genetically homozygous state. The clinical presentation comprised of the findings seen in the people who carry the sickle cell hemoglobin in homozygous or heterozygous state or who carry it with other hemoglobins is called "sickle cell syndromes." Inheritance of HbS from one parent and another hemoglobinopathy (for example beta thalassemia or HbC) from the other parent can result in many sickle cell syndromes. The most common of these syndromes are HbSC disease, HbS/Beta thalassemia, HbS/DPunjab, HbS/OArab, and HbS/E. The clinical findings vary based on the accompanying mutation.

Now, the programs for screening and prevention of thalassemia are widespread, their acceptance depends on the regional distribution and cultural factors. Various screening programs and premarital screening are carried out nationwide. These screening programs are carried out in line with the recommended algorithms using the complete blood count and electrophoresis or HPLC methods. The DNA analysis is required to confirm the diagnosis of thalassemia and hemoglobin variant. In Turkey, in our central laboratories where the prenatal diagnosis is performed, the final diagnosis can be established using the advanced molecular methods such as ARMS, RFLP, Gene Sequencing (classical/new generation).

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Course-02

What is LC-MS/MS ? What not?

Taner Ozgurtas

Department of Medical Biochemistry, Head and Professor, Gulhane Faculty of Medicine, University of Health Sciences, Ankara, Turkey

Standard techniques of analyte detection in clinical chemistry rely on indirect characteristics of an analyte, e.g. its absorption of light, chemical reactivity or physical interaction with macro-molecules. In mass spectrometric methods, in contrast, analytes are detected directly from molecular characteristics as molecular mass and molecular disintegration patterns.

Beginning in the 1970s, gas chromatography-mass spectrometry (GC-MS) instrumentation has evolved to an essential tool for both biomedical research and some important routine clinical chemistry applications.

This technology seems to be of similar novelty for clinical chemistry as immunoassays in the 1970s and PCR in the 1980. The use of HPLC-MS/MS systems in bio-analytical research started already in the late 1980s. Tandem mass spectrometry found its way into clinical laboratories in the early 1990s when first flow injection analysis (FIA)-MS/MS methods were introduced for neonatal screening assays. First implementations in clinical routine laboratories started about a decade ago with realizing the first therapeutic drug monitoring (TDM) assay.

HPLC-MS/MS systems are expensive analytical tools. Investments ranging from 300.000 € to 500.000 € have to be expected to purchase systems suitable for above mentioned routine applications in clinical laboratories. This roughly corresponds to twenty ultrasounds instruments, ten intensive care respirators, of half a modern CT scanner and exceeds the costs for immunoanalyzer systems wide spread in routine laboratories.HPLC-MS/MS systems require substantial hands on time of skilled technicians-typically one instrument occupies one person fully.

It is optimistic but not unrealistic to expect that the typical lifetime of a HPLC-MS/MS is about 10 years. Given a degree of utilization which is

rather typical today for most laboratories (e.g. 250 days per year, 15 h per day, 5 min per sample) about 500.000 sample could be analyzed during these 10 years. Taken together, in the highest through put scenario, overall expenses of about 2 € would result for one LC-MS/MS analysis, while about 6 € per sample are required in a standart throughput scenario.

State of the art HPLC-MS/MS instruments with one – or two dimensional chromatography set ups allow to run up to 20 analyses per hour. Consequently, within 24 h several hundred quantitative analyses can be performed with one HPLC-MS /MS system in a continuous work mode. In most clinical laboratories far smaller series are run in Daily routine, especially if switching from one assay to another requires hardware changes (e.g. of HPLC columns) causing significant down times.

LC-MS/MS is attractive for laboratory medicine for three main reasons

- The development of new methods is independent from the diagnostic industry
- Highly multiplexed analyses are feasible with very low current costs
- When applying the principle of isotope dilution internal standardisation, analyses on a reference method-level of accuracy can be performed in a routine laboratory setting.

Summarizing, it has to be stated, that present day routine HPLC-MS/MS assays are no "turnkey" applications. Both costs and response delays are significantly higher from MS industries.

Course-03

Validation and Verification Applications, Method Comparison and ROC Analysis on the Basis of CLSI Guidelines

Fatih Yesildal[1], Metin Uyanik[2], Erdim Sertoglu[3]

[1]Department of Medical Biochemistry, Istanbul Medeniyet University, Goztepe Education and Research Hospital, Istanbul, Turkey

[2]Department of Medical Biochemistry, Corlu State Hospital, Tekirdag, Turkey

[3]Department of Biochemistry, University of Health Sciences, Gulhane Faculty of Medicine, Ankara, Turkey

Introduction

Existing tests in clinical laboratories have gone through several stages before they were put into use, and after that they were used for diagnostic purposes. These steps refer to the same process in tests produced or modified in clinical laboratories as in commercial manufacturers. This process is examined in the CLSI evaluation protocol (EP) guidelines under two main headings: establishment stage and implementation stage.

CLSI guidelines play an important role in ensuring harmonization between clinical laboratories through standardization of laboratory procedures. During evaluation of measurement procedures, basic information about when and which CLSI guideline to use are defined in CLSI EP19. Establishment stage of the tests consists of feasibility, design, development and validation steps. Implementation stage includes preliminary evaluation, verification, measurement procedure launch and maintenance by the user and measurement procedure retirement (Figure 1) [1].

Establishment stage

1. Feasibility assessment step: It is a preliminary assessment of existing tests and alternative tests in a particular area, potential market, estimated production costs and new demands.
2. Design step: The manufacturer's commercial needs and the intended test performance are evaluated to meet the user's requirements.
3. Development step: The method is developed by making continuous improvements to all measuring procedure components.
4. Validation step: It is the validation of the product through a standardized process in a given population for the intended situation during the establishment stage. These performance characteristics for the measurement procedure are the performance claims that the manufacturer will provide for this method. The main elements and documents used in this scope can be listed as follows:

a. CLSI EP05 (Quantitative tests) and EP12 (Qualitative tests) provide useful information for precision evaluation. [2, 3].

b. Bias (accuracy): It is recommended to evaluate the accuracy using at least 100 patient samples in CLSI EP09 [4].

c. Measurement range (CLSI EP06): According to linearity, precision and quantitation limit values; the measuring range is determined [2, 5].

d. Reference range (CLSI EP28): It is determined within 90% confidence interval by using at least 120 samples, covering 95% of the reference individuals [6].

e. Analytical sensitivity (CLSI EP17): It is determined by limit of blank (LoB), limit of detection (LoD) and/or LoQ values [7].

f. Analytical specificity (CLSI EP14): It is the ability of a test to accurately identify and measure an analyte [8]. This ability is tested as described in CLSI EP07 with different sources of interference possible to affect the test. The effect of hemolysis, icter and lipemia indices and their end-user confirmation processes are described in CLSI C56 [9, 10].

g. Total analytical error (CLSI EP21): It is evaluated by comparisons with patient samples or reference materials; considering a predetermined error target [11].

h. Reagent stability (CLSI EP25): The stability of the reagent is assessed based on conditions such as storage conditions, packaging or transfer conditions [12].

i. Diagnostic sensitivity and specificity: In clinical trials, the diagnostic performance of the test is evaluated by determining the appropriate cut-off value using ROC analysis as specified in CLSI EP24 [13].

Implementation stage

1. Preliminary evaluations (CLSI EP10): In quantitative tests, bias, linearity, carry over and precision data are evaluated by repeated measurement of 10 samples. For qualitative testing, CLSI EP12 is used [3]. If the results are appropriate, the user passes to the verification step.
2. End-user verification: It is the verification of the manufacturer's presented data by the end-user (CLSI EP06, CLSI EP28, CLSI EP17, CLSI EP15) [5-7, 14].
3. Measurement procedure launch and maintenance: This is the process followed to ensure that the test performs properly. This process includes proficiency tests, internal quality control, periodic calibration and verification of calibration.
4. Measurement procedure retirement: It is the termination of the clinical use of a measurement procedure.

Conclusions

The CLSI evaluation protocol (EP) documents define and explain a variety of evaluation parameters for the establishment and implementation of a method. The relevant guidelines were briefly introduced in this text in order to manage and statistically evaluate the validation and verification process of the tests or measurement procedures produced by manufacturers or produced in our laboratories. These applications will also contribute to efficiency and quality management in clinical laboratories.

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Table 1. EP guidelines and evaluations during the establishment of measurement procedures (QMS=quality management system) [1]

CLSI Guideline	Establishment											
	1. Step: Feasibility and design	2. Step: Development	3. Step: Validation									
			Precision	Accuracy	Measuring Interval	Reference Range	Detection Capability	Analytical Specificity	Clinical Validation	Reagent/ Sample Stability	Risk Assessment	General
EP05[2]												QMS01; QMS02; QMS13
EP06[5]												
EP07[9]												
EP09[4]												
EP10[15]												
EP12[3]												
EP14[8]												
EP15[14]												
EP17[7]												
EP18[16]												
EP21[11]												
EP23[17]												
EP24[13]												
EP25[12]												
EP26[18]												
EP27[19]												
EP28[6]												
EP30[20]												
EP31[21]												

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2. CLSI. Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
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11. CLSI. Estimation of Total Analytical Error for Clinical Laboratory Methods; Approved Guideline. CLSI document EP21-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2003.
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13. CLSI. Assessment of the Diagnostic Accuracy of Laboratory Tests Using Receiver Operating Characteristic Curves; Approved Guideline-Second Edition. CLSI document EP24-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.
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15. CLSI. Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures; Approved Guideline-Third Edition. CLSI document EP10-A3-AMD. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
16. CLSI. Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline-Second Edition. CLSI document EP18-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

Table 2. EP guidelines and evaluations during the implementation of measurement procedures (QMS=quality management system) [1]

CLSI Guideline	Implementation															
		5. Step: Verification								7. Step: Measurement Procedure Launch and Maintenance by the end User					
	4. Step: Preliminary Evaluation	Prec.	Acc.	Meas. Interval	Ref. Range	Detect. Capabil.	Risk Assess.	Qual.	6. Step: Preparation for Measurement procedure launch	Prec.	Acc.	Other	Results review and follow up	Gen.	8. Step: Measurement Procedure Retirement
EP05[2]															
EP06[5]															
EP07[9]															
EP09[4]															
EP10[15]															
EP12[3]															
EP14[8]															
EP15[14]															
EP17[7]															
EP18[16]															
EP21[11]															
EP23[17]															
EP24[13]															
EP25[12]															
EP26[18]															
EP27[19]															
EP28[6]															
EP30[20]															
EP31[21]															
													QMS01; QMS02; QMS13		

17. CLSI. Laboratory Quality Control Based on Risk Management; Approved Guideline. CLSI document EP23-A™. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.
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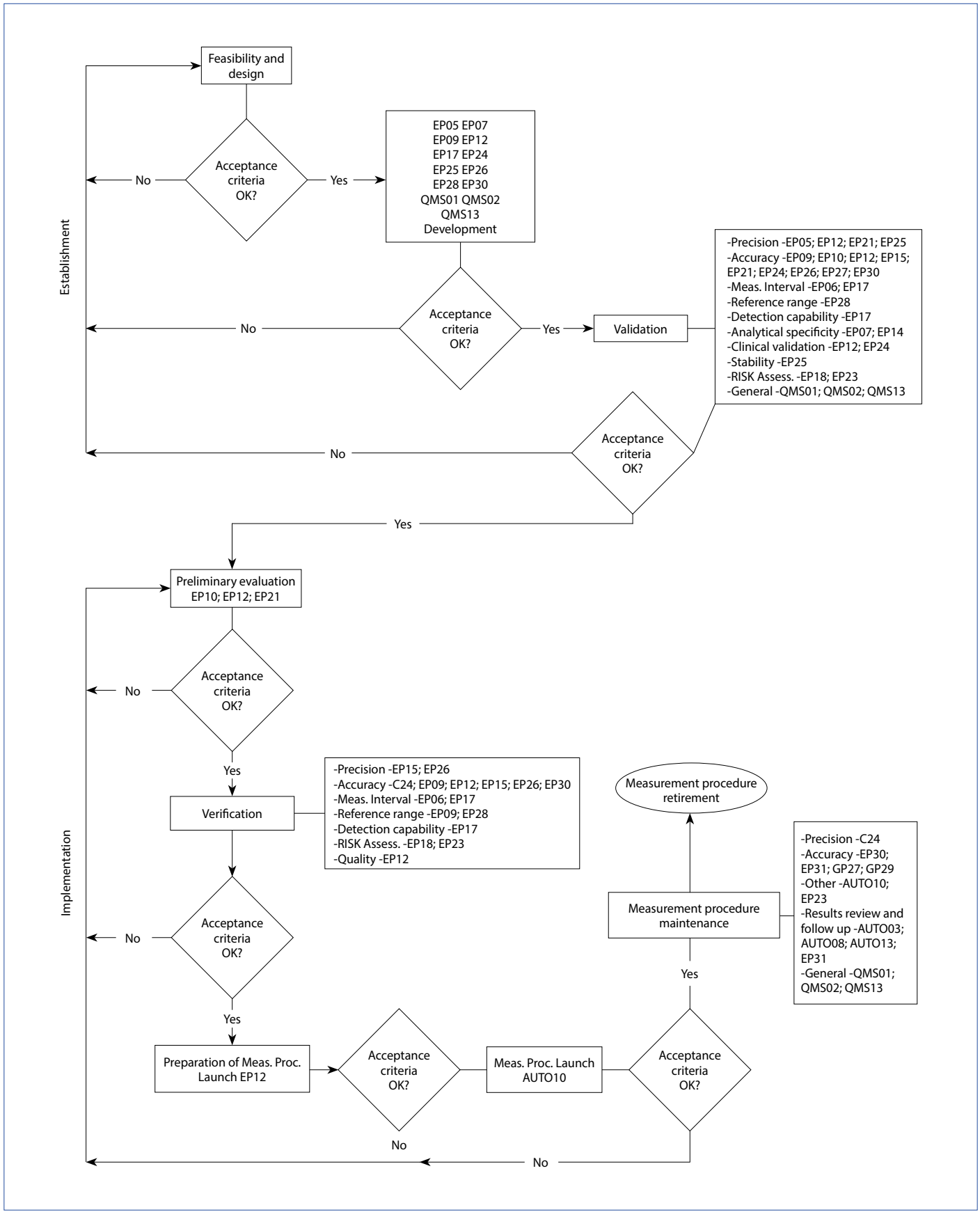

Figure 1. Flow chart of lifecycle of a measurement procedure [1].

Oral Presentation

OP-01

Assessment of laboratory parameters and prediction of mortality in septic premature infants

Hakan Ongun[1], Meltem Demir[2]

[1]Department of Child Development, Istinye University Faculty of Health Sciences, Istanbul, Turkey

[2]Department of Medical Biochemistry, Istinye University Faculty of Medicine, Istanbul, Turkey

Objective: To conduct a study on septic prematures (gestational age<32 weeks) to determine risk factors and predict mortality using clinical signs and laboratory work-up.

Materials and Methods: Out of 914 prematures who were admitted to NICU of İstinye University-affiliated Antalya Medical Park Hospital between 2014-2018, 198 patients were identified septic. Demographics, clinical signs and laboratory findings, body fluids cultures, CBC and hsCRP at different time points (hsCRPinitial, hsCRP24hours) were collected. hsCRP change at two time points was calculated. Depending on blood culture positivity, infants were categorized into two groups (proven or suspected sepsis). SPSS-23 was used for statistical analysis. Mortality risk factors were assessed using multiple regression models.

Results: Analysis verified male predominance (53%), gestational age 28.91±2.67 weeks and birth weights 1240.15±440.76 grams. Rate of proven sepsis (blood culture positivity) was 39.9%. Total length of NICU stay was 55.75±35.06 days with mortality rate of 23.7%. Prematures with proven sepsis demonstrated higher out-of-hospital referrals (p=0.045), frequent intubation rates and longer CPAP respiratory supports (p=0.031, p=0.002). They also presented higher umblical venous catheterization (p=0.012), significant hsCRP alterations and thrombocytopenia (p=0.022, p<0.001) with longer NICU stay (p=0.006). Gestational age and birth weight was associated with mortality (p<0.001, p<0.001). The evidence of lower five-minutes Apgar scores (p<0.001), higher and elongated intubation rates (p<0.001, p<0.001) and frequent catheterizations were observed. Deceased neonates presented significant hsCRP alterations, thrombocytopenia and leukocytosis. ROC analysis indicated an alteration rate of 5.34 times at 24th hour hsCRP measurement predicted mortality with a sensitivity of 91% and specifity of 81% (AUC=0.942, %95 CI: 0.894-0.990, p<0.001). Early thrombocytopenia also increased the odds of mortality by 4.14 times (adjusted ratio: 0.623; OR: 4.140; %95 CI 1.469-11.671; p=0.007).

Conclusion: Early recognition of sepsis with interpretation of clinical signs and laboratory work-up (hsCRP alterations, thrombocytopenia) and timely antibiotherapy initiation is essential for survival.

OP-02

Possible relationship between umbilical cord blood gas and acid-base analysis and dynamic thiol-disulfide levels in newborn infants

Selcuk Gurel[1], Ayse Ozdemir[2], Ozcan Erel[3]

[1]Departement of Pediatrics, Usak Medical Park Hospital, Usak, Turkey

[2]Departement of Biochemistry, Usak University, Faculty of Medicine, Usak, Turkey

[3]Department of Biochemistry, Ankara Atatürk Training and Research Hospital, Yıldırım Beyazıt University, Ankara, Turkey

Objective: Inorder tominimize death and neurological sequelae due to fetal asphyxia, it is important to evaluate intrauterine fetal status anddistress. APGARscoring alone is not sufficient in antepartumevaluation of fetalhypoxia and acidosis as itmay differ among individuals. In addition,an optimaltest has notyet been fully defined. In ourstudy, weaimed todetermine therelationship between thiol(-SH)-disulfite(-S-S)levelsand fetal status in umbilical cord bloodduring delivery,to determine the effect of various perinatalandobstetric factors ontheseparameters and to contribute toearlydetection of fetalhypoxia andacidosis andprognosiscontrol.

Materials and Methods: After the approval of the ethics committee, 108 newborns (F:51, M:57) who were born in3rdStage Neonatal Intensive Care Unit between June 2018 and June 2019 were included in our study. After obtaining written informed consent, APGAR scoring, EC (necrotizing enterocolitis), sepsis and ROP (Retinopathy of Prematurity) intervention anddemographic information were collected. Metabolic and other congenital anomalies were excluded. Blood was collected for the measurement of umblical cord blood gases, thiol (-SH)-disulfide(-S-S) amounts and thiol ratios in umbilical cord blood on the same newborn. Blood gas analysis was performed from each collected sample within 10 minutes of delivery. Cord blood pHwas measured potentiometrically and evaluated separately for term and premature infants. After this evaluation, newborn babies were divided into3 groups. pH<7.21was considered as acidic, pH7.21-7.30 as normal pH <7.0. Study data were evaluated statistically using mean and standard deviations.

Results: In premature babies, disulfide, index 1 and index 2 levels were lower than in term babies, while index 3 was found to be higher in premature babies compared to term babies. The total thiol level was higher in cord blood of 12 newborns with Rh incompatibility (p<0.05.IMA, albumin, disulfide, total thiol, native thiol, index 1, index 2, index 3 levels were not statistically significant.

Conclusion: According to the data of our study,it can be said thatnewborns may be susceptible to oxidative damage and this may increase the risk of disease that starts in the prenatal period, especially in preeclamptic babies. Thiol height in infants with Rh incompatibility was seen as an interesting finding. Although the index 3 level was found to be increased in the infants who were admitted to the newbornunit (n=48), sincethiol levels were not studied after the intervention,no comparison could be made. The absence ofliterature comparing thiol efficacy with umbilical cord blood gas and acid-base analysison the samefetus makes our studyoriginal.

OP-03

Determination of TSH and free T4 reference ranges in pediatric age groups

Mehmet Kalayci[1], Musa Yilmaz[2]

[1]Department of Medical Biochemistry, Elazig Fethi Sekin City Hospital, Elazig, Turkey

[2]Department of Medical Biochemistry, Hitit University, Faculty of Medicine, Corum, Turkey

Objective: In clinical practice, the reference intervals help clinicians to decide whether the laboratory results of patients are normal or not. Laboratory test results are commonly interpreted based on population-based reference ranges or decision limits developed based on clinical outcome studies. However, the need for robust evidence-based reference ranges for the accurate interpretation of laboratory test results has been largely overlooked. This problem is particularly evident in the pediatric laboratory medicine, where age-specific reference ranges based on healthy children and adolescents are not readily available [1]. The aim of this study is to determine the TSH and free T4 reference ranges, measured

Table 1. Manufacturer and calculated reference ranges for TSH

TSH (mIU/L)	Roche manufacturer	Roche calculated (n)	Beckman (caliper)	Beckman calculated (n)
0-6 days	0.7-15.2	0.7-12.6 (275)	0.79-5.85	0.46-9.50 (122)
7 days-1month	0.72-11	0.73-9.07 (545)		0.63-7.20 (414)
1-3 months		0.74-6.10 (215)		0.86-5.50 (233)
3-12 months	0.73-8.35	0.68-4.58 (311)		0.61-4.07 (329)
1-6 years	0.7-5.97	0.74-4.57 (2780)		0.71-4.17 (3224)
6-12 years	0.6-4.84			
12-18 years	0.51-5.30	0.67-4.01 (2365)	0.68-3.35	0.56-3.44 (2622)

Table 2. Manufacturer and calculated reference ranges for free T4

fT4 (ng/dL)	Roche manufacturer	Roche calculated (n)	Beckman (caliper)	Beckman calculated (n)
0-6 days	0.86-2.49	1.01-2.75 (300)	0-20 days=1.35-4.48	0.99-2.15 (160)
7 days-1month	0.89-2.20	1.04-2.24 (562)		0.78-1.61 (372)
1-3 months		1.05-1.76 (217)	20 days-3 years=0.74-1.38	0.79-1.28 (239)
3-12 months	0.92-1.99	1.0-1.68 (315)		0.71-1.16 (3566)
1-6 years	0.96-1.77	1.06-1.71 (2674)	3-18 years=0.61-1.06	
6-12 years	0.97-1.67			
12-18 years	0.98-1.63	0.99-1.64 (1779)		0.65-1.12 (2165)

by different immunoassay devices, in children between 0 and 18 years of age who were admitted to our hospital.

Materials and Methods: The TSH and fT4 results of patients, who had applied to Elazig City Hospital between 01.10.2019 and 01.08.2019 and Elazig Training and Research Hospital between 01.08.2017 and 31.07.2018, were obtained from the Laboratory Information System. TSH and fT4 measurements were done with the device Beckman Coulter DxI-800 in Elazig City Hospital and with Roche Cobas 8000 (e602) in Elazig Training and Research Hospital. Children between the age of 0 and 18 years, who had applied to the outpatient clinics, were included in the study. The outliers were excluded with the Tukey method. The calculation of the reference intervals was done with the MedCalc version 18.11.6 (trial version) according to the C28-A3 protocol (non-parametric percentile method) recommended by CLSI.

Results: In this study, 6.693 TSH and 5.948 fT4 data were analyzed on the Cobas-e602 device, while 7.251 TSH and 6.593 fT4 data were analyzed on the DXI-800 device. Based on these analyzes, the TSH reference ranges calculated using the Cobas-e602 device were 0-6 day=0.7-12.6, 7 days-1 month=0.73-9.07, 1-3 months=0.74-6.10, 3 months-1 year=0.68-4.58, 1-12 years=0.74-4.57 and 12-18 years=0.67-4.01; and the TSH references ranges calculated using the DXI-800 device were 0-6 days=0.46-9.50, 7 days-1 month=0.63-7.20, 1-3 months=0.86-5.50, 3 months-1 year=0.61-4.07, 1-12 years=0.71-4.17 and 12-18 years=0.56-3.44 (table 1). The fT4 reference ranges calculated using Cobas-e602 device were 0-6 days=1.01-2.75, 7 days-1 month=1.04-2.24, 1-3 months=1.05-1.76, 3 months-1 year=1.0-1.68, 1-12 years=1.06-1.71 and 12-18 years=0.99-1.64; and the fT4 reference ranges calculated using the DXI-800 device were 0-6 days=0.99-2.15, 7 days-1 month=0.78-1.61, 1-3 months=0.79-1.28, 3 months-12 years=0.71-1.16 and 12-18 years=0.65-1.10 (table 2).

Discussion: The laboratory test results are mostly interpreted according to the population-based reference intervals or the decision limits based on clinical study results. In the clinical practice, the reference intervals are intensively used by clinicians to determine whether the laboratory results are normal or not [2]. Taking into consideration the importance of the reference intervals in the health service shows that valid and comprehensive reference intervals should be readily available for the clinical laboratories and clinicians. In fact, the necessity for reliable and evidence-based reference intervals regarding the correct interpretation of the laboratory results is usually ignored [3]. Instead, the majority of the efforts to develop the laboratory quality systems were focused on the analytic test performance. However, these huge efforts to improve the test performance go to waste if inappropriate reference intervals are used for the interpretation of the laboratory results. This problem is particularly prominent in the field of the pediatric laboratory, where age-specific reference intervals established for children and adolescents are not readily available [2].

The use of the reference intervals developed for adults for the pediatric test results may lead to erroneous and misleading interpretations. The recommendations of the device and kit manufacturers about the reference intervals related to the pediatric population are also rather limited [2]. Therefore, in this study, we determined the reference intervals of TSH and fT4 for children between the age of 0 and 18 years. We determined the reference intervals of TSH and fT4 in the pediatric age groups with two different devices. The following intervals were determined for TSH: Roche Cobas-e602: 0-6 days= 0.7-12.6; 7 days-1 month=0.73-9.07; 1-3 months=0.74-6.10; 3 months-1 year=0.68-4.58; 1-12 years=0.74-4.57, 12-18 years=0.67-4.01. The reference intervals recommended by the manufacturer were as follows: 0-6 days=0.7-15.2; 7 days-3 months=0.72-11; 3 months-1 years=0.73-8.35; 1-6 years=0.7-5.97; 6-12 years=0.6-4.84; 12-18 years=0.51-5.30. We determined the following intervals for TSH with Beckman DXI-800: 0-6days=0.46-9.50; 7 days-1 month=0.63-7.20; 1-3 months=0.86-5.50; 3 months-1 years=0.61-4.07; 1-12yıl=0.71-4.17; 12-18yıl=0.56-3.44. The reference intervals we determined for fT4 were as follows: Cobas-e602: 0-6 days=1.01-2.75; 7 days-1 month=1.04-2.24; 1-3 months=1.05-1.76; 3 months-1 years=1.0-1.68; 1-12 years=1.06-1.71; 12-18 years=0.99-1.64. The reference intervals recommended by the manufacturer were as follows: 0-6 days=0.6-2.49; 7 days-3 months=0.89-2.20; 3 months-1 years=0.92-1.99; 1-6 years=0.96-1.77; 6-12 years=0.97-1.67; 12-18 years=0.98-1.63. We determined the following intervals for fT4 with Beckman DXI-800: 0-6 days=0.99-2.15; 7 days-1 month=0.78-1.61; 1-3 months=0.79-1.28; 3 months-12 years=0.71-1.16; 12-18 years=0.65-1.10. The manufacturer of Beckman DXI-800 has no recommendation for TSH and fT4 reference intervals related to the pediatric population. These results indicated that each laboratory/country has to determine its own reference intervals. Currently many laboratories are using the reference intervals developed for adults also for the pediatric population.

In this study, the TSH and fT4 reference intervals were not classified according to the genders. In most of the studies, no differences for genders were reported regarding the TSH and fT4 [4-7]. However, in a study conducted by Dijemli et al., a significant difference was determined between the genders for fT4 in the age group 15-17 months [8].

Conclusion: In the last decade, many national- and global-level initiatives have begun to establish pediatric reference ranges with the aim of filling critical gaps with regards to the reference ranges in the pediatric laboratory medicine. In the present study, differences were found between the reference ranges provided by the manufacturer and those of our own population. This makes it to necessary to determine the reference ranges of our own society (particularly among pediatric patients).

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OP-04

The effect of urine creatinine/internal standard ratio change on urine organic acid analysis

Yuksel Gulen Cicek, Soner Erdin, Alev Kural, Nilgun Isiksacan, Zeynep Levent Cirakli, Sehide Baz, Sebnem Tekin Neijmann

Department of Biochemistry, Sadi Konuk Training and Research Hospital, Istanbul, Turkey

Objective: Urine organic acid analysis is used in the diagnosis and follow-up of many hereditary metabolic diseases. The internal Standard (IS) (4-phenylbutyric acid) is added to quantify the organic acids detected in the analysis. The amounts of organic acid are calculated by dividing the sub-curve area of the organic acid by the sub-curve area of the IS, multiplying by 20000, then dividing the molecular weight of the substance. The aim of this study was to determine how the results would be affected by amount of IS over a diagnosed patient.

Materials and Methods: In this study, a urine sample known to belong to a patient diagnosed with 2-OH glutaric aciduria was used. Urine creatinine was measured on the Beckman Coulter AU480 analyzer (Beckman Coulter, Inc. U.S.A). Organic acid analysis was performed with Thermo Scientific Trace GC Ultra/Thermo Scientific ISQ (GC/MS) (Thermo Fisher Scientific, USA). Preparation of the analysis was performed twice by adding the IS both as required and 10 times of this value. Both chromatograms were evaluated and organic acids in the urine were quantified.

Results: Urine creatinine value was 5.1 mg/dL. The values were; 2-OH glutaric acid 169.5 and 6.3 mmol/mol creatinine (n<26.8), succinic acid 722 and 21.4 mmol/mol creatinine (n<79.2), glutaric acid 6.7 and 2 mmol/mol creatinine (n<5.3) and ethylmalonic acid were calculated as 31.9 and 4.6 mmol/mol creatinine (n<14.6), respectively for appropriate amount and 10 times more IS values.

Conclusion: According to the formula, an increase in the amount of IS was predicted to cause a decrease in the amounts of organic acids and the results supported this. However, this decrease did not occur proportional. Such a change may cause false negative results. In this study, we have shown that calculation errors can cause serious changes in the results in such analyzes with more manual procedures.

OP-05

Case report: a newborn with hyperammonemia

Soner Erdin[1], Yuksel Gulen Cicek[1], Melike Ersoy[2], Alev Kural[1], Nilgun Isiksacan[1], Sehide Baz[1], Sebnem Tekin Neijmann[1], Zeynep Levent Cirakli[1], Asuman Gedikbasi[1]

[1]Department of Biochemistry Laboratory and [2]Pediatric Metabolism, University of Health Sciences, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

Objective: Citrullinemia type I (MIM 215700) is a rare autosomal recessive inborn error of distal urea cycle caused by mutation in the ASS1 (Argininosuccinate synthase 1) gene, presents as a clinical spectrum that includes an acute neonatal form (the "classic" form), a milder late-onset form (the "non-classic" form). It is biochemically characterised by accumulation of citrulline and ammonia.

Materials and Methods: Our case was admitted to our hospital at day 6 with poor suckling, vomiting, respiratory distress and drowsiness. In the first five days, patient have had only vomiting with mucus but not poor feding and drowsiness. The pregnancy was uneventful and she was born at 38th week without complication.

Results: At initial laboratory evaluation plasma ammonia was 4261 µg/dL. After that hemodialysis and medical treatment started immediately. The amino acid profile revealed very highly increased citrulline (3460 µmol/L) and increased glutamine (2223 µmol/L), alanine (1599 µmol/L), methionine (350 µmol/L), tyrosine (391 µmol/L) and proline (488 µmol/L) levels. Dried blood spot amino acid/acylcarnitine profile analysis with tandem MS confirmed very high citrulline levels (1439 µmol/L). We determined increased orotic acid (454 mmol/mol creatinine) and uracil (21.2 mmol/mol creatinine) in urine organic acid analysis. All these results were consistent with citrullinemia type 1. In this context genetic consultation was done and DNA sequence analysis is planned. Our patient is now in the 12th day of admission to hospital.

Conclusion: The clinical outcome of citrullinemia depends on the degree of hyperammonaemia on initiation of effective treatment. So early diagnosis and treatment of the disease is vital especially in acute neonatal form. This situation raises the importance of expanded newborn screening (ENS). Turkey have not yet implemented the ENS. Introduction of ENS can improve the early detection and clinical outcome of neonatal onset citrullinemia without significant increase of costs for follow-up or treatment.

OP-06

Case report: 3-metylglutakonık acidure

Sehide Baz, Yuksel Gulen Cicek, Soner Erdin, Alev Kural, Nilgun Isiksacan, Sebnem Tekin Neijman, Zeynep Levent Cirakli

Department of Biochemistry, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

Objective: 3-Methylglutaconic acid is an intermediate in leucine metabolism. It occurs as inherited metabolic diseases of different types and appearance, independent of each other. However, the disease types share a similar biochemical phenotype, while they are clinically quite different.

Type VI MGCA (MEGDEL) caused by mutation in the SERAC1 gene on chromosome 6q25 includes deafness, encephalopathy and a Leigh-like syndrome. The aim of this study was to present a very rare case of MEGDEL syndrome with laboratory findings.

Materials and Methods: Our case was a 5-year-old boy who came to the pediatric metabolism clinic with suspicion of deafness and cerebellar ataxia. The patient was asked for urine organic acid analysis, quantitative serum amino acid analysis, extended neonatal screening test, routine biochemistry, lactate, very long chain fatty acid analysis and magnetic resonance and abdominal ultrasonography for imaging.

Results: Cerebellar atrophy and basal ganglion involvement and stage 1 fatty liver were detected. Extended neonatal screening test and serum amino acid profile were normal, lactate was slightly elevated and liver enzymes were high. In urine organic acid analysis, 3-methylglutaconic acid was 78 mmol/mol creatinine (n<19) and 3-methylglutaric acid was 20 mmol/mol creatinine (n=0). The level of excretion was found to be compatible with 3-methylglutaconic acidurides other than type 1. As a result of all these findings, the patient was referred to the genetics and as a result of the analysis, he was diagnosed with MEGDEL by SERAC1 gene mutation.

Conclusion: When the patient's clinical, imaging and laboratory findings were taken into consideration, all these findings suggested that the diagnosis was one of the 3-methylglutaconic aciduria types and the diagnosis was confirmed by genetic analysis. We have emphasized the importance of clinical and laboratory cooperation in the diagnosis of metabolic tests combined with genetic analysis and clinical findings.

OP-07

Biochemical diagnostic approach to inherited metabolic disorders in hypoglycemia clinic

Melike Ersoy[1], Soner Erdin[2], Yuksel Gulen Cicek[2], Asuman Gedikbasi[3]

[1]Department of Pediatric Metabolism and [2]Biochemistry, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

[3]Department of Medical Genetics, Institute of Child Health, Pediatric Basic Sciences, Istanbul University, Istanbul, Turkey

Objective: Appropriate test order and rapid interpretation of clinical biochemistry tests are crucial for the diagnosis of inherited metabolic disorders (IMD). Because of the confusion with sepsis, especially in the neonatal period, it often results in mortality and morbidity before the underlying metabolic disease can be detected. Our aim is to emphasize the importance of early diagnosis and treatment with algorithmic approach to biochemical tests in a newborn with refractory hypoglycemia.

Case: A 28-day-old male patient was admitted to the neonatal intensive care unit with decreased breastfeeding, respiratory distress and fever. The patient had a pre-diagnosis of sepsis at postnatal 10th hour and had a 13-day follow-up in intensive care unit. Because of hypoglycemic convulsions, metabolic acidosis and high lactate levels, the examinations were planned for IMD. Blood gas analysis revealed pH 7.30, HCO_3 10.9, anion gap 50, Lactate 6.6. In biochemical tests, glucose is too low to be measured (1 mg/dl), creatinine, uric acid and and sodium levels were high. Complete urine test revealed +4 ketone and +2 protein and ammonia level was also high (467 µmol/L). Blood and urine samples were taken to study Tandem MS, organic acid and quantitative amino acids for basal values of advanced metabolic tests and emergency treatment was started. Lactate, ketone bodies and 5-oxoprolin were high in urine organic acid analysis. In the quantitative amino acid profile, alanine and glutamine were low and glutamic acid was high. The metabolic picture was consistent with severe metabolic energy crisis and ATP depletion. Lactate and ammonia levels decreased in the first 5 hours with urgent metabolic treatment and other metabolic tests improved on the second and fourth days. After the acute symptoms improved, further analysis was performed and the patient was followed up with the diagnosis of Glycogen Storage Disease Type 1A.

Conclusion: Ammonia levels should be included in laboratory tests for differential diagnosis of IMD, since acute sepsis is more rare as the first clinical diagnosis in healthy term newborn. If laboratory tests for the underlying cause are not performed during symptomatic hypoglycemia, the patient may be lost without a definitive diagnosis. Therefore, algorithmic approach to biochemical tests, effective communication with the clinical laboratory specialist and the interpretation of the results together is important in the early and definitive diagnosis of IMD.

OP-08

Is there a difference between two PSA results in a patient with follow-up?: reference vhange value

Okan Dikker

Department of Medical Biochemistry, Istanbul Okmeydanı Training and Research Hospital, Istanbul, Turkey

Objective: Prostate specific antigen (PSA) is a tumor marker used in the diagnosis and follow-up of prostate adenocarcinoma. The numerical value that expresses the clinical significance of the change between two consecutive test results is the reference change value (RDD). Giving this value together with patient results is useful in detecting significant differences between serial measurements. In my study, I aimed to calculate the reference change value of the PSA test in our laboratory, and to evaluate the clinical use of RDD in a patient who was followed up with PSA elevation.

Materials and Methods: In our laboratory, two level internal quality control results of the PSA test in 2019 were obtained from the laboratory information system. Westgard rules were used for the acceptance and rejection criteria of the control results. The standard deviation was calculated from these internal quality control data for two levels of PSA test and the averages were taken. Then the coefficient of variation (CV) was calculated using the formula ''Standard deviation (SD)/ Average *100''. The mean CVA values of the two levels were calculated. The CVI (coefficient of intra-individual variation) was obtained from the database at the Westgard site. The RDD value was calculated using the formula (%)=(z. 2½. [CVA^2+CVI^2] ½).

Results: The CVI value for the PSA test was 18.1. The CVA value calculated from the internal quality control data of the test is 11.8%. The calculated RDD for the PSA was 50.2%.

Conclusion: RDD may be useful in a patient with follow-up. When the difference between the two PSA test results exceeds the RDD, it should be interpreted as a significant change. There is a need for further prospective studies on the use of RDD in patients with prostate adenocarcinoma for biological variation calculations.

OP-10

Development of fully automatic malate dehydrogenase enzyme activity measurement kit

Omer Faruk Ozer, Sahabettin Selek

Department of Biochemistry, Bezmialem Vakıf University, Faculty of Medicine, Istanbul, Turkey

Objective: Malate dehydrogenase is one of the NAD+ dependent enzymes of the TCA cycle and its activity varies especially in liver and cancer diseases. We aimed to develop a fully automated Malate dehydrogenase (MDH) enzyme activity measurement kit which is suitable for routine use and has high specificity and sensitivity.

Materials and Methods: The most suitable buffer and pH to obtain the maximum reaction was determined by using different buffer and pH levels. The best activity was taken at pH=8.1 in Tris buffer. MDH activity was achieved by measuring the decrease in absorbance at 340 nm resulting from oxidation of NADH during malate formation from oxaloacetate. MDH activity was increased by using surfactants such as glycerol and triton X. Specific LDH inhibitors such as CuSO4, Cobalt, Oxamate and Oxalate were tested to eliminate LDH interference of our kit and Oxalate was found to completely inhibit LDH activity. After determining the specificity, sensitivity and linearity of our developed MDH kit, it was subjected to all known performance criteria and passed all of them successfully.

Results: The linearity of the test was between 15-3000 U/L (r=0.999). The same sample was tested 20 times at one time and the intra-assay coefficient of variation (CV%) was 2.05, the same sample was tested in 20 consecutive days and the inter-assay CV% was 5.2. Two solutions containing 6 and 60 U/L MDH were added to the serum pool and provide 95-105% recovery. The reference range was <58 U/L. The shelf life at 2-8 °C was 12 months and the reagents were stable for at least 30 days on the autoanalyzer.

Conclusion: A new, stable, reliable, fast and fully automated MDH test that meets the clinical use criteria has been developed as a cheaper and easier to use alternative to complex methods.

OP-11

Evaluation of analytical quality of immunoassay tests by using sigma metrics in Karapinar State Hospital

Saadet Kader

Department of Biochemistry, Karapinar State Hospital, Konya, Turkey

Objective: The Six-Sigma Methodology is a quality measurement method in order to evaluate the performance of the laboratory. In the present study, we aimed to evaluate the analytical performance of our emergency laboratory by using the internal quality control data of cardiac biomarkers and by calculating process sigma values.

Materials and Methods: Biological variation database (BVD) are used for Total Allowable Error (TEa). Sigma levels were calculated using [permissible error (TEa) -Bias]/coefficient of variation (CV). If the sigma values are≥6, between 3 and 6, and <3, they are classified as »world-class«, »good« or »un -acceptable«, respectively.

Results: When the sigma values were analyzed by calculating the mean of 01.01.2019-04.30.2019, of all the hormonal parameters (ferritin, B12, free T4, free T3, thyroid stimulating hormone (TSH), prolactin, estradiol, follicle stimulating hormone (FSH), luteinizing hormone (LH) were found <3.

Conclusion: The "poor quality" levels of hormonal parameters sigma values, decision is taken for the improvement of hormonal parameters in our laboratory. It is possible to determine the test with high error probability by evaluating the fine sigma levels and the tests that must be quarded by a stringent quality control regime. In clinical chemistry laboratories, an appropriate quality control scheduling should be done for each test by using Six-Sigma Methodology.

OP-12

How do therapeutic enzymes affect immunosuppressant drugs measured by LC-MS/MS?

Ataman Gonel[1], Nihayet Bayraktar[1], Ismail Koyuncu[1], Cuneyt Tayman[2], Osman Bardakci[3], Ali Uzunkoy[3]

[1]Department of Biochemistry, Harran University, Faculty of Medicine, Sanliurfa, Turkey

[2]Department of Neonatology, Health Sciences University, Zekai Tahir Burak Maternity Hospital, Ankara, Turkey

[3]Department of General Surgery, Harran University Faculty of Medicine, Sanliurfa, Turkey

Objective: Although LC-MS/MS is preferred as a reliable method, some drugs in the blood matrix may lead to false results. The aim of this article is to investigate the effect of five different enzyme drugs on blood immunosuppressant levels.

Materials and Methods: Five different enzyme drugs (galsulfase, alglucosidase alpha, imiglucerase, elosulfase alpha, laronidase) were added to control materials containing tacrolimus, everolimus, sirolimus, and cyclosporine A drugs. Measurements were performed using an LC-MS/MS instrument. The amount of deviations from the target values was calculated.

Results: Blood Immunosuppressant levels significantly changed after the administration of enzyme drugs. Four different enzyme drugs led to false positive results in the tacrolimus levels at a rate of 10.58% to 37.28%. The highest deviations were observed with the administration of galsulfase and alglucosidase alpha in the sirolimus levels at rates of 336.54% and 395.88%, respectively. Imiglucerase was the least effective enzyme for the sirolimus level. Different deviations between the ratios of - 9.37% and 8.33% were determined at the cyclosporin A level.

Conclusion: False immunosuppressant results associated with enzyme injection may result in immunosuppression failure, organ rejection, and toxicity. For the measurement of immunosuppressant levels, sampling should be done before the enzyme infusion.

OP-13

The comparison of 24-hour urine and spot urine tests in the evaluation of glomerular proteinuria

Dilara Karacan[1], Serkan Yildiz[2], Ali Riza Sisman[1]

[1]Department of Medical Biochemistry, Faculty of Medicine, Dokuz Eylül University, Izmir, Turkey

[2]Department of Internal Medicine, Faculty of Medicine, Dokuz Eylül University, Izmir, Turkey

Objective: The reference method for proteinuria is measurement of the level of protein in the urine for 24 hours. However collecting urine for 24 hours is difficult and error-prone. In our study, we aimed to compare

protein levels in the 24 hours urine and ratio of protein/creatinine in the spot urine in patients with chronic kidney disease (CKD).

Materials and Methods: One hundred patients diagnosed with Type2-DM, amyloidosis, crescentic nephropathy, membranous nephropathy, IgA nephropathy, C3 nephropathy, focal segmental glomerulosclerosis (FSGS) in Dokuz Eylul University Hospital were included in the study. Protein levels in 24-hour urine and protein/creatinine ratio were determined before biopsy. Patients were classified according to the stage of CKD and primary disease subgroups. The correlations between 24-hour urine protein and protein/creatinine ratio were determined at each stage.

Results: A significant correlation was found between protein/creatinine ratio and 24-hour urine protein levels in whole group. The significant correlations were found in stages 1-4 but not in stage 5. When patients were classified according to their glomerular pathologies, high correlations in type2-DM and C3 nephropathy; moderate in membranous nephropathy, IgA nephropathy and FSGS. In the ROC analysis, when taken the 300 mg/day protein threshold in 24-hour urine for pathological proteinuria, the sensitivity and specificity were determined as 93% and 75% in patients with protein/creatinine ratio ≥0.755.

Conclusion: While moderate correlation was found in all CKD patients, no significant correlation was found in stage 5, indicating that the urine protein/creatinine ratio could be safely used instead of 24-hour urine in all groups except stage 5. When classified according to glomerular pathology, the lack of correlation between amyloidosis and crescentric nephropathy subgroups may be due to insufficient number of cases in these groups. Therefore, in the future, it will be appropriate to re-evaluate these subgroups with higher number of cases.

OP-14

Is ischemia responsible for the formation of white matter lesions in migraine?

Alevtina Ersoy[1], Cuma Mertoglu[2], Hasan Yasar[1], Ural Koc[3], Selcuk Akturan[4], Gamze Gok[5], Ozcan Erel[5]

[1]Department of Neurology, Erzincan Binali Yildirim University, Faculty of Medicine, Erzincan, Turkey

[2]Department of Clinical Biochemistry, Erzincan Binali Yildirim University, Faculty of Medicine, Erzincan, Turkey

[3]Department of Radiyology, Golbasi Sehit Ahmet Ozsoy State Hospital, Ankara, Ankara, Turkey

[4]Department of Medicine Education, Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey

[5]Yildirim Beyazit University, Faculty of Medicine, Clinical Biochemistry, Ankara, Turkey

Objective: White matter lesions (WMLs) are more common in migraine patients than in the normal population. Ischemia/hypoxia and oxidative stress are considered to play a role in WML formation. This study aimed to investigate ischemia-modified albumin (IMA), ferroxidase and thiol/disulfide homeostasis in migraineurs with and without WML.

Materials and Methods: Sixty-two migraineurs with WML, 59 migraineurs without WML and 61 controls were included in the study. All participants underwent brain MRI. WML was evaluated according to the Fazekas scale. IMA, ferroxidase, total thiol, native thiol and disulfide measurement was carried out in all participants.

Results: The IMA levels were higher in the migraine groups compared to the control group ($p<0.001$) and in the WML group compared to non-WML ($p<0.001$). The total and native thiol levels were higher in the non-WML group compared to the control and WML groups ($p<0.001$ for both). The disulfide levels were similar between the control and non-WML groups, but they were significantly lower in the WML group compared to the control and non-WML groups. There was no significant difference between the groups in terms of the ferroxidase levels ($p=0.092$). The thiol/disulfide, IMA and ferroxidase levels were not significantly correlated with the frequency and duration of attacks, severity of pain and disability due to migraine.

Conclusion: Increased serum IMA levels in migraineurs point to the role of ischemia/hypoxia, and increased total thiol and decreased disulfide levels indicate an oxidant/antioxidant imbalance in migraine. Ischemia/hypoxia may play a role in WML formation in migraine.

OP-15

Investigation of GALT enzyme mutation on patients with kongenital cataract

Beri Hocaoglu Bozarslan[1], Fatma Birgul Isik[2], Selahattin Tekes[3], Yildirim Beyazit Sakalar[4]

[1]Department of Biochemistry, Diyarbakir Children Hospital, Diyarbakir, Turkey

[2]Department of Biochemistry, Dicle University, Faculty of Medicine, Diyarbakir, Turkey

[3]Department of Genetics, Dicle University, Faculty of Medicine, Diyarbakir, Turkey

[4]Department of Ophthalmology, Kocaeli Derince Training and Research Hospital, Kocaeli, Turkey

Objective: The purpose of this investigation is to analyze GALT (Galactose-1-phosphate uridyl transferase) enzyme mutation in patients with congenital cataract.

Materials and Methods: Q188R, K285N and N314D mutations in the GALT enzyme is researched in 33 (13 girls and 20 boys between the ages of 2 months-9 years) children who are diagnosed with congenital cataracts and therefore operated in Ophthalmology Clinic of Dicle University Faculty of Medicine, and in the healthy subjects of the same number.

2 cc of whole blood sample with EDTA was taken for analysis of GALT enzyme. DNA was isolated from these blood and, DNAs of all samples were amplified with polymerase chain reaction (PCR) and amplified samples were examined for possible mutations with restriction fragment length polymorphism (RFLP). Restriction endonuclease digestion method was used.

Results: As a result, homozygous Q188R mutation was detected in the GALT enzyme of two children (6% of patients) on congenital cataract group.

Conclusion: The frequency of classic galactosemia is 23.775/1 and the incidence of Q188R mutation is %57 in our country, we believe it would be beneficial for public health to generalize galactosemia screening along with other metabolic diseases such as Phenylketonuria, Biotinidase deficiency etc. and that ophthalmologists should not ignore metabolic diseases in congenital cataract patients in newborn period.

OP-16

Evaluation of the association between 25-OH-D3 and total cholesterol levels

Cigdem Yucel, Sebla Ertugrul, Erdim Sertoglu, Taner Ozgurtas

Department of Clinical Biochemistry, University of Health Sciences, Ankara Gülhane Training and Research Hospital, Ankara, Turkey

Objective: Vitamin D deficiency is a major public health problem worldwide. The prevalence of vitamin D deficiency about 50% in all age groups in Turkey. As we know, vitamin D is synthesized from cholesterol and therefore vitamin D levels are thought to be affected by cholesterol metabolism. The purpose of the study was to evaluate association between cholesterol and 25-hydroxy Vitamin D (25-OH-D3) levels in different age groups.

Materials and Methods: Patients aged between 18-65 years who were admitted to our hospital in the last 3 months and who were asked to examine 25-OH-D3 and cholesterol panels were included in the study. The patients were grouped according to age between 18-45 (Group 1) and 45-65 years (Group 2) and according to gender [Male (M): Group 1a and Group 2a; Female (F): Group 1b and Group 2b]. The correlation the differences between 25-OH-D3 and Cholesterol levels and differences between 25-OH-D3 and Cholesterol levels in groups was evaluated.

Results: There was no significant difference between Group 1 and Group 2 and their subgroup according to age distribution.When all age groups were evaluated, a significant difference was observed between 25-OH-D3 and cholesterol in terms of F (n=2136), M (n=1198) ($p=0.026$; $p<0.01$ respectively).In correlation analysis, there was a positive correlation between 25-OH-D3 and cholesterol levels in patients group ($r=0.078$; $p<0.01$).

Conclusion: The assessment of 25-OH-D3 levels with cholesterol levels is thought to be significant, especially in older age patients.

OP-17

The measurement of HbA1c level in diabetic patient with homozygous Hb G-Coushatta variant

Hulya Unal, Aysenur Atay, Muammer Yucel, Huriye Erbak Yilmaz

Department of Medical Biochemistry Laboratory, Izmir Kâtip Celebi University, Ataturk Training and Research Hospital, Izmir, Turkey

Objective: Glycosylated hemoglobin (HbA1c) measurement is widely used in the diagnosis and follow-up of Diabetes Mellitus. Patients with abnormal hemoglobin (hemoglobinopathies) due to inherited coding errors and de novo mutations may have problems with HbA1c measurements. In such cases, fructosamine testing may be useful for glycemic control. We aimed to report the rare case of Hb G-Coushatta variant with low HbA1c level incompatible with fasting blood glucose.

Materials and Methods: A 48-year-old male patient with the diagnosis of Diabetes Mellitus applied to our laboratory. EDTA blood sample was taken and studied HbA1c level by ion-exchange-HPLC assay. In duplicate study, HbA1c was found to be incompatible with fasting blood glucose. Hemoglobin chain analysis was performed to confirm the possibility of any hemoglobin variant. Based on the database of the device, the chromatogram was compatible with the variant 'Homozygous G-Coushatta. In order to evaluate the patient's glycemic control for 2-3 weeks, serum fructosamine level measurement and hemoglobinopathy were planned for family screening.

Results: It was found that HbA2: % 75.4, HbA0: % 4.0, HbF: % 16.8, and Hb: 16.5 g/dL, Hct: % 48.4, RBC: 6.93 million/mm3, MCV: 69.8 fL, MCH: 23.8 pg in complete blood count, and in routine biochemistry fasting blood glucose: 112 mg/dL, HbA1c: 3.1%. Fructosamine level compatible with fasting blood glucose was high (332 µmol/L, Reference range: 205-285).

Conclusion: In patients with any hemoglobin variant, HbA1c measurements by HPLC method may be found incompatible with clinical findings. Unlike chromatographic methods, serum fructosamine measurement should be preferred to evaluate the patient's glycemic control.

OP-18

Comparison of Westergren method with Starrsed Interlinear Sedim Analyzer Device in erythrocyte sedimentation rate

Mustafa Orkmez, Mehmet Akif Bozdayi, Seren Orhan, Mehmet Tarakcioglu

Deparment of Biochemistry, Gaziantep University, Turkey

Objective: The erythrocyte sedimentation rate (ESR) test is one of the most widely studied tests in laboratories. The recommended reference method for ESR measurement is Westergren method. In clinical laboratories, the need for closed and automated systems in terms of safety and ease of the operation of the laboratory's staff and the need to obtain results in a shorter period of time; therefore, the development of new measurement techniques for ESR has become mandatory in recent years.

In this study, we aimed to evaluate the Starrsed analysis method according to the results obtained with the classic Westergren method, from whole blood samples were taken from the same patient.

Materials and Methods: The study included 151 patients who were referred to Gaziantep University Medical Faculty Hospital for ESR measurement and 5 healthy individuals for CV analysis. The results were classified as 0-<20 mm/h, 20-80 mm/h and >80 mm/h according to Westergren method.

Results: The concordance between Starrsed Interliner and Westergren method was evaluated according to Intraclass Correlation method. Westergren result was moderate between 0-<20 mm/h, high between 20-80 and >80, and very high concordance was observed when all the results were evaluated together.

Conclusion: Our results showed that there might be some differences in ESR values obtained from Westergren and Starssed interliner. Unlike the Westergren method, this difference in mean may be due to two different anticoagulants used in Starssed devices and different measurement times. Starrsed interliner ESR method results should be more compatible with the gold standard Westergren method results.

OP-19

Irisin and chemerin levels in patients with Type 2 diabetes mellitus

Yasemin Akgul Balaban[1], Mehmet Kalayci[2], Nisbet Yilmaz[3], Mustafa Unal[4], Turan Turhan[5]

[1]*Department of Internal Medicine, Mecitozu State Hospital, Corum, Turkey*

[2]*Department of Medical Biochemistry, Elazig Fethi Sekin City Hospital, Elazig, Turkey*

[3]*Department of Internal Medicine, Ankara Numune Training and Research Hospital, Ankara, Turkey*

[4]*Department of Endocrinology, Istinye University Medical Park Gaziosmanpasa, Istanbul, Turkey*

[5]*Department of Biochemistry, Ankara Numune Training and Research Hospital, Ankara, Turkey*

Objective: Diabetes mellitus is a chronic disease, with a rapidly increasing global prevalence, characterized by hyperglycemia with disturbances of carbohydrate, protein and fat metabolism [1, 2]. In general, the main problem implicated in the pathogenesis of the disease is insulin deficiency or insulin resistance without an insulin deficiency and many recent studies have reported that the disease was directly associated with adipokines [3-6]. The irisin molecule consisting of 112 amino acids synthesized from muscle tissue and the chemerin molecule, a chemoattractant protein with a molecular weight of 16.6 kDa mainly released from adipose tissue, are among the adipokines [7, 8].

According to the literature review, there was no study that evaluated both irisin and chemerin levels in diabetic patients. This study aimed to investigate the relationship of the irisin and chemerin levels with insulin resistance and/or with the pathogenesis of DM in patients newly diagnosed with type 2 DM (T2DM).

Materials and Methods: After approval was obtained from the ethics committee of Ankara Numune Training and Research Hospital, a total of 90 subjects, 41 patients newly diagnosed with T2DM who presented to the internal medicine outpatient clinics and 49 control subjects, were included in the study (Table 1).

All participants provided written consent after they were informed about the study. Detailed medical history was obtained from all subjects and their age, height, weight and waist circumferences were noted.

Plasma irisin levels were measured using the Human Irisin ELISA kit (Hangzhou Eastbiopharm, China), while plasma chemerin levels were measured using the Human Chemerin ELISA kit (Boster Biological, USA) in an ELx800 device (Biotek, USA) with the ELISA method.

Data obtained in the study was expressed with mean±standard deviation values. Chi-square test was used for qualitative parameters. Student's t test was employed in intergroup comparisons and Pearson's correlation coefficient was used to investigate the relationships between the parameters in the groups. $p<0.05$ was considered statistically significant.

Results: Table 1 shows the demographic and biochemical data of the groups. Irisin levels in the control and patient groups were 3.34±0.97 µg/ml and 2.79±0.83 µg/ml, respectively. Irisin levels in the group of patients newly diagnosed with T2DM were lower than in the control group. Chemerin level was 6.44±2.31 ng/ml in the newly diagnosed patient group, which was statistically significantly higher than that in the control group (5.37±2.23 ng/ml) (Fig. 1).

There was a statistically significant positive correlation between chemerin levels and BMI (r=0.352, p=0.024), HOMA-IR (r=0.359, p=0.021) and insulin (r=0.377, p=0.015) levels in patients with T2DM. Moreover, there was a negative correlation between irisin levels and BMI (r=-0.275, p=0.082), insulin (r=-0.303, p=0.054), HOMA-IR (r=-0.261, p=0.099) and triglyceride (r=-0.338, p=0.031) levels. Although there was a negative correlation between chemerin and irisin levels, it was not statistically significant (r=-0.283, p=0.073).

Discussion: Changes in the secretion of signaling molecules that originates from adipose tissue and inflammation draw attention in the pathogenesis of T2DM. Chemerin, one of the signaling molecules of adipose origin, and irisin, defined as the Renaissance of the metabolism, are

Table 1. Demographic and biochemical properties of the control and patient groups

	Control n=49	Type 2 DM n=41	p
Sex (F/M)	28/21	24/17	p>0.05
Age (years)	40.18±14.14	47.24±9.8	p<0.01
BMI (kg/m^2)	26.47±3.53	29.80±5.94	p<0.01
Waist-circumference (cm)	79.0±12.35	102.97±14.04	p<0.001
Glucose (mg/dl)	86.67±8.41	178.29±79.86	p<0.001
HbA1C (%)	5.21±0.57	8.51±2.69	p<0.001
Insulin (µIU/ml)	6.05±1.46	10.08±4.88	p<0.001
HOMA-IR	1.22±0.29	4.33±2.83	p<0.001
Cholesterol (mg/dl)	212.24±32.33	223.09±46.69	p>0.05
HDL-Cholesterol (mg/dl)	46.83±11.37	40.73±8.19	p<0.01
LDL- Cholesterol (mg/dl)	133.61±26.47	141.44±34.74	p>0.05
Triglyceride (mg/dl)	163.12±73.31	203.75±86.66	p<0.05

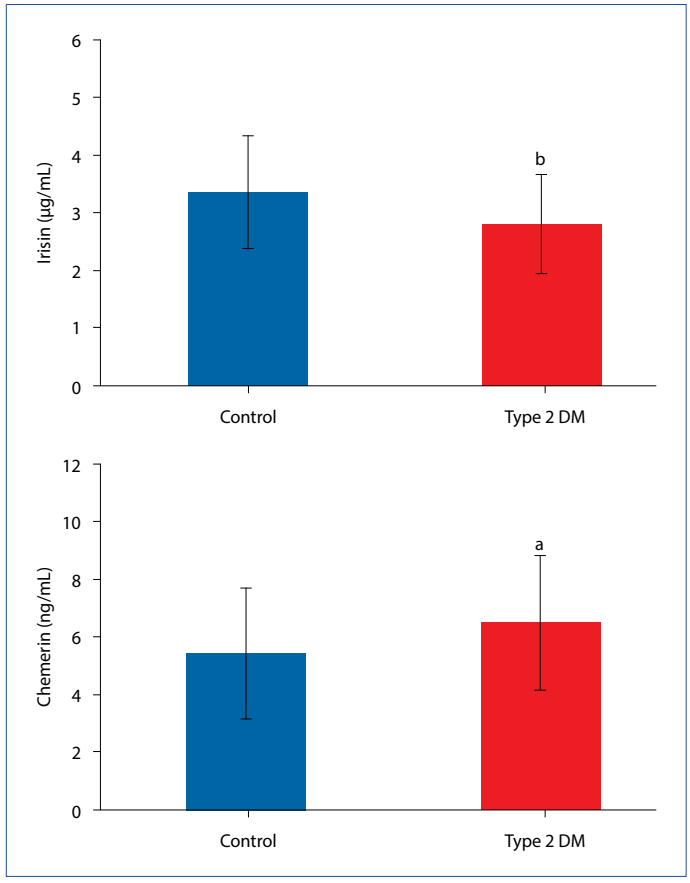

Figure 1. Plasma irisin and chemerin levels of the control and patient groups.
a: p<0.05; compared with the control group.
b: p<0.01; compared with the control group.

among these molecules [13]. Accordingly, this study was planned in order to compare the changes in serum irisin and chemerin levels in patients newly diagnosed with T2DM and in healthy subjects.

It was observed that the level of irisin, a very popular molecule in the recent years, was significantly lower in patients with T2DM than in healthy controls. These results are consistent with the findings of many previous studies [6, 19, 20]. In experiments conducted by Boström et al., it was found that exogenous administration of irisin to mice induced white-to-brown adipose tissue conversion and increased energy expenditure (7), which resulted in improved glucose tolerance and weight loss. In the light of this information, it is thought that irisin can prevent the development of T2DM, since exercise promotes increased irisin synthesis from the skeletal muscle.

Studies comparing serum irisin levels in controls with normal glucose tolerance and newly diagnosed T2DM patients have shown that serum irisin levels were lower in patients newly diagnosed with T2DM [19, 20]. Moreover, elevated irisin levels were linked to a lower risk of developing T2DM. The fact that circulating irisin levels were lower both in newly diagnosed patients and in patients who had T2DM for a long time suggests that irisin can be a T2DM marker [25, 26].

In this study, the change in chemerin levels was also investigated in patients newly diagnosed with T2DM because chemerin is thought to have an impact on insulin-mediated glucose regulation. It was observed that chemerin levels were significantly higher in patients newly diagnosed with T2DM than in the control group. There are many studies reporting that chemerin levels were higher in patients with T2DM than in healthy controls, which is consistent with the results of this study [5, 27, 28].

Chemerin regulates the key effectors of glucose and lipid metabolism such as diacylglycerol acyltransferase enzyme that plays a role in triglyceride synthesis, adipokines and GLUT-4 in mature adipocytes [29]. In 3T3-L1 adipocytes, a moderate increase of insulin-induced glucose uptake and IRS-1 phosphorylation was reported after a short stimulation by low concentrations of chemerin, while longer stimulation by higher chemerin concentrations decreased insulin-induced glucose uptake in the same cells [30]. In addition, it was found that injecting rats with chemerin led to the inhibition of glucose uptake in adipose tissue, liver and skeletal muscle and to increased glucose intolerance.

According to this study, chemerin levels had a positive correlation with insulin and HOMA-IR. Considering the information provided here and the results of this study and other recent studies, it is clear that chemerin plays an important role in glucose metabolism and in the pathogenesis of T2DM. Therefore, it is necessary to understand the role of chemerin and the associated receptors in glucose homeostasis. In addition, cell-based studies and studies conducted on animals and humans support the regulatory role of this adipokine in the metabolism.

Conclusion: Consequently, our knowledge on the mode of action of chemerin and irisin and their effect on the development of diabetes is gradually expanding. The above-mentioned mechanisms and diabetes-dependent changes in chemerin and irisin concentrations suggest that these two hormones have a role in the pathophysiology of DM.

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OP-20

Evaluation of hsCRP, thiamine, and serotonin in fibromyalgia syndrome

Muzaffer Katar[1], Koksal Deveci[1], Hulya Deveci[2]

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

[2]Department of Physical Therapy and Rehabilitation, Tokat Gaziosmanpasa University, Faculty of Medicine, Tokat, Turkey

Introduction: Fibromyalgia syndrome (FMS) is a clinical condition with unknown etiology and determined with chronic, diffuse muscle pain, fatigue, sleep disturbance, cognitive dysfunction and depressive attacks. FM often affects women aged 30-50 years. It's prevalence was found to be 1-4% of the total population, ranging from 0-4% in men and 2.5-10.5% in women [2]. Many mechanisms such as central nervous system, immunological, neurohormonal, psychological, genetic predisposition and environmental factors are thought to play important roles in it's etiopathogenesis [3].

Objective: Fibromyalgia has no physical findings and usually locomotor system and neurological examination are normal. The most important physical examination findings are the presence of multiple tender points in palpation, skinfold sensitivity, cutaneous hyperemia and reticular pigmentation of the skin. Researches reveal that antidepressants such as tricyclic and SSRI may be helpfull in the treatment of the disease.

AIM:The aim of this study was to evaluate inflammation and neuropathy related indicators; high sensitive C-reactive proein (hsCRP), thiamine (B1) and serotonin in the etiopathogenesis of fibromyalgia.

Materials and Methods: Fifty patients with clinical diagnosis of FM and 35 healthy controls were recruited from the patients who applied to Gaziosmanpaşa University Faculty of Medicine Physical Therapy and Rehabilitation (FTR) outpatient clinic. Beck Depression Scale (BDI) and Quality of Life scales were applied to patients and controls, and Fibromyalgia Impact Questionnaire (FIQ) was applied to the patients in addition to other tests. Vitamin B1 levels were measured with Agilent 1100 HPLC-UV device by HPLC (High Performance Liquid Cromotography) method, hsCRP levels with commercial mass photometric method, by Roche Dianostiks Cobas C 501 device and serotonin with commercial kits ELISA (Enzyme-LinkedImmuno-SorbentAssay) method by Chromate Microplate Reader 4300 (Awareness Technology Inc., USA). This project was supported by Scientific Reseach Projects Support Fund of Tokat Gaziosmanpasa University.

Table 1. Displaying variables in groups

Variables	Total	Fibromyalgia (n=53)	Control group (n=35)	p
Age	37±5.58	38.34±5.5	35.09±5.19	-
VAS	7.88±1.84	7.88±1.84	-	-
Tender points	13.46±2.7	13.46±2.7	-	-
BDS	23.34±10.3	23.34±10.3	-	-
FIQ	65.12±12.7	65.12±12.7	-	-
CRP	2.78±3.68	3.19±4.28	2.2±2.54	0.227
Vit B1	44.5±15.24	46.39±16.9	41.64±11.99	0.153
Serotonin	19.85±29.91	20.36±31.7	19.09±27.47	0.847

Data were expressed as mean±standard deviation. The independent sample t test was used to compare continuous normal data between the groups. Tukey HSD was used for post-hoc comparisons of the paired groups. Categorical variables were expressed as numerical or percentage Pearson correlation coefficient was used for correlation between variables. p values less than 0.05 were considered statistically significant. Analyzes were performed using SPSS 19 (IBM SPSS Statistics 19, SPSS inc., An IBM Co., Somers, NY).

Results: The results of our study are summarized in Table 1.

Discussion: FMS is characterized by extensive pain and identified with 11 to 18 finger palpation-sensitive points [4]. Serotonin is found in the rafe nucleus of the brain stem and is synthesized from tryptophan. It is a neurotransmitter involved in non-REM sleep, pain and mood regulation. Decrease in non-REM sleep leads to deterioration of somatic complaints, depression and increased pain. There is an inverse relationship between pain severity and subjective morning pain and serum tryptophan levels. Tryptophan mechanisms, a serotonin precursor, were found to be abnormal in patients with FMS. In some studies, serum serotonin levels decreased in FM patients compared to healthy controls and the number of serotonin re-uptake receptors increased in platelets. Dysfunction of serotonin and neuradrenaline delivery mediating endogenous analgesic mechanisms through descending pain inhibitor pathways in the central nervous system may play a role in the pathophysiology of FM [5]. Treatment with serotonin-neuradrenaline reuptake inhibitors (SNRIs) increases the transmission of neurotransmitters and may improve disease states associated with fatigue and impaired perception [6].

In 1989, IJ Russell found that serotonin levels were low in a group of FMS patients [7]. In another follow-up study, Russel found that serotonin degradation metabolites were low in cerebrospinal fluid (CSF) in a group of FMS patients and in a group of rheumatoid arthritis (RA) patients [8]. In a large review of the neurochemical pathogenesis of FMS; Tryptophan and serotonin levels were found to be low in serum and 5-HTP levels in CSF were low. Low levels of serotonin in serum were found to be inversely correlated with clinical measures of perceived pain [9]. There are studies showing high levels of metabolites in the pathway of kynurene that remove tryptophan from serotonin production in CSFs of FMS patients [10]. Emerging evidence suggests that FMS is associated with irregular processing of pain by the central nervous system (CNS). FMS patients often overreact to the painful stimulus (hyperalgesia) and perceive non-painful stimuli as pain (allodynia) [11]. In our study, no significant difference was found between patients and controls in terms of serotonin.

In many publications, high concentrations of CRP levels were found in FM patients compared with controls. Groven et al. [12] found high concentrations of hsCRP in chronic fatigue syndrome (CFS) and FM patients. In another study investigating systemic inflammatory and stress response in FM, Bote et al. [13] found significantly higher hsCRP and lower serotonin levels in patients compared to age-matched controls. In our study, no significant difference was found between the patients and controls in terms of hsCRP.

Costantini et al. [14] showed that fatigue and related symptoms regressed after high-dose thiamine treatment in ulcerative colitis patients. They hypothesized that chronic fatigue associated with inflammatory and autoimmune diseases may be due to mild thiamine deficiency caused by intracellular transport dysfunction or enzymatic abnormalities and will respond well to high-dose thiamine. Since then, they have begun using thiamine in diseases accompanied by fatigue. As a conclusion, thiamine treatment of 600-1800 mg/day resulted in a significant reduction in chronic widespread pain, fatigue and all other complaints. Monroe et al. [15] suggested that there are many similarities between FM and thiamine deficiency. In our study, we compared FM patients with healthy controls in the light of this information, but we could not determine a significant difference.

Conclusion: It is seen that an in inflammation marker hsCRP levels are high in FMS. Serotonin and vitamin B1 associated with neuropathy are low, but we could not find statistically significant results in our study.

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OP-21

Iron deficiency and iron deficiency anemia frequency in patients with musculoskeletal system pain

Fatih Baygutalp, Ayhan Kul

Department of Physical Medicine and Rehabilitation, Atatürk University School of Medicine, Erzurum, Turkey

Objective: Iron deficiency and iron deficiency anemia are very common and preventable nutritional problems in our country as well as all over the world. There are very few studies available investigating the possible relationship between iron deficiency and pain. The aim of this study was to determine iron deficiency and iron deficiency anemia frequency of patients who have musculoskeletal system pain, retrospectively.

Materials and Methods: Five hundred and fifty patients admitted to our outpatient clinic within the last five years were evaluated retrospectively. After the exclusion criteria (infections, inflammatory diseases, rheumatologic diseases, malignancy, depression, pregnancy and breastfeeding) were applied, the study was conducted with the data of the remaining 338 patients. Serum ferritin levels was measured by enzyme immunassay method and serum iron levels was measured by electrochemiluminescence immunoassay (ECLIA) method.

Results: Mean ages were as follows; all patients: 44.76±14.43 years (n=338), female patients: 45.09±14.22 years (n=311) and male patients: 40.93±16.48 years (n=27). Mean serum iron level was 70.22±30.64 ug/dl in female and 90.33±41.60 ug/dl in male patients (p=0.002).Serum ferritin level was 35.90±36.73 ng/ml in female and 72.93±55.47 ng/ml in male patients (p<0.001). Patients with serum ferritin values below 15 ng/dl were defined as iron deficient (35.79%). In addition to iron deficiency, patients with hemoglobin values below 12 g/dl in premenopausal women and 13 g/dl in postmenopausal women and men were defined as iron deficiency anemia (10.65%). Serum total vitamin B12 concentrations below 300 pg/ml were defined as vitamin B12 deficiency (43.49%) and <200 pg/mL as vitamin B12 deficiency (9.17%).

Conclusion: Considering the rates of iron deficiency and iron deficiency anemia in patients with musculoskeletal system pain, we suggest that serum ferrum, ferritin and vitamin B12 levels should be measured and, if necessary, treated in patients with musculoskeletal system pain to improve treatment success.

OP-22

Apolipoprotein E Allele distribution in Western black sea region: comparison with other populations

Selma Duzenli[1], Ozgur Mehmet Yis[2]

[1]Department of Medical Genetics and [2]Medical Biochemistry, Bolu Abant Izzet Baysal University, Faculty of Medicine, Bolu, Turkey

Objective: Apolipoprotein E is a key protein in lipid metabolism with three major isoforms, i.e. alleles, E2, E3 and E4. APOE allele frequencies show non-random global distribution with high APOE E3 frequency. APOE has been associated with increased risk of cerebrovascular and cardiovascular diseases and is a major genetic susceptibility locus for Alzheimer's disease. It is known that APOE allele frequencies vary widely with demographic factors such as sex, ethnicity and geography. Studies undertaken in different populations have shown different association patterns between APOE allele distribution. Therefore we aimed to evaluate APOE allele frequencies of healthy populations/subjects from the Western Black Sea Region (Bolu and near area) of Turkey and compare them with some other regions of Turkey and the world.

Materials and Methods: The APOE genotypes of 356 healthy individuals from Western Black Sea Region (Bolu and near area) were determined by RFLP and/or RT-PCR after conventional extraction of DNA from whole blood from venopuncture. The subjects' demographic data, ages from 5-87 years, equal gender number, without chronic illness and without apparent sickness or former diagnose relevant to any disease related to APOE. In this study statistical data is shown as allele and genotype frequencies.

Results: This is the first report to have examined the APOE allele frequency of Western Black Sea Region (Bolu and near area) of Turkey. In this study APOE allele distribution appeared as E2=9.97%, E3=82.58% and E4=7.44% in 356 healthy individuals.

Conclusion: Our results show apparent difference in Turkey itself and throughout the world. Turkish alles distribution is similar to the far eastern population. It is postulated that these differences are caused by ancient mankind migration. Our data is important in terms of disease susceptibility and preventive medicine.

OP-23

Lack of immunassay harmonization: prostate-specific antigen (PSA) assay example

Seyda Ozdemir, Fatma Ucar, Ali Yalcindag

Department of Clinical Biochemistry, University of Health Sciences, Yildirim Beyazit Training and Research Hospital, Ankara, Turkey

Objective: Comparability of tumor marker is critical in the interpretation of patients' results for clinical decision-making. Prostate-specific antigen (PSA), which play an important role in prostate cancer screening and diagnosis tests, yield frequently different results among measurement procedures. Currently, most PSA assays are standardized to the Hybritech PSA method or to standards introduced by the World Health Organization (WHO). The objective of the present study was to indicate a lack of harmonization in the PSA tests even when a standard reference material is available.

Materials and Methods: According to the Randox International Quality Assessment Program (RIQAS, 2018), with 3 different levels of external quality samples result for 12 cycles, were evaluated. Total PSA (tPSA) assays were measured with Roche (Cobas 6000/8000, Cobas 4000/e411), Abbott (Architect/Alinity), Siemens (Centaur XP/XPT/Classic), Beckman Coulter (DXI standardized to Hybritech, DXI standard to WHO IRP96/670), DiaSorin (Liaison, Liaison XL).

Results: Peer group means show a wide range in low level 0.426–2.002 ng/mL, in medium level 4.179-15.407 ng/mL and in high level 8.970-31.262 ng/mL. CV% results show a wide range in low level 4.1-18.4, in medium level 4.1-13.2, in high level 4.5-10.2. Generally, the lowest CV% was obtained by Roche Cobas 6000/8000 and the highest CV% was obtained by DiaSorin Liaison.

Conclusion: According to our findings, harmonization of the tPSA results has not yet been revealed. Achieving harmonization of tPSA results requires broad international agreement about identifying a traceable to a reference method and/or a reference material and defining antibody specifities. Laboratories should determine assay details (kit/method/calibration) in each report and clinicians should be alerted to the potential misclassification of patients through PSA variation.

OP-24

Urinary irisin, alpha 1-microglobulin and retinol-binding protein levels in response to regular exercise

Zafer Bayraktutan[1], Ebubekir Bakan[1], Nurcan Kilic Baygutalp[2], Mehmet Ali Gul[1], Murat Ozan[3], Muhammet Celik[1], Sena Erduhan[1], Zuhal Umudum[1]

[1]Department of Medical Biochemistry, Ataturk University, Faculty of Medicine, Erzurum, Turkey

[2]Department of Biochemistry, Ataturk University, Faculty of Pharmacy, Erzurum, Turkey

[3]Department of Physical Education and Sports, Ataturk University, Kazım Karabekir Faculty of Education, Erzurum, Turkey

Objective: Irisin is a thermogenic protein released from skeletal muscle in response to exercise and plays role in converting white fatty tissue into brown fatty tissue. Through these effects, irisin is thought to improve glucose homeostasis and insulin resistance by providing energy consumption. Retinol-binding protein (RBP) is considered as a biomarker of proximal tubular dysfunction with its low molecular weight and it is known that urinary RBP levels are increased in patients with diabetes. Impaired absorption of low molecular weight proteins such as alpha-1 microglobulin is correlated with the degree of renal tubulointerstitial damage in diabetic patients and has predictive value in follow-up of treatment response.This study was aimed to measure urinary irisin, RBP and alpha 1-microglobulin levels during 4 weeks of regular exercise program in sporters and to evaluate the possible effects of exercise on these parameters.

Materials and Methods: 30 male boxers were subjected to regular exercise program for 3 days/week,for four weeks. Spot urine samples were taken at the end of the 1st week, 2nd week, 3rd week and 4th week of exercise program. Urinary irisin, retinol-binding protein and alpha 1-microglobulin levels were measured in all urine samples by ELISA.

Results: After 4 weeks of regular exercise; urine irisin, retinol binding protein and alpha 1-microglobulin levels did not differ significantly from pre-exercise level.

Conclusion: We had previously reported significantly increased serum irisin levels through 3 weeks of regular exercise with the same sporters using the same exercise protocol.It can be concluded that plasma levels of irisin may be considered as an indicator of long-term regular exercise, but urinary levels of irisin may not. Additionally, further studies to be conducted with regular exercise program longer than 4- week duration is needed for determination of urinary alpha 1-microglobulin and retinol-binding protein levels in response to exercise are needed.

OP-25

Comparison of Roche Cobas 601 and Beckman Coulter DXI 800 analysis results in procalcitonin measurement

Fikret Akyurek

Department of Medical Biochemistry, Selcuk University, Faculty of Medicine, Konya, Turkey

Objective: In routine service laboratories, changes in analytical devices and methods are very common.

The impact of these changes on clinical decision processes should be determined. The acceptability of the new system and method results should be proved. In addition, some tests are very limited in alternatives. The number of antibody producers in the procalcitonin test is very limited. In this study, we aimed to compare a new system for the procalcitonin test with the accepted and widely used system.

Materials and Methods: This study was conducted with 120 patient sera sent to the biochemistry laboratory of our hospital for procalcitonin test analysis. Analizler Roche Cobas 601 cihazında elektrokimilüminesans yöntemi ve Beckman Coulter dxı 800 cihazı ile chemiluminessans yöntemi kullanılarak incelendi. Comparisons were made quantitatively and qualitatively (<0.5, 0.5-2, >2 µg/L according to clinical decision thresholds).The results were analyzed by SSPS 21 statistical program.

Results: The results were compared with 120 patients. There was no statistically significant difference between the systems in both quantitative and qualitative comparisons [(p=0.058), (p=0.45)]. Both systems were correlated (r=0.984, p<0.001).

Conclusion: Most of the companies providing routine services for procalcitonin testing are dependent on a single center. The availability of new methods is important in terms of both analytical diversity and price and quality competition. The high correlation of the new system with the old system, which we have compared, established that the new system can be used safely for routine analysis.

OP-26

Average test request in the emergency department and affecting factors

Murat Alisik

Department of Medical Biochemistry, Polatli State Hospital, Ankara, Turkey

Objective: In the emergency department (ED), effective, accurate and prompt intervention is required. For this reason, in many places, supervised laboratories, which only run the tests needed in the emergency department, have been established.Within the scope of the rational laboratory, it is necessary to calculate and evaluate the average rate of test request (ARTR). In this context, it was aimed to investigate the mean test requirements and the factors affecting this situation in ED.

Materials and Methods: The number of patients who applied to ED, patients with test requests, tests requested and on-call physicians between February-August 2019 were noted.It was also noted whether the examiner physician was an emergency medical specialist(ES) or general practitioner (GP).

Results: The total number of patients admitted to ED was 84643, the number of patients with requested tests was 13805 (16%), and the total number of tests was 302246. The ARTR of physicians in ED was 4.02±1.98. While the ARTRs of ES was 3.12±1.22, this rate was 5.14±2.18 for GPs and was significantly higher in GPs than ES (p<0.001). The rate of patients in whom tests were requested was significantly lower in ES (15±5%) than GP (22±10%) (p<0.001). A multiple regression analysisi was run to predict ARTR from patients admitted to ED (B=-0.0005; p=0.577), physician being an GP (B=1.457; p<0.001), number of on-call physicians (B=-0.225; p=0.115) and the number of patients examined by the physician (B=-0.008; p<0.001).

Conclusion: ARTRs should be calculated and these data should be examined within the scope of rational laboratory approaches. The number of patients examined by the physician and whether the physician was ES or GP were independent factors on ARTR.In conclusion, it is suggested that inadequate/incomplete test requests may affect the diagnosis and treatment, and unnecessary test requests won't be cost-effective.Therefore, it is suggested that emergency room planning should be made considering the factors affecting ARTR.

OP-27

Spexin: A novel candidate biomarker for differentiating diabetic cataract and cataract disease with diabetic retinopathy

Meltem Yardim[1], Yavuz Oruc[2], Suleyman Aydin[3]

[1]Department of Medical Biochemistry, Yerköy State Hospital, Yozgat, Turkey

[2]Department of Ophthalmology, Health Science University, Elazig, Turkey

[3]Department of Medical Biochemistry and Clinical Biochemistry, Firat Hormones Research Group, Faculty of Medicine, Firat University, Elazig, Turkey

Objective: Diabetes mellitus (DM) is an endocrinological disease of genetic origin associated with chronic hyperglycemia that causes changes in protein, fat, electrolyte, and especially carbohydrate metabolism, occurring as a result of the insufficient release or inadequate use of insulin hormone. Microvascular, macrovascular, and neuropathic complications may occur during the course of the disease and reduce the quality of life [1, 2]. Diabetic retinopathy is one of the most common complications of diabetes, and it is microangiopathy and neuropathy in which the capillaries, venules, and arterioles in the retina are affected [2]. Chronic hyperglycemia is associated with vascular pathologies. Its risk of development increases with glycemic control and the duration of diabetes [2, 4]. A cataract is generally observed over the age of 50. It is the most important cause of reversible decreased vision. While its etiopathogenesis is not fully known yet, conditions such as kidney disease, glaucoma, hypertension, and diabetes play a role in the etiopathology of cataract [3, 5]. Spexin (SPX) is an endogenous neuropeptide consisting of 14 amino acids, which was described by Mirabeau et al. in 2007 and is also called neuropeptide Q [6]. It is encoded in the c12orf39 gene in humans [7]. As a result of the studies carried out by Kim et al., the SPX gene was demonstrated to be located near the GAL and KISS gene family [8]. Studies demonstrated that SPX was expressed in the brain, heart, lung, liver, muscle, adrenal gland, adipose tissue, kidney, ovary, testis, pancreas, stomach, and different parts of the gastrointestinal tract [9, 10]. The expression of SPX in these tissues may indicate that it is associated with various physiological processes [11, 12]. However, its biological effect and function have not been fully clarified. It was demonstrated by the studies that serum SPX level was negatively correlated with HbA1c, blood glucose, triglyceride, and low-density lipoprotein (LDL) cholesterol levels in Type 2 DM and was low [11-13]. Based on these results, it was concluded that spexin plays a role in glucose and lipid metabolism. A cataract is known to be associated with glucose metabolism. In the literature, there is no study examining the relationship between SPX and cataract and investigating its level in aqueous humor. In this study, we aimed to investigate the level of SPX hormone in aqueous fluids taken during cataract surgery and to reveal whether it was associated with cataract.

Materials and Methods: The study was carried out after the approval of Firat University Faculty of Medicine Local Ethics Committee was obtained. Forty-five patients, who were admitted to the ophthalmology outpatient clinic of Elazig Fethi Sekin City Hospital with the complaint of blurred vision, were diagnosed with cataract and underwent cataract surgery, were included in the study. The patients were divided into 3 groups: Group 1 (Control group): 15 people who were operated for cataract and had no additional disease, Group 2: 15 people who were diagnosed with diabetes and had no retinopathy, and Group 3: 15 people who were diagnosed with diabetes and had retinopathy. Patients with corneal ulcer, corneal scar, retinal dystrophies, age-related macular degeneration, macular edema, vascular disease, and hypertension were excluded from the study. During the cataract operation performed by the phacoemulsification technique, 0.1 mL of aqueous humor was taken from the anterior chamber and transferred to plain biochemistry tubes. It was centrifuged at 4000 rpm (1792 g) for 5 minutes and then stored at -80 °C until biochemical analysis. Biochemical assay validity experiments (linearity, recovery, specificity, sensitivity, intra- and inter-assay experiments) were performed as described by Aydin to confirm the accuracy of spexin measurements in aqueous humor (14). It was determined that SPX measurement in aqueous humor had the same sensitivity as blood. SPX levels in aqueous humor were analyzed by the ELISA technique, Human SPX ELISA Kit (Bioassay Technology Laboratory; Catalog no. E3507Hu Shanghai, CHINA). While Intra-Assay: CV value of the kit was <8%, Inter-Assay: CV value was <10%. Automatic washer BioTek ELX50 (BioTek Instruments, USA) was used in plate washes. Absorbances were spectrophotometrically read at 450 nm with a Chro-Mate, Microplate Reader P4300 instrument (Awareness Technology Instruments, USA). Considering the dilution rate with phosphate buffered saline (PBS), the results were calculated by multiplying the dilution factor. The test results were indicated in pg/mL. The measuring range of the kit (standard curve range) was 10 pg/mL–4000 pg/mL, minimum measurable level (sensitivity) was 4.95 pg/mL.

Statistical analysis: SPSS 22 package program was used for statistical analysis, and the Mann Whitney-U test was used for the analysis of variables between the groups. The cases in which the p-value was less than 0.05 were considered significant.

Results: When the control group and (diabetes+cataract) group were compared, the level of SPX was statistically significantly higher compared to the control group. However, There was no statistically significant differences when the control group and (diabetic retinopathy+cataract) group were compared.

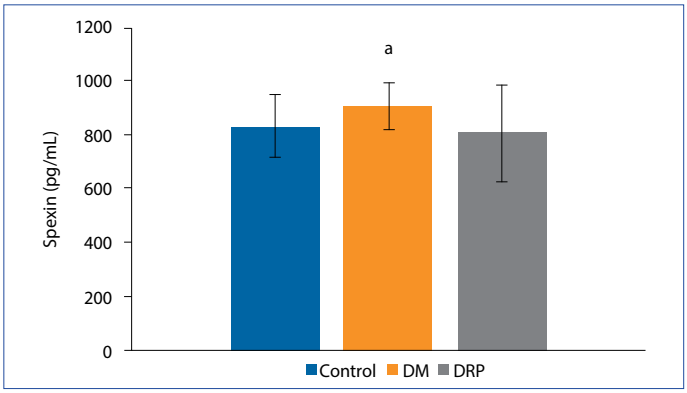

Figure 1. Spexin levels in the studied groups. DM: Diabetes. DRP: Diabetic retinopathy. a: Control versus DM groups (p<0.05).

Table 1. Spexin levels in the controls and diabetic patients

	Control	DM	DRP
SPX (pg/mL)	830.67±115.70	904.37±86.86[a]	807.43±176.82

DM: Diabetes; DRP: Diabetic retinopathy.

Conclusion: SPX, a 14-amino-acid peptide which has been discovered in recent years, is synthesized in many biological tissues, and plays a role in type 2 DM [10, 12]. Therefore, it is a new molecule that regulates glucose metabolism. In this study, the fate of SPX in diabetic cataract and cataract with diabetic retinopathy was investigated since glucose metabolism is impaired in diabetic cataract and cataract with diabetic retinopathy. Aqueous humor fluid SPX was higher in diabetic cataract than that of circulated SPX. It is considered that it was high in our study probably because SPX was synthesized in the lacrimal glands of the eye or it was transferred to the aqueous fluid by diffusion since its molecular weight was low, or we thought that both assumptions were possible. Based on these results, SPX was considered to play a role in the etiopathology of diabetes+cataract rather than diabetic retinopathy and to be a novel marker that may play a role in differentiating cataract with diabetic retinopathy from diabetes+cataract.

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OP-28

Evaluation of preoperative and postoperative s100B and neuron specific enolase levels in liver transplantation

Bora Dinc[1], Ilker Onguc Aycan[1], Necmiye Hadimioglu[1], Zeki Ertug[1], Abdullah Kisaoglu[2], Ismail Demiryilmaz[2], Mutay Aslan[3]

[1]Department of Anesthesiology and Reanimation, [2]General Surgery and [3]Medical Biochemistry, Akdeniz University, Faculty of Medicine, Antalya, Turkey

Objective: This study aimed to evaluate plasma neuron specific enolase (NSE) and S100β levels in liver transplantation.

Materials and Methods: A total of 56 patients who underwent liver transplantation were divided into three groups. Healthy donors (group D), end-stage liver failure (ESLF) patients (recipient, group R) and ESLF patients diagnosed with hepatic encephalopathy (HE) (Group HE). Prognosis, preoperative routine laboratory findings, serum NSE and S100β in samples obtained at preoperative, postoperative -first and -sixth months were analyzed.

Results: Serum NSE and S100β levels were significantly higher in ESLF patients compared to healthy donors, particularly during the preoperative period. There was a significant decrease in serum NSE and S100β in ESLF patients during the postoperative measurement periods compared to preoperative levels. Serum NSE and S100β levels measured at three different time points showed no significant difference between ESLF patients and ESLF patients with HE. However, recent Model of Endstage Liver Disease (MELD) and Child-Turcotte-Pugh (CTP) scores showed a significant correlation with serum NSE and S100β in ESLF patients diagnosed with HE. Serum NSE and S100β levels in healthy donors significantly increased within the first month following hepatectomy and decreased in the sixth month following surgery.

Conclusion: Although serum NSE and S100β levels significantly decreased with improved liver function in recipients following liver transplantation, there was no complete recovery within 6 months after surgery. The increase in serum levels of NSE and S100β in donors measured following hepatectomy were detected to remain slightly higher in the post-operative sixth months.

OP-29

Evaluation of measurement uncertainty of clinical biochemistry analytes in Mus state hospital

Muhammed Fevzi Kilinckaya[1], Mustafa Taner Yeler[2]

[1]Department of Laboratory of Public Health, Mardin, Turkey

[2]Department of Biochemistry Laboratory, Mus State Hospital, Turkey

Objective: Quality control of analytical measurement is a step used to evaluate whether measurement method meets the criteria required for patient care. Quality Control has both internal and external content. Measurement uncertainty is an important issue expresses a measurement for each test. Calibrators and control materials of analytes, reagents affect many factors measurement.

In our study, evaluation of measurement uncertainty of clinical biochemistry analytes in Mus State Hospital's Clinical biochemistry laboratory and aimed to evaluate the meeting criteria of the analytical quality objectives derived from biological variations Ricos and EuBIVAS.

Materials and Methods: In this study, Cobas 6000 Modular Analysis Series (Roche Diagnostics, USA) autoanalyser in Mus State Hospital Medical Biochemistry Laboratory was used. Measurement uncertainties of Urea, Uric Acid, Direct and Total Bilirubin, Phosphorus, HDL, Calcium, Chlorine, Magnesium, Potassium, Total Protein, Sodium analytes were calculated. Two levels of internal quality control data and one-year external quality control data provided by KBUDEK were used for each analyte. In this study, measurement uncertainty calculation model was used according to NORDTEST guideline. "desirable" analytical quality target was calculated according to both EuBIVAS and Ricos biological variation databases.

Results: Urea, uric acid, total and direct bilirubin measurement uncertainties are within the desired limits according to both EuBIVAS and Ricos. Although the measurement uncertainty of the phosphorus analyte is within the desired limits according to Ricos, it is exceeded desired limit of EuBIVAS. HDL, Calcium, Chlorine, Magnesium, Potassium, Total Protein and Sodium analytes are excedded desired uncertainty limit of EuBIVAS and Ricos.

Conclusion: Analytical Quality Indicators are one of the factors that should be taken into consideration by the medical biochemistry specialists managing medical biochemistry laboratories. In this context, internal and external quality control data should be examined carefully and necessary precautions should be taken in case of precaution status.

OP-30

Time-dependently evaluation of "Storage Lesions" in stored red blood cells: the protective effect of rosmarinic and alpha lipoic acid

Mehmet Ramazan Sekeroglu[1], Erdem Cokluk[1], Zubeyir Huyut[2]

[1]Department of Medical Biochemistry, Sakarya University, Faculty of Medicine, Sakarya, Turkey

[2]Department of Medical Biochemistry, Van Yuzuncu Yil University, Faculty of Medicine, Van, Turkey

Objective: Erythrocytes for transfusion can be stored at 2-8°C for up to 42 days under suitable conditions. Starting from the first stage of storage, morphological, biochemical and functional changes are occured in erythrocytes thats' called storage lesions. We aimed to investigate the protective effects of Rosmarinic and Alfalipoicacid, against time-dependent biochemical storage lesions in stored human erythrocytes.

Materials and Methods: For this purpose, one unit of blood was taken from each of 10 healthy volunteers to blood bags containing CPDA (citrate-phosphate-dextrose-adenine) and leukocytes were removed and erythrocyte package was divided into three equal parts and stored in bags containing SAGM (saline, adenine, glucose, mannitol). No procedure was performed on the erythrocytes that were accepted as control group (n=10). 10 µg/mL of rosmarinicacid was added to the second group of erythrocyte and 10µg/mL of alphaaipoicacid was added to the third group of erythrocyte packs(respectively Rosmarinic Acid and Lipoic Acid group). At the beginning, 14, 28, 42 and 56 days erythrocyte oxidation sensitivity, Total Antioxidant Status (TOS), Total Antioxidant Status (TAS), Oxidative Stress Index (OSI), ATP, 2,3-biphosphoglycerate, catalase (CAT)), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), reduced glutathione (GSH), mean erythrocyte count and volume were determined.

Results: The means of the measurands in the groups were compared with the beginning day the MDA and invitro oxidation susceptibility levels were increased with time in all three groups ($p<0.05$) and catalase and GSHPx levels increased on the 14th and 56th day ($p<0.05$). ATP was decreased in the control group ($p<0.05$) but not in rosmarinicacid group ($p>0.05$) and also lipoicacid group was significantly decreased at 56 days ($p<0.05$). SOD, ATP, 2,3 BPG, MCV, HGB, MCH, MCHC levels did not change in time ($p>0.05$).

Conclusion: These results shown that; although rosmarinic acid and lipoic acid show some protective effects on ATP in storage erythrocytes, neither oxidant-antioxidant status nor biochemical storage lesions have been shown to have a favorable effect on erythrocyte quality of life.

OP-31

Determination of individuality index and reference change value in the parameters that is used to evaluate the calcium metabolism

Erdem Cokluk[1], Nagehan Esra Aydin[1], Mehmet Ramazan Sekeroglu[1], Abdulkadir Aydin[2], Fatima Betul Tuncer[1]

[1]Department of Medical Biochemistry, Sakarya University, Faculty of Medicine, Sakarya, Turkey

[2]Department of Family Medicine, Sakarya University, Faculty of Medicine, Training and Research Hospital, Sakarya, Turkey

Objective: Individual reference interval values can be generated by calculating and using individual and interindividual biological variation values, which provides significant benefits for clinicians to accurately evaluate laboratory results. In this study, it is aimed to determine the reference change value (RCV) and individuality index(II) of serum calcium, phosphorus, magnesium, PTH and 25(OH)Vitamin D that is used to evaluate the calcium metabolism.

Materials and Methods: Five samples taken from 20 healthy volunteers (10 female, 10 male), between the ages of 19 and 52, on day 0, day 1, day 7, day 14 and day 28 in a one-month period were studied twice to eliminate the analytic variation between days. Analytic variation(CVA), within-subjects biological variation(CVI) and between-subjects biological variation (CVG) values were calculated by using the arithmetic mean and standard deviation found for the evaluated parameters. II and RCV values were derived with these calculated values. Data were analyzed using the CV-ANOVA statistic program.

Results: Individuality index was calculated as 0.12 for calcium, 0.85 for phosphorus, 0.17 for magnesium, 0.09 for PTH and 0.39 for 25(OH)Vitamin D; and RCV values were calculated as (95%/99%) 3.5/4.6; 5.0/6.5; 8.0/10.5; 14.3/18.8; 27.8/36.6 respectively.

Conclusion: Because the II values calculated for calcium, magnesium, PTH and 25(OH) Vitamin D were less than 0.6; employing RCV may be more appropriate than employing the population based reference range for these parameters. However, since the calculated values of II for phosphorus was between 0.6 and 1.4, using both population based reference interval and RCV values may be appropriate for this parameter. Considering the lack of data in the BV database for many parameters such as the 25(OH) Vitamin D, that we evaluated in our study, we believe that more comprehensive studies are needed to similarly contribute to the database and encourage further employment of RCV.

OP-32

Comparison of glucose measurement uncertainty in 4 different autoanalyzers and reporting to the patient

Mustafa Sahin

Department of Medical Biochemistry Laboratory, Hitit University, Erol Olcok Education and Research Hospital, Corum, Turkey

Objective: The uncertainty of measurement is a quantitative indicator of laboratory result quality and shows to what extent the test result represents the real value. In our study, we aimed to calculate measurement uncertainty of glucose test studied with the same brand 4 different routine biochemical autoanalyzers in our laboratory, compare our findings and evaluate how uncertainty value is reported to patients.

Materials and Methods: In the study, the internal and external quality control data of glucose test measured by hexokinase method in Beckman Coulter brand 4 biochemistry autoanalyzer (2 autoanalyzers in central laboratory, in emergency laboratory 2 autoanalyzers) was used. With the calculation model based on Nordest guide, measurement uncertainty of glucose test was calculated using 1440 internal quality control data at 6-month pathological and normal levels for 4 autoanalyzers and 24 external quality control data at 6 cycles and 1 level at each cycle. The results were compared with allowable limits.

Results: Measurement uncertainty values for glucose were determined as 8.59% for the Beckman Coulter AU5800-1 autoanalyzer, 8.19% for Beckman Coulter AU5800-2 autoanalyzer in the central laboratory, 7.84% for Beckman Coulter AU680-1 autoanalyzer, and 9.33% for Beckman Coulter AU680-2 autoanalyzer in the emergency laboratory. In the study, the extended measurement uncertainty values for glucose were found in total allowable error (+/-10%, CLIA'88) in 4 autoanalyzers.

Conclusion: Laboratories with multiple autoanalyzers running the same test should keep in control the analytical difference among the autoanalyzers. Laboratories must determine the measurement uncertainty calculation model and evaluation criteria. In addition, laboratories must provide test results that do not exceed the targeted total allowable error (%TEa) values and inform the clinician about measurement uncertainty. Measurement uncertainty results can be reported in patient reports based on autoanalyzer or in the form of arithmetic mean of all autoanalyzers.

OP-33

Determination of carryover in random error research process for calcium test results

Pınar Eker

Department of Central Lab2, Istanbul Provincial Health Directorate Chairman of Public Hospital Services-2, Istanbul, Turkey

Objective: Calcium is the most abundant mineral in the body and its results often lead to further clinical research. It was decided to carry out "carryover" study due to randomized problems in Ca results in 8 Biochemistry autoanalysers available in Istanbul Presidency2 Central Laboratory.

Materials and Methods: We performed carryover experiment on Abbott Architect c16000 Biochemistry Autoanalysers for Archem (ArsenazoIII) calcium reagent in Fatih Sultan Mehmet Training and Research Hospital Central Laboratory2. The simple carryover evaluation study was designed based on CLSI EP10-A3 and "Assay Applications Guide. A homogeneous serum pool was prepared representing the reference range. Serum pool was studied in 5 replicates and the mean target value was recorded. This

value was called the "Non-Contaminated Measurement Mean". All tests on the clinical biochemistry panel except Archem calcium were called "donors". Ca values were recorded as "contaminated recipient". The same serum pool was used in each cycle. First, the non-contaminated calcium value, then the donor test in 5 replicates and the third sample of contaminated calcium were studied.

Results: % Bias was calculated according to the target calcium value for each test. Bias values of 3.5% and above were considered as carryover for calcium. Following the smart washing procedure, the study was repeated. Carryover was detected for magnesium (4.3%), amylase (6.45%), albumin (4.3%), alkaline phosphatase (4.3%), creatinine (4.3%), urea (8.6%), triglyceride (4.3%), iron (5.38%)) and total protein (4.3%).

Conclusion: The Carryover study is a procedure used to evaluate transport between reagents and to minimize transport if detected. At the end of the study, extra washing was defined for the necessary tests. As a safety enhancing procedure, device 1 was reserved for Ca testing only. By means of Abbott Alin IQ, it was automatically sent to the device number 1 when Ca-test was rerun.

OP-34

Trimester specific reference intervals for serum TSH and free T4 among Turkish pregnant women

Mehmet Fatih Alpdemir, Medine Alpdemir

Department of Clinical Biochemistry Laboratory, Balikesir State Hospital, Balikesir, Turkey

Objective: Laboratory measurement of thyroid function plays an important role in the assessment of maternal thyroid health. We aim to investigate the reference intervals (RIs) of thyrotropin (TSH), free thyroxine (FT4) and triiodothyronine (FT3) in pregnant women

Materials and Methods: The study was conducted at Balıkesir State Hospital, during 2018 and 2019 using results from samples submitted to our laboratory for routine clinical examinations. Only healthy pregnant women were included in the study. This study was included 135 non-pregnant women and 395 pregnant women (130 for 1st trimester, 130 for 2nd trimester, and 135 for 2rd trimester) aged between 18 and 45 years. TSH, FT4 and FT3 levels were measured using the Abbott Architect i2000SR analyzer. 1st trimester, 2nd trimester and 3rd trimester was defined as 4–12, 13–24, and >25 weeks, respectively.

Results: Mean±SD age of subjects were 32.4±8.3 years for non-pregnant women, 30.4±6.3 years pregnant women. Gestational weeks of the pregnant women were mean weeks of 7.7, 19.1 and 31.6 for 1st trimester, 2nd trimester, and 3rd trimester, respectively In the non-pregnant women, RIs (median) of TSH, FT4 and FT3 were 0.63-2.85 mIU/L (1.48), 0.87-1.25(0.98) ng/dL, and 2.11-3.51(2.86) pg/mL. In the 1st trimester, RIs (median) of TSH, FT4 and FT3 were 0.41-2.49 mIU/L (1.29), 0.80-1.50(0.98) ng/dL, and 2.42-3.55(3.06) pg/mL. In the 2nd trimester, RIs of TSH, FT4 and FT3 were 0.62-3.41 mIU/L (1.85), 0.77-1.16 ng/dL (0.95), and 2.59-3.52(3.12) pg/mL. In the 3rd trimester, RIs of TSH, FT4 and FT3 were 0.67-2.98 (1.65) mIU/L, 0.73-0.98 (0.82) ng/dL and 1.61-3.66 (3.01) pg/mL. TSH and FT3 concentration were significantly different in the all trimesters compared with non-pregnant women

Conclusion: The present results demonstrate that serum TSH and FT3 RIs are differenced by trimester specific. Our study is the first to determine trimester-specific RIs of TSH, FT4, and FT3 in Turkish women with pregnancies.

OP-35

Total analytical error or measurement uncertainty?

Kubranur Unal

Department of Biochemistry, Gazi Mustafa Kemal Public Hospital, Ankara, Turkey

Objective: Total analytical error (TAE) is commonly used to evaluate analytical performance in laboratory medicine. TAE is a simple and practical procedure. However, there has been a criticism that the theoretical basis of TAE is lacking and it cannot fully determine the analytical performance. This study is designed to compare the validity of TAE and Measurement uncertainty (MU) in analytical performance evaluation.

Materials and Methods: TAE and MU of glucose was estimated from internal and external quality control results. TAE is expressed linear sum of the random and systematic errors. MU defines coverage interval that is contained the true value of result. Allowable Total Error (TEa) is analytical quality goal that determines acceptable limits for result with a single measurement for both random error and systematic error.

Results: The TAE and MU of glucose was estimated were estimated to be 4.12% and 3.05%, respectively. Estimating MU by 'Root Sum of the Squares' allows the TAE values which use linear method to be higher than the MU values. Moreover, when evaluating analytical performance, comparison of TAE and MU results with TEa limits is widely used. The TAE and MU values of glucose test did not exceed the TEa limits in this study. But now, it is recommended to evaluate MU with a new analytical quality specification 'permissible MU'.

Conclusion: When evaluating analytical performance, both MU and TAE theory have some their own advantages and challenges. MU evaluates trueness and precision separately and allows to detected possible error sources in cause effect relationship. But, TAE composes performance characteristics by combining of trueness and precision in a single expression.. Moreover, different methods are used to calculate MU and there is still no standardization of the calculation. However, TAE and MU continue to be complementary methods each other and are frequently used in evaluating analytical performance.

OP-36

"Atypical cell" analysis in urine with automated flow cytometry method

Nalan Gokalp, Banu Isbilen Basok, Fatma Demet Arslan, Inanc Karakoyun, Ayfer Colak

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

Objective: Significant advances have been made with new technologies in fully-automated urinalysis. One of the best examples is a potential for non-invasive and early detection of urinary tract cancers through the atypical cells(aC)' presence with urinary flow cytometry (FC). We aimed to confirm morphologically aC detection of the FS system and to evaluate the accordance of aC presence in compliance with bladder cancer through the patient records retrospectively.

Materials and Methods: The aC -research parameter- was detected by the FC method on the fully-automated urine analyzer (Sysmex UF 5000; Sysmex Corporation,Kobe, Japan). The cut-off value for aC positivity was defined as "a 1 aC or more per 10 high power field". The urinary aCs were confirmed morphologically in urine sediment preparations stained with "Sternheimer&Malbin" dye -prepared in house- and through the system's digital images. The relationship of aC with other urine parameters and

preliminary diagnosis/diagnosis data was statistically evaluated with SPSS 24.0.

Results: aC was detected in 122 (7.7%) of 15.782 urine samples that analyzed between May and August. FS graphs, microscopic, and digital images of aCs were given in graph 1, figure 1, and 2, respectively. Since patients with urinary system cancers in our cohort was recorded as 2.5% and the shortness of the diagnosis data, accordance of aC presence in bladder cancer cases could not be evaluated. A significant correlation was found between aC and leukocyte positivity (r 0.230; p=0.011).

Conclusion: The bladder cancer incidence arising and there is currently no validated or valid non-invasive protocol for early diagnosis. Leukocyte positivity and the urinary tract infection (UTI) should be considered when evaluating the aC presence in UTI/presence of leukocytes in urine. In summary, aC detection with urinary FS has been morphologically confirmed, but aC's utility and efficacy in bladder cancer screening should be monitored and supported by further prospective studies.

OP-37

An evaluation of critical laboratory values procedure by clinicians

Rahile Akin[1], Fatma Birgul Isik[2]

[1]Department of Medical Biochemistry, Bitlis State Hospital, Bitlis, Turkey

[2]Department of Medical Biochemistry, Dicle University Faculty of Medicine, Diyarbakir, Turkey

Objective: Critical values are the laboratory test result that require the clinicans to be informed as soon as possible in cases where there is a risk for the patient's diagnostic, therapeutic and/or preventive medical intervention is required. İn accordance with the "Regulations on Improvement and Assessment of Health Care Quality" published in the official gazette in 27.06.2015 with issue number of 2939; medical laboratories should ensure that critical values are reported to the physician in a timely and efficient manner. In this study; we aimed to investigate and improve the effectiveness of critical laboratory value reporting between our laboratory and clinicians.

Materials and Methods: A questionnaire on 'Critical values and reporting' was applied to 56 specialist physicians working in our hospital clinics and the results were evaluated.

Results: 28 of the participants were from pediatrics and internal medicine, while 16 from surgery and 12 from emergency department. The ratio of clinicans thinking that 'critical laboratory value reporting' contributed to diagnosis and treatment was found to be 76.0% and 89.0% respectively. Critical laboratory value reporting was found to be insufficient at 40.0%. Although 56% of the participants did not find the critical value reporting in the hospital information system (HIS) sufficient, 74% stated that they learned the results from the HIS.

Conclusion: For faster and more effective diagnosis and treatment, each hospital should make communication methods and parameter arrangements according to their own conditions in the critical value declaration and support this with educations.

OP-38

The role of CETP Taq1B polymorphism in young atherosclerotic heart disease

Bilal Ilanbey[1], Meral Kayikcioglu[2], Ebru Demirel Sezer[3], Sacide Pehlivan[5], Ferhan Girgin Sagin[3], Feristah Ferda Ozkinay[4], Eser Yildirim Sozmen[3]

[1]Department of Medical Biochemistry, Kirsehir Ahi Evran University, Faculty of Medicine, Kirsehir, Turkey

[2]Department of Cardiology, [3]Medical Biochemistry, [4]Medical Genetics, Ege University, Faculty of Medicine, Istanbul, Turkey

[5]Department of Medical Biology, Istanbul University, Faculty of Medicine, Istanbul, Turkey

Objective: There is increasing evidence that oxidative modification of LDL plays a central role in atherogenesis and HDL-cholesterol levels is negatively related to the risk of coronary artery disease (CAD). Previously, it has been shown that Cholesteryl ester transfer protein (CETP) is involved in the regulation of plasma HDL-cholesterol levels. The role of CETP during atherosclerotic process is still debated; since it may induce both anti-atherogenic and pro-atherogenic consequences. Although several mutations and polymorphisms in the CETP gene have been identified, Taq1B polymorphism has been the most studied one, which is consistently associated with HDL levels. In this study, we conducted a case control study to investigate known risk factors and pathogenesis parameters such as oxidized-LDL and paraoxonase (PON) activity in young Turkish population (<50 years) with CAD embracing different genotypes of CETP Taq1B.

Materials and Methods: The study group consisted of 97 patients (age <50 years) who were hospitalized for CAD. 43 healthy volunteers constituted the control group. Fasting blood samples were drawn. Serum PON activities, oxidative markers of LDL (LDL-diene and LDL-TBARS) were determined along with the routine biochemical parameters in all groups. Following DNA extraction from leukocytes, CETP Taq1B polymorphism was determined by PCR amplification and restriction enzyme digestion.

Results: LDL-diene and TBARS levels and stimulated LDL-TBARS levels were higher in patients compared with control group. The distribution of the three genotypes of CETP within control group didn't show any statistical significance difference, while the frequency of B1B2 genotype was 10.536 times higher in the patients. There was no significant difference between three genotypes in the patient group in respect of BMI, and other biochemical parameters.

Conclusion: We conclude that the genetic polymorphism of CETP has no significant effect on CETP function and CETP polymorphism may not be proposed as an independent risk factor for cardiovascular events.

OP-39

The effect of 15-lipoxygenase gene transfer on immunomodulation ability of mesenchymal stem cells

Alper Tunga Ozdemir[1], Rabia Bilge Ozgul Ozdemir[2], Ayse Nalbantsoy[3], Afig Berdeli[4]

[1]Department of Medical Biochemistry Laboratory, Merkezefendi State Hospital, Manisa, Turkey

[2]Department of Immunology and Allergy Clinic, Manisa City Hospital, Manisa, Turkey

[3]Department of Bioengineering, Ege University, Faculty of Engineering, Izmir, Turkey

[4]Department of Pediatrics, Ege University, Faculty of Medicine, Molecular Medicine Laboratory, Izmir, Turkey

Objective: The metabolites derived from membrane phospholipids play an important role in the initiation and resolution of inflammation. 15-lipoxygenase (15-LOX) is an enzyme responsible for the synthesis of lipoxin (LX) and resolvins (RV) that involved in the resolution of inflammation. In this study, we aimed to the comparison of effects of mesenchymal stem cells (MSCs) which 15-LOX enzyme gene transferred, and naive MSCs on immune cells.

Materials and Methods: We co-cultured 15-LOX-MSCs and nMSCs with PHA-activated-PBMCs that obtained from healthy volunteers (n=3) at 1:1, 1:5 and 1:10 E:T ratios for 48 hours. We measured the inhibition of proliferation by WST-1. We evaluated the changes of IFN-g, IL-4, IL-10, IL-17a, LXA4, and RVD1 in medium supernatants by ELISA.

Results: We found that IFN-g and IL-4 levels were significantly suppressed in 1: 1 co-culture groups, but there was no significant difference in other groups. IL-10 levels of 15-LOX-MSCs in the 1:10 group were significantly higher than the other groups. IL-17a levels were significantly increased in both nMSC and 15-LOX-MSC groups compared to the control group, but the increase in 15-LOX-MSC groups was significantly lower than nMSC groups. The LXA4 and RVD1 levels of the nMSC groups were significantly lower than those of the 15-LOX-MSC groups. In WST-1 analysis, we found that 15-LOX-MSCs suppressed PBMC proliferation, especially at a 1:10 culture ratio, more effectively and significantly than nMSC.

Conclusion: We showed that 15-LOX-MSCs can increase the expression of immune suppressive cytokine IL-10 in proportion to the severity of inflammation, but reduce IL-17a expressions, which are closely associated with autoimmune diseases, and 15-LOX-MSCs have been shown to be superior in suppressing activated PBMCs. In conclusion, our findings suggested that MSCs may perform effective suppression especially in severe inflammation by 15-LOX gene transfer. However, in order to reach a more conclusive judgment, our data should be supported by in-vivo studies.

OP-40

Serum vitamin B12 levels in presence of helicobacter pylori in gastric mucosa

Levent Deniz[1], Enver Yarikkaya[2], Hale Aral[1], Merve Senyuzlu[1]

[1]Department of Medical Biochemistry, Istanbul Training and Research Hospital, Istanbul, Turkey

[2]Department of Medical Pathology, Istanbul Training and Research Hospital, Istanbul, Turkey

Objective: In patients categorized according to Helicobacter pylori (H. pylori) positivity, serum vitamin B12 levels and inflammation status were investigated, retrospectively.

Materials and Methods: Patients (>18 years) reported with H.pylori positivity were included the study. Data was retrieved from the hospital records of four months through February-May 2019. Patients with gastric malignancies were excluded. With suspicion of malnutrition or any other causes of deficiency, patients with B12<150 ng/L were also excluded.Instead of gradual sampling, endoscopic sampling was performed only in the antral region of the stomach; the absence of H.pylori is unclear, so we had no control group. Patients were categorized according to histopathological and histochemical (semiquantitative) examination of H. pylori, as following; Group-1:1 positive (n=97), Group-2:2 positive (n=117), Group-3:3 positive (n=67) out of 3 positive. Liver enzymes and B12 (Beckman Coulter Inc.), and hemogram parameters (Sysmex Corp.) previously studied (at maximum 6 months prior to or after then endoscopy) were taken.

Results: We could reach biochemical data in only one third of the patients who underwent endoscopic examination; 252 of all (281) patients had chronic active gastritis. There was no difference in alanine amino transpherase, gamma-glutamyl transpherase, mean corpuscular volume, hemoglobin, white blood cell counts and neutrophil/lymphocyte ratio between the groups. When Group-1 was compared to Group-3; although mean age was higher in Group-1 (53 vs. 47 years), B12 levels were found significantly higher ($p<0.05$) in Group-1 (244 vs. 217ng/L), respectively. Linear regression analysis revealed that H.pylori positivity significantly correlated with B12 levels ($r=-0.166$; $p<0.05$).

Conclusion: We had no difference in liver or inflammation markers between 3 groups. In presence of H. pylori, serum B12 levels should be monitored. Conversely, investigating gastric H. pylori is recommended in decreased serum B12 levels.

OP-41

Measurement uncertainty in complete blood count

Hatice Bozkurt Yavuz[1], Suleyman Caner Karahan[2], Huseyin Yaman[2], Asim Orem[2], Yuksel Aliyazicioglu[2]

[1]Department of Biochemistry, Sebinkarahisar State Hospital, Giresun, Turkey

[2]Department of Medical Biochemistry, Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey

Objective: Measurement uncertainty is defined as a magnitude representing the distribution of measured values.It is recommended that uncertainty be calculated and reported with the results. Different methods have been identified for calculation, Australasian Association of Clinical Biochemists (AACB) and Nordtest (Handbook for Calculation of Measurement Uncertainty in Environmental Laboratories) are common guidelines. The aim of the study was to determine the uncertainty of two different complete blood count device models accordance with two different guidelines.

Materials and Methods: Measurement uncertainty values were calculated for four complete blood count autoanalysers, Beckman Coulter LH780 [R1, R2]; Beckman Coulter DXH800 [A1, A2] found in KTU Farabi Hospital clinical biochemistry laboratory. Nordtest,AACB guidelines were used,with data of 2017 year. 10 parameters (HCT, HGB, MCH, MCHC, MCV, MPV, PLT, RBC, RDW, WBC) in the external quality control (EQC)program (BIORAD-EQAS Hematology) were selected.Two guidelines recommend calculating separate uncertainty for different levels.However,target values of internal quality control (IQC-Beckman Coulter Control) samples of MCV,MCH,MCHC,RDW,MPV were so close to each other for all three levels.Single uncertainty value was calculated for these parameters.

Results: Rilibak, CLIA and BV-Desirable total allowable error limits (TEa) were used for evaluation. WBC, RBC, HGB, HCT and RDW were within and MCH, MCHC and MPV were above the TEa limits for all analyzers. The uncertainty of platelet at LH780 devices for $70x10^3/\mu L$ level with AACB guideline was 4.74% and 4.63%; with Nordtest guideline was11.49% and 14.81%. These are the highest values in all parameters.

Conclusion: WBC subgroups were not included because they could not be evaluated with EQC.We observed QC was insufficient for MCV, MCH, MCHC, RDW, MPV. The presence of only BV-Desirable limits for MCH, MCHC, MPV may be the reason for uncertainty to appear above TEa. In device instructions, CV% value at low levels of platelet is considerably higher than other tests, and LH780 has a greater CV% than DXH800. When uncertainties were calculated with AACB,it was found close to each other and low for two models. This indicates the importance of the use of EQC data in uncertainty calculation.

OP-42

The relationship between pneumatic tube transport system and hemolysis at emergency department

Sibel Cigdem Tuncer

Aksaray University Faculty of Medicine, Aksaray, Turkey

Objective: The objective of this study was to compare the effect of pneumatic tube system with manual transport on hemolysis of emergency department blood samples.

Materials and Methods: It is found that a total of 121741 samples were transported to the laboratory of emergency department in the 8-month period between November 2018 and June 2019. Samples were transferred manually (Group I) in the first 4 months while in the last four months they were transferred by pneumatic tube system (Group II). Percentages of the rejected sample causes were calculated separately by the formula of 'the number of the rejected sample causes/the number of the total samples X 100'.

Results: 121741 samples were transported to the laboratory of emergency department in the 8-month period. 1.44% of samples were rejected by laboratory technicians due to preanalytical error. Number of the total samples in Group I was 54323, rejected sample number due to preanalytical error was 942. 181 samples of the 942 were rejected because of hemolysis. The proportion of those rejected for hemolysis was 19% of the total rejected. Number of the total samples in Group II was 67418, rejected sample number due to preanalytical error was 813. 170 samples of the 813 were rejected because of hemolysis. The proportion of those rejected for hemolysis was 18.04% of the total rejected.

Conclusion: Pneumatic tube transport system is more faster and reliable than the manual method.

In our study blood samples transported to the emergency laboratory by pneumatic tube system was found to have a lower percentage of hemolysis than samples transported manually contrary to some other studies.

OP-43

Repurposing of alexidine dihydrochloride as an apoptosis-initiator and cell cycle inhibitor in human pancreatic cancer

Esra Aydemir Coban, Fikrettin Sahin

Deparment of Genetics and Bioengineering, Yeditepe University, Istanbul, Turkey

Objective: Highly aggressive and resistant to chemotherapy, pancreatic cancers are the fourth leading cause of cancer-related deaths in the western world. The absence of effective chemotherapeutics is leading researchers to develop novel drugs or repurpose existing chemicals. Alexidine dihydrochloride (AD), an orally bioavailable bis-biguanide compound, is an apoptosis stimulating reagent. It induces mitochondrial damage by inhibiting a mitochondrial-specific protein tyrosine phosphatase, PTPMT1. The aim of this study was to test AD as a novel compound to induce apoptosis in a human pancreatic adenocarcinoma cell lines, Panc-1, MIA PaCa-2, AsPC-1, and Psn-1.

Materials and Methods: After IC50 value of the AD was determined by cytotoxicity assay, apoptosis was observed by a variety of methods including the detection of early apoptosis marker Annexin V and the proteomic profile screening by apoptosis array. Multicaspase and mitochondrial depolarization were measured and changes in cell cycle were analyzed.

Results: AD is found to initiate apoptosis by activating the intrinsic pathway and inhibit cell cycle in pancreatic cancer cell lines.

Conclusion: As a conclusion, considering its anti-cancer properties and bioavailability, Alexidine dihydrochloride can be considered as a potential candidate against pancreatic adenocarcinomas.

OP-44

Serum periostin values in STAGE 4 and 5 chronic renal failure patients

Ayla Yildiz, Esma Yucetas, Ibrahim Yilmaz, Gozde Turhan, Macit Koldas

Department of Medical Biochemistry Laboratory, H.S.U. Haseki Education and Research Hospital, Istanbul, Turkey

Objective: Periostin is a recently described new biomarker for chronic kidney disease (CKD). Periostin is a matricellular protein of 90 kDa, which is abundant in bone and dental tissues and contributes to inflammation and fibrosis in different disease states. These include myocardial infarction, cardiac hypertrophy, idiopathic lung diseases, asthma, skin sclerosis, hepatic fibrosis, muscle dystrophy and kidney diseases. In recent years, it has been emphasized that periostin contributes to the progression of CKD. We compared serum periostin levels in patients with renal failure Stage 4 (eGFR: 30-15 ml/min/1.73 m^2) and Stage 5 (eGFR:<15 ml/min/1.73 m^2) with healthy control groups.

Materials and Methods: The study included 21 patients stage 4, 9 patients stage 5 diagnosed with chronic renal failure and 30 healthy subjects. Periostin levels were measured by ELISA (enzyme-linked immunosorbent assay) method. Periostin values of the patients and healthy groups were compared using Mann-Whitney U test.

Results: The median periostin values of the patient and healthy groups were 8.219 and 8.402 ng/ml, respectively. There was no statistically significant difference between the two groups in terms of periostin values (p=0.666).

Conclusion: Periostin was expressed abnormally in several forms of CKD (lupus nephritis, focal segmental glomerulosclerosis, IgA nephropathy, polycystic kidney disease, transplant rejection, etc.) and interstitial fibrosis is associated with the degree and decrease in renal function.

In this study, we found no significant change in periostine levels in stage 4 and 5 renal failure patients however, we believe that periostin levels should be investigated in other stages of chronic renal failure and early fibrosis.

In our study blood samples transported to the emergency laboratory by pneumatic tube system was found to have a lower percentage of hemolysis than samples transported manually contrary to some other studies.

OP-45

Comparison of ischemia-modified albumin values between patients with age-related macular degeneration and healthy population

[1]Mehmed Ugur Isik, [2]Murat Alisik

[1]Department of Ophthalmology, Balikligol State Hospital, Ankara, Turkey

[2]Department of Biochemistry, Polatli Duatepe State Hospital, Ankara, Turkey

Objective: To investigate ischemia-modified albumin levels in patients with age-related macular degeneration (AMD) compared to age-matched healthy controls.

Materials and Methods: The study was designed in three groups. Eleven healthy volunteers without known systemic (diabetes mellitus, rheumatoid arthritis, vasculitis, etc.) and intraocular disease (AMD, uveitis, glaucoma, etc.) were included in the first group. Eighteen patients with non-treated dry-type AMD in any eye were included in the second group, and 18 patients with non-treated wet-type AMD in any eye were included in the third group. All patients underwent a complete ophthalmologic examination (best corrected visual acuity, intraocular pressure, biomicroscopy, dilated fundus examination). Albumin, ischemia-modified albumin (IMA) and ischemia-modified albumin/albumin ratio (IMAR) were measured in all patients.

Results: There was no difference between the mean ages of the first, second and third groups (63.1±4.0 years, 62.3±3.8 years, 61.3±3.8 years, respectively) (p=0.480). When albumin, IMA and IMAR values between groups were compared, albumin values were similar (p=0.133), however, there was a significant difference in IMA and IMAR values (p=0.004, p=0.003, respectively). In paired comparisons, IMA and IMAR values were significantly higher in wet-type AMD patients than in the healthy group (p=0.003, p=0.002, respectively). In dry-type AMD patients, there was no significant difference in IMA and IMAR values compared to healthy controls (p:0.083, p:0.125, respectively). There was no significant difference between IMA and IMAR values between wet and dry type AMD patients (p=0.592, p=0.359, respectively).

Conclusion: Higher IMA and IMAR values in wet-type AMD patients compared to the healthy group can be shown as a supportive finding of oxidative stress in AMD pathogenesis. Apart from that, the lack of difference between IMA and IMAR values in dry and wet AMD patients may suggest that oxidative stress does not play an active role in the stages after the onset of the disease.

OP-46

The effects of initial procalcitonin levels on mortality rates in geriatric patients undergoing surgery

Belkiz Ongen Ipek[1], Mustafa Erinc Sitar[1], Asli Karadeniz[2]

[1]Department of Medical Biochemistry and [2]Infectious Diseases, Maltepe University Faculty of Medicine Research and Education Hospital Central Laboratory, Istanbul, Turkey

Objective: Aging is an inevitable and continuous process which develops with accumulation of ongoing damage. Due to easily available and qualified health care services, vaccination rate success, increased communication skills and education of general population on preventive medicine, average life expectancy is increasing every day. Health care providers are focusing on healthy aging rather than preventing aging. Medical laboratories had their role in this issue by supporting clinicians using robust biomarkers. Estimation of comorbidities and mortality rates can provide valuable information to physicians. This study aimed to evaluate procalcitonin analysis for its possible role on predicting mortality in geriatric patients with bacterial infection risk and/or surgery.

Materials and Methods: The study included three groups with 101 patients, who are older than 65 years of age. Group I composed of patients who had surgery and then mortality within one month. Group II composed of hospitalized patients who had operation and then no post-op mortality. Group III composed of out-patients, who were evaluated as having bacterial infection risk. Serum procalcitonin, c-reactive protein, blood urea nitrogen, creatinine, albumin, total protein, aspartate aminotransferase activity, alanine aminotransferase activity, erythrocyte sedimentation rate and complete blood count were analyzed retrospectively for all the aforementioned patients by using laboratory information system.

Results: Procalcitonin and mortality rate had no statistically significant relationship (p>0.05). But there were statistically significant differences on the levels of c-reactive protein and sedimentation rates between Group I and III.

Conclusion: Fast, less labor intense, inexpensive, highly sensitive and specific biomarker search should never end in current medical era. Clinical laboratories should take important part in this geriatric medicine issue that will be much more substantial in future health care system.

OP-47

Investigation of sortilin-1 level in obese mouse livers

Huseyin Avni Uydu[1], Mehtap Atak[1], Tolga Mercantepe[2], Tuba Celik Samanci[2], Hande Cekici[3], Ahmet Alver[4]

[1]Department of Medical Biochemistry, [2]Histology and Embiryology, and [3]Dietetics, Recep Tayyip Erdogan University, Rize, Turkey

[4]Department of Medical Biochemistry, Karadeniz Technical University, Trabzon, Turkey

Objective: Obesity, defined as excessive body fat, is a serious public health problem that is increasingly prevalent in developed and developing countries and characterized by dyslipidemia (high LDL-C and TG levels, low HDL-C levels) and inflammation.Recent genome-wide association studies (GWAS) have identified new gene regions associated with plasma cholesterol and lipoprotein levels. The Sort1 gene product from these gene regions has been shown to be closely related to both lipoprotein metabolism and inflammatory cytokine levels. However, the effect of increased hepatic expression on plasma level of triglyceride-rich lipoproteins levels is controversial.The aim of this study was to determine the relationship between serum triglyceride load (TG, VLDL) and TNF- levels in obese mouse liver.

Materials and Methods: C57BL/6J male rats (15-25 g) were divided into two groups as control and obese. Serum TG and VLDL levels were measured spectrophotometrically after decapitation. Sortilin-1 and TNF-α levels in liver homogenates were determined by ELISA.

Results: Liver sort-1 and TNF-α levels were significantly higher in the obese mice compared to the control group (97±3/62±4, p=0.000; 143±12/100±11, p=0.000). There was a statistically significant decrease in serum levels of TG and VLDL (55±10/67±9, p=0.028; 11±2-14±2, p=0.028).

Conclusion: The increase in hepatic sortilin-1 level might affect plasma lipid homeostasis, as it can induce endogenous lipid degredation and proinflammatory process, And so it may be an important player in the pathogenesis. Thus, it is considered that sortilin-1 may have an important target biomolecule potential for therapeutic agents to be developed.

OP-48

Evaluation of biochemistry parameters in fasting and nonfasting group of medical faculty students

Berna Kus[1], Abdullah Arpaci[2]

[1]Department of Molecular Biochemistry and Genetics, Mustafa Kemal University, Institute of Health Sciences, Hatay, Turkey

[2]Department of Medical Biochemistry, Mustafa Kemal University, Faculty of Medicine, Hatay, Turkey

Objective: Patients' fasting blood samples are traditionally delivered to laboratory in the mornings. However, blood samples are drawn from patients at all hours of the day and fasting can not be certainly assured. In this study, we aimed to compare the fasting-nonfasting biochemical parameters of a group of medical faculty students.

Materials and Methods: Morning fasting and afternoon nonfasting blood samples were drawn from students (n=721, 297 female, 426 male). The samples were analysed with biochemical autoanalysers (Siemens Advia-1800) in the central laboratory of the university hospital and results are statistically analyzed. Paired-t was evaluated by SPSS (21) using Wilcoxon Sign Rank tests. The groups were seperated according to BMI, gender and a general group, then the relationship between fasting and nonfasting status were evaluated.

Results: Our resullts indicate that based on BMI, when we compared the underweight groups' fasting and nonfasting results, there were differences only in the value of BUN, while in the normal weight group there were differences in the value of Ca, BUN and TG. However we did not see any differences in the overweight group. When we compared the subjects according to gender (male and female), the differences were in the value of GLU, BUN and TRIG. When we grouped total subjects for fasting and nonfasting situations, we observed notable differences in GLU, BUN, Ca and TG ($p<0.05$).

Conclusion: Our study showed that there is no significant difference between a majority of fasting and nonfasting parameters. So it can be proposed that people can give fasting or nonfasting blood samples during the day unless they have a crucial disease.

OP-49

Determination of reference intervals of the thyroid function tests in geriatric population

Hakan Ayyildiz[1], Mustafa Timurkaan[2]

[1]Department of Biochemistry Laboratory, Elazig Fethi Sekin City Hospital, Elazig, Turkey

[2]Department of Internal Medicine, Elazig Fethi Sekin City Hospital, Elazig, Turkey

Objective: Reference intervals, used in the evaluation of laboratory results, facilitate distinguishing between the healthy population and patient subjects. Reference intervals which are reliable in terms of diagnosis and treatment are significantly essential to evaluate the results belonging to a patient accurately. Reference intervals, presented by the producer company, are utilized in routine laboratory practice. IFCC suggests that every laboratory is required to determine its own reference intervals. This study AIM to determine reference intervals of thyroid function tests (TFT) in the geriatric population.

Materials and Methods: TFT results of the patients applying our hospital between the dates 01.09.2018 and 31.08.2019 were obtained from the Laboratory Information System. Thyroid function tests were analyzed in DxI800 device by using commercial kits belonging to the firm. Out of the patients applying the policlinics, the ones who are over 65 years old were included in the study. The reference intervals were determined using MedCalc programme in accordance with C28-A3 as suggested by CLSI.

Results: 8816 TSH, 8171 fT4, 5796 fT3 data were analyzed in the study. Although the producer firm had noted the reference interval of TSH as 0.32-5.33 mIU/L, the study indicated it to be 0.23-3.44 mIU/L. Furthermore, the reference interval of fT4 had been presented as 0.61-1.12 ng/dL; however, the study revealed it to be 0.61-1.19 ng/dL. Lastly, the firm had presented the reference interval of fT3 as 2.6-4.37 ng/L, but it was found to be 2.47-4.15 ng/L.

Conclusion: The method, frequently used in the evaluation of the clinic test results, is the analysis of reference interval. This study found out some differences between the reference values presented by the producer firm and the ones of our own population. Therefore, reference intervals should be calculated as peculiar to each region or laboratory by taking all controllable or uncontrollable factors into consideration.

OP-50

Mutual evaluation of four different internal quality control materials of two different brands

Omer Kaya

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

Objective: One of the most important steps in determining the analytical method performance is the Internal Quality Control (IQC) process. One of the ways of assessing the IQC is to use commercially available materials prepared for this purpose. These materials should mimic the matrix of the analyte, should be in clinical decision levels, should have satisfactory storage life, and the variability should be small enough. In this study, we aimed to verify by comparing four commercial IQC materials in accordance with CLSI documents.

Materials and Methods: BioRad (Irvine, USA) and the Serocon (Konya, Turkey) brand the ICC materials were evaluated by Progesterone, Thyroid Stimulating Hormone (TSH), Free T4 (fT4), Troponin I (TnI) and Mass CKMB measurands at two concentration levels. We evaluated the results of intraassay and interassay studies comparatively.

Results: In the intraassay study, the coefficient of variation (CV) values were obtained between 2.25-17.27% and in the interassay study between 2.26-23.42%. The results were evaluated for Total Allowable Error (TEa). Of the total 40 CVs in the form of 5 analytes, two brands, two levels and two working patterns, 16 were found outside the TEa limits.

Conclusion: For results outside the TEa limits, it should be determined whether the error is due to the IQC material, the work order or the method. Improvement of error sources should be done. Criteria should be clearly defined in the selection of IQC material. Steps should be defined for verifying the IQC material.

OP-51

Comparison of immature platelet fraction between Sysmex XN-9000 and Mindray BC-6200 hematology analyzers

Ozlem Dogan[1], Emre Ispir[2]

[1]Department of Biochemistry, Ankara University, Ankara, Turkey

[2]Department of Biochemistry, Balikesir State Hospital, Turkey

Objective: Immature platelets (reticulated platelets) which are analogous of erythroid reticulocytes are newly released platelets from bone marow and may help to diferentiate the bone marrow failure and increased platelet (PLT) consumption at the vascular system. Immature platelet fraction (IPF) is a new parameter of haematology analyzers that shows young and reticulated platelets in peripheral blood. In our study we aimed to compare Sysmex XN-9000 and Mindray BC-6200 for platelet and IPF measurements.

Materials and Methods: 82 EDTA-anticoagulated blood samples of hospitalised patients and outpatients for routine laboratory testing were included. The samples were analysed in duplicate for PLT and IPF with Sysmex XN-9000 (Sysmex, Kobe, Japan) and Mindray BC-6200 (Mindray, Shenzhen, China) within 6 hours of samples arrival to the laboratory. The mean PLT and IPF values were used for correlation analysis.

Results: The XN-9000 and the BC-6200 showed good correlation for the measurement of platelet. The correlation coefficient (r) was 0.998 with 95% confidence interval of 0.997 to 0.999. However, The XN-9000 and the BC-6200 showed moderate correlation for the measurement of overall IPF values. The correlation coefficient (r) was 0.679 with 95% confidence interval of 0.555 to 0.775. The correlation of IPF between analyzers increased at normal (PLT count between 100 to 450×10^9/L) and higher PLT numbers (PLT count of>450×10^9/L) and decreased at lower PLT numbers (PLT count of<100×10^9/L) that r values were 0.733, 0.946 and 0.564, respectively.

Conclusion: In our study, we evaluated the standardization of IPF measurement by comparison of two methods and especially new standardization efforts are needed at lower PLT numbers.

OP-52

The effect of normalization method on the diagnostic performance of serum levels of miRNAs in prostate cancer

Yakup Dulgeroglu

Department of Medical Biochemistry, Kulu State Hospital, Konya, Turkey

Objective: The aim of this study was to evaluate the effect of endogenous (miR-93, RNU6) and exogenous (ce-miR-39) controls used for normalization on the diagnostic performance of miRNAs in prostate cancer.

Materials and Methods: Thirty-three patients with prostate cancer and 25 patients with BPH were included in the study. Serum examples were obtained within the scope of thesis on medical specialty in Dışkapı Yildirim Beyazit Research and training hospital in 2013. The serum samples were stored at -80°C until the study day. Serum levels of miR-26b-5p, miR-375, let-7c-5p, miR-223-5p, miR-93, ce-miR-39, and RNU6 were measured on qRT-PCR device (Agilent Aria MX). Fold change calculations were made online through the Qiagen data center. The p value was accepted as <0.005 for statistical significance.

Results: When ce-miR-39 was used for normalization, compared to BPH in prostate cancer, in serum levels of miR-26b-5p 18.5 fold ($p<0.001$), miR-375 5.6 fold ($p<0.001$), let7-c-5p 20.7 fold ($p<0.001$) and miR-223-5p 10-fold ($p<0.001$) downregulation was observed. When miR-93 was used for normalization, miRNA levels in prostate cancer were not significant compared to BPH ($p>0.05$). When RNU6 was used for normalization, compared to BPH in prostate cancer, in serum levels of miR-26b-5p 25.2 fold ($p<0.001$), let-7c-5p 28.1 fold ($p<0.001$), miR-223-5p 13.6 fold downregulation was observed, but the change in miR-375 was not significant ($p>0.05$).

Conclusion: The use of miRNAs in cancer diagnosis has been shown to be highly affected by the normalization method. Since there is no consensus for the normalization method, it is considered that the normalization method should be taken into consideration when evaluating the studies on the use of miRNAs in the diagnosis of prostate cancer.

OP-53

Cost effectiveness study on blood gas analyzers for multiple external quality membership

Medeni Arpa

Department of Medical Biochemistry, Recep Tayyip Erdogan University, Rize, Turkey

Objective: Arterial bloodgas (ABG) analysis, is used in many diseases because of its efficiacy in management of acid-base status and oxygenation. It can be placed as bedside as well as in laboratories. Separate external-quality-membership is provided for each ABG analyzer. The aim of the study was to investigate whether single membership would be sufficient for multiple analyzers.

Materials and Methods: A total of four ABL800 (Radiometer, Denmark) ABG analyzers, two in each laboratory, located different areas at Recep Tayyip Erdoğan University Training and Research Hospital were included in study. The study was carried-out with two identical external-quality samples (OASYS-OneworldAccuracy) with pH, pCO_2, and pO_2 tests between August 2018-June 2019. It was evaluated howmuch costs would decrease with changes to be made according data obtained. Study Design: One of identical external-quality-control samples of each month was applied to analyzers in first laboratory and then to analyzers in second laboratory,respectively. Similarly, other sample was applied to analyzers in second laboratory and then to first, respectively.Results were evaluated with external-quality-performance data.

Results: In November2018, April2019 periods, pH, pCO_2 and in August 2018,November 2018 periods pO_2 were found to be outside evaluation criteria for the second laboratory in both studies.Likewise,in May 2019 the pH was excluded.There were only two periods in which first laboratory was excluded;first study November2018-pCO_2, Ma y2019-pH.

Conclusion: For some months, pH, pCO_2 and pO_2 tests in second laboratory were excluded. However, the pCO_2 test was excluded in November2018 for the first laboratory. It was found the related analyzer was defined to wrong peer-group in external-quality-program. Similarly, pH test for the first laboratory was excluded in May2019 period. As a result, it was seen that first external-quality applications carried-out in same laboratory analyzers were in accordance with the evaluation criteria. It can be concluded that one membership is sufficient for each laboratory. Thus, the costs can be reduced by half. However, it is not known that the same result will be obtained for different device combinations, since present study, is performed only for four devices located in two areas.Therefore, considering each hospital's own device placement, it may help to determine the appropriate external-quality-membership

Poster Presentations

PP-01

Evaluation of vitamin D status and its association with thyroid disease

Rukiye Nar, Esin Avci

Department of Biochemistry, Pamukkale University, Faculty of Medicine, Denizli, Turkey

Objectives: Vitamin D is recognized to be an essential element for calcium metabolism and bone health; however, recent studies have shown that its deficiency has been identified as a risk factor for cancers, autoimmune diseases, and cardiovascular disorders. The aim of this study was to determine whether Vitamin D levels have any effects on thyroid diseases.

Materials and Methods: A total of 1197 adults, aged 18-45 years were enrolled in this retrospective study. Serum levels of Vitamin D, FT3, FT4 and TSH were measured. According to the thyroid hormones levels individuals were classically divided into 4 groups as Euthyroid State (n=940), Subclinical Hypothyroidism (n=180), Clinical Hypothyroidism (n=26) and Hyperthyroidism (n=51). These groups were compared according to the vitamin D status.

Results: Study population had mean serum Vitamin D concentrations of 18.33±14.53 ng/ml. The mean Vitamin D level was 16.01±14.37 ng/ml in women (n=921) and 26.04±12.26 ng/ml in men (n=276) ($p<0.001$). The mean Vitamin D levels were in the groups of euthyroid, subclinical hypothyroidism, clinical hypothyroidism and hyperthyroidism were 18.79±15.04 ng/ml, 16.15±12.08 ng/ml, 12.77±9.18 ng/ml and 20.4±14.23 ng/ml, respectively. There was a statistically significant difference between hyperthyroidism and clinical hypothyroidism groups ($p=0.042$).

Conclusion: Vitamin D deficiency is an important public health problem all over the world. The vitamin D levels in patients with hypothyroidism were lower compared to the other groups. Several studies found a correlation between autoimmune thyroid diseases and vitamin D deficiency. Vitamin D supplementation should be considered for thyroid disease and further prospective studies with a larger number of subjects are needed.

PP-02

Comparison of hematologic inflammation parameters in gestational diabetes mellitus patients

Ayse Hedef[1], Emine Araz[2], Filiz Alkan Baylan[1], Suleyman Murat Bakacak[3], Fatma Inanc Tolun[1], Sebnem Aka[2]

[1]Department of Medical Biochemistry, Kahramanmaras Sutcu Imam University, Faculty of Medicine, Kahramanmaras, Turkey

[2]Kahramanmaraş Sutcu Imam University, Institute of Health Sciences, Kahramanmaras, Turkey

[3]Department of Obstetrics and Gynecology, Kahramanmaras Sutcu Imam University, Faculty of Medicine, Kahramanmaras, Turkey

Objectives: Gestational diabetes mellitus (GDM) is the first glucose intolerance that occurs during pregnancy. Another mechanism underlying pregnancy-related insulin resistance is the production of inflammatory mediators. In our study, we aimed to compare hematological inflammation parameters and serum glucose levels in gestational diabetes mellitus patients and healthy pregnant women.

Materials and Methods: The data of 40 pregnant women who were admitted to Kahramanmaraş Sütçü İmam University Hospital Pregnancy Outpatient Clinic between 01.01.2018 and 01.12.2018 were evaluated. 50 healthy pregnant women were included in the study as a control group. The hematological parameters MPV, PLT, Lymphocyte and Neutrophil potassium EDTA were studied. Glucose values were measured as 0 min, 60 min and 120 min. NLO (Neutrophil lymphocyte ratio) and PLO (platelet lymphocyte ratio) were calculated and the results were compared statistically. Descriptive statistics were expressed as Mean±SD. Statistical significance was accepted as $p<0.05$.

Results: There was no difference in MPV and NLO levels between the groups. PLO values were 174.69±4.25 in the patient group and 127.12±2.01 in the control group. There was a significant difference between the patient and control groups in terms of PLO parameters ($p<0.05$).

Conclusion: NLR and PLO show a significant relationship with chronic inflammation. PLO parameter is a simpler and cheaper test compared to OGTT. Consequently, it may be useful to use secondary to OGTT in differentiation of gestational diabetes mellitus patients.

PP-03

Investigation of endotoxin and DNA damage level in patients with H.pylori (+) peptic ulcer

Nihayet Bayraktar[1], Islim Guler[2], Ismail Koyuncu[3], Ataman Gonel[4]

[1]Department of Medical Biochemistry, Nihayet Bayraktar, Harran University, Faculty of Medicine, Sanliurfa, Turkey

[2]Department of Medical Biochemistry, Islim Guler, Harran University, Faculty of Medicine, Sanliurfa, Turkey

[3]Department of Medical Biochemistry, Ismail Koyuncu, Harran University, Faculty of Medicine, Sanliurfa, Turkey

[4]Department of Medical Biochemistry, Ataman Gonel, Harran University, Faculty of Medicine, Sanliurfa, Turkey

Objectives: Helicobacter pylori, the first bacterium found to be carcinogenic, despite the acidity of gastric juice the protective mucus layer of the stomach mucosa of more than half of the world's population colonized with this bacterium. It is responsible for different gastro-dudenol clinical pictures and complications (gastritis, gastric and peptic ulcers and gastric cancers). Gastric cancer is considered as a major public health issue and ranks as the third most common cause of cancer-related mortality triggering the bad prognosis. It is incriminated in more deaths than half a million people worldwide every year. Our aim is to dermine the level of DNA damage level and analyse bacterial endotoxin through cellular dimension in positive peptic ulcer patients as well as to find whether there is a correlation between them. If there is a correlation, to assess it and to determine whether or not the cells affected in molecule basis in the pathogenesis caused by H. pylori.

Materials and Methods: In this study, 8-OHdG (Hydroxideoxyguanosine) was used as reference to DNA damage markers in serum samples. The DNA damage level was performed using the 8-OHdG ELISA kit using the method reported by the manufacturer (Fine Test, EU2548). The obtained data were analyzed.

Results: According to the data, significant difference found between patient and control group and between these two parameters observed there is a weak correlation.

Conclusion: Nowadays, perfect successful treatment for H.pylori infection and gastric cancers is difficult, so there a need to develop new treatment approaches and strategies and to contribute in such efforts in the fighting against gastric cancer. The major disadvantages of anticancer drugs are they are not original and have harmuful side effects.

PP-04

Neutrophil lymphocyte ratio and mean platelet volume in diabetic microvascular complications

Gulsah Siranli[1], Cuma Mertoglu[1], Alevtina Ersoy[2], Yucel Karakurt[3], Adalet Ozcicek[4]

[1]Department of Clinical Biochemistry, Erzincan Binali Yildirim University Faculty of Medicine, Erzincan, Turkey

[2]Department of Neurology, Erzincan Binali Yildirim University Faculty of Medicine, Erzincan, Turkey

[3]Department of Ophthalmology, Erzincan Binali Yildirim University Faculty of Medicine, Erzincan, Turkey

[4]Department of Internal Medicine, Erzincan Binali Yildirim University, Faculty of Medicine, Erzincan, Turkey

Objectives: The role of new inflammatory markers such as neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), mean platelet volume (MPV), and platelet distribution width (PDW) in diabetic microvascular complications were investigated.

Materials and Methods: A total of 266 (172 female, 94 male) individuals were divided into five groups; Group 1; who have diabetes without any complications for at least 10 years, group 2; only diabetic nephropathy, Group 3; only diabetic neuropathy, Group 4; only diabetic retinopathy, Group 5; control group. Among the groups, MPV and PDW were obtained directly from the hemogram results of the individuals, and NLR and PLR values were calculated by dividing the neutrophil and platelet values by lymphocytes, compared.

Results: Glucose and HbA1c were higher in retinopathy, neuropathy and nephropathy groups than the control group ($p<0.001$). NLR in neuropathy group was higher than in retinopathy and uncomplicated diabetic groups ($p=0.018$, $p=0.001$ respectively) and PLR was higher than in retinopathy group only ($p=0.001$). In the retinopathy group, MPV and PDW were higher than the control group and the uncomplicated diabetic group (MPV; $p=0.009$, $p=0.003$, PDW; $p<0.001$, $p=0.003$ respectively). Also, lymphocyte value in the retinopathy group was higher than in the control and the neuropathy groups ($p=0.008$, $p=0.009$ respectively). Furthermore, the lymphocyte value was higher in the uncomplicated diabetic group than in the control and the neuropathy groups ($p=0.033$, $p=0.046$ respectively).

Conclusion: Patients with diabetic neuropathy and retinopathy have subclinical inflammation. However, the question of whether this inflammation is responsible for the development of these complications or whether the inflammation has increased because these complications have not been clarified in this study.

PP-05

The need for assay harmonization: carbohydrate antigen 19-9 (CA 19-9) assay example

Fatma Ucar, Seyda Ozdemir, Gulfer Ozturk, Ali Yalcindag

Department of Clinical Biochemistry, University of Health Sciences, Yildirim Beyazit Training and Research Hospital, Ankara, Turkey

Objectives: The carbonhydrate antigen 19-9 (CA 19-9) assay is widely used biomarker for the detection and monitorization of pancreatic cancer. CA 19-9 assays often yield different results. The objective of the present study was to characterize the harmonization problem in immunoassays CA 19-9 testing.

Materials and Methods: According to the 2018 external quality assessment (EQA) program by the RIQAS (Randox International Quality Assessment Scheme), pooled serum samples containing three levels of CA19-9 were evaluated. The results of 4 assays: Abbott Architect, Beckman Access DXI600/800, Roche Cobas 6000/8000, and Siemens Advia Centaur XP/XPT/Classic, were compared.

Results: Data both from EQA schemes demonstrate significant variation in CA 19-9 assay results obtained for the same specimen using different assays. The mean CA 19-9 measurements of the peer groups varied among all 4 systems, and the interlaboratory CVs varied. In general, the highest peer groups mean values were obtained using the Abbott Architect system, followed by Siemens Centaur XP/XPT/Classic; the lowest means were obtained using the Roche Cobas system. Serum CA 19-9 assays show also a wide range in CV, which vary from 4.5-10.1%.

Conclusion: According to our findings, harmonization of the CA 19-9 results obtained using the 4 immunoassays has not yet been achieved. The concentration of CA 19-9 in a given specimen, determined with assays from different manufacturers, can vary owing to differences in assay methods, antibodies used, and reagent specificity etc. The lack of an international reference standard for use by the different manufacturers to appropriately calibrate their kits may account for these discrepancies. Clinicians should be aware of the inconsistency of the various commercially available methods/device and assays so that they can critically interpret results reported by different laboratories. Consequently, we suggest that the assay/method used to determine CA 19-9 concentrations should be noted in the laboratory result report.

PP-06

Evaluation of second trimester screening test

Muzaffer Katar[1], Osman Demir[2]

[1]Department of Clinical Biochemistry, School of Medicine, Tokat Gaziosmanpasa University, Tokat, Turkey

[2]Department of Medical Statistics, School of Medicine, Tokat Gaziosmanpasa University, Tokat, Turkey

Objectives: We aimed to evaluate the ability of maternal serum beta-human chorionic gonadotropin (ß-hCG), alfa feto protein (AFP) and unconjugated estriol (uE3) values measured in the second trimester screening test to predict complications that may develop in later gestational weeks.

Materials and Methods: The study included 692 women between 16-44 years old of age. Their gestational ages were between 14 weeks and 6 days to 21 weeks and 4 days. They had a single live pregnancy, and no any complicated obstetric history and chronic systemic disease. The results of pregnants, applied to the Biochemistry Laboratory of GaziosmanpasaUniversity Faculty of Medicine between 2017 and 2019, were evaluated retrospectively. P values less than 0.05 were considered statistically significant.

Results: The mean age of the patients was 27.46±5.85and their weight was 67.37±14.82 kilograms. Bi-parietal diameters (BPD) were determined as 37.02±3.41mm. ß-hCG levels were 25295.22±16564.10 mIU/ml, AFP values were 40.44±18.98 IU/ml and uE3 values were 0.87±0.36 ng/ml. BPD measurement was determined as 37.02±3.41. None of patients had age risk. Only 1 patient (% 0.001) had Trisomy 18 risk while 28 patient (% 0.40) had Trisomy 21 risk.

Conclusion: As well as first trimester screening tests, the accuracy and performance of second trimester screening tests, should be improved. Since they are used in the diagnosis of neural tube defects and chromosomal anomalies and guide for further interventional procedures, their measurements should be performed with strict internal and external quality programs.

PP-07

Retrospective evaluation of vitamin D levels: Bursa study

Aylin Beyaz[1], Yesim Ozarda[1], Melehat Dirican[1], Robab Ahmadian[2]

[1]Department of Medical Biochemisty, Bursa Uludag University, Faculty of Medicine, Bursa, Turkey

[2]Department of Biostatistics, Bursa Uludag University, Faculty of Medicine, Bursa, Turkey

Objectives: Vitamin D deficiency is an important public health problem that is thought to play a role in the development of many chronic diseases. According to current data, values below 12 ng/mL are considered deficiency, 12-20 ng/mL insufficiency and values above 20 ng/mL are considered sufficient. The aim of this study was to determine 25(OH) vitamin D3 (25(OH)D) levels in the clinical biochemistry laboratory of Bursa Uludag University Hospital and to determine the rates of vitamin D deficiency in adults.

Materials and Methods: The results of 25(OH)D levels were collected from the laboratory information system for a period of 3 years (2015-2017). Chemiluminescent Microparticle Immunoassay on Architect i2000SR analyzer of Abbott was used for the measurement of 25(OH)D levels. The Architect 25(OH)D assay demonstrated linearity from 3.4 to 155.9 ng/mL. The results of the patients who were repeated within 1 year were excluded with the possibility of being followed-up. Data from adult age group (18-65 years) and obtained only from outpatient clinics were evaluated.

Results: Of the 64068 patients evaluated, 48176 (75.2%) were women. The mean age was 45.5±13.1 years, and 25(OH) vitamin D levels were 19.65±15.93 ng/mL. 25(OH)D levels were <12 ng/mL in 20576 patients (32.12%), 12-20 ng/mL in 18336 patients (28.62%), 20-50 ng/mL in 22664 patients (35.37%), and >50 ng/mL in 2492 patients (3.89%).

Conclusion: The prevalence of vitamin D deficiency is increasing globally. Our study also showed that approximately 61% of the individuals who applied to the hospital had 25(OH)D levels below 20 ng/mL. This ratio shows that vitamin D deficiency and insufficiency in adult Turks is significantly high and widespread.

PP-08

Evaluation of blood count based inflammatory indexes in patients with idiopathic sudden sensorineural hearing loss

Medine Alpdemir[1], Mehmet Fatih Alpdemir[1], Yusuf Burak Kapucu[2]

[1]Department of Clinical Biochemistry, Balikesir State Hospital, Balikesir, Turkey

[2]Department of Otorhinolaryngology, Balikesir State Hospital, Balikesir, Turkey

Objectives: Recently, Idiopathic sudden sensorineural hearing loss (ISSHL) has been focused on chronic inflammation as the cause. The aim of this study was to determine whether the inflammatory index [neutrophil/lymphocyteratio(NLR), platelet/lymphocyte ratio (PLR), mean platelet volume (MPV) levels were elevated in patients with ISSHL.

Materials and Methods: This study was conducted of 98 patients with ISSHL diagnosed and 98 age- and sex-matched healthy control subjects. An automatic blood cell counter was used for the cell blood count (Sysmex XE-2100, Kobe, Japan). Hearing evaluations were performed with an audiometer. The severity of hearing loss in patients was classified as mild (<40 dB for any frequency loss), moderate (up to 80 dB), and severe (deep, >80 dB).

Results: The male/ female percentage of the patients and control group were 47/53 and 43/57. Mean age of the patients and the control group was 46.22±12.88and 46.56±18.05 years. According to the audiometry results, 20.4% mild, 32.6% moderate, 46.93% severe hearing loss were detected. NLR and PLR values of patients (2.14±1.56 and 121.01±37.71) were significantly higher than control group (1.44±0.27 and 105.5±28.28) (p<0.001). There was no significant difference in MPV between the two groups (10.33±0.78 fL for control, 10.27±0.78 for ISSHL). However, therewas not significant difference in NLR, PLR, and MPV among audiographically distinct ISSHL patients

Conclusion: NLR and PLR which is an indicator of inflammation are associated with ISSHL. It is a great advantage that these markers are readily available. However, they could not be used to distinctly ISSHL audiographically.

PP-09

Mean platelet volume/platelet count ratio as a diagnostic marker in children with acute appendicitis

Inanc Karakoyun[1], Mustafa Onur Oztan[2]

[1]Department of Medical Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Turkey

[2]Department of Pediatric Surgery, Izmir Katip Celebi University, Izmir, Turkey

Objectives: Acute appendicitis is the most common abdominal surgical emergency in the pediatric population. This study evaluates the diagnostic value of mean platelet volume/platelet count (MPV/PC) ratio in pediatric acute appendicitis.

Materials and Methods: This retrospective study included a total of 440 patients, 176 in the uncomplicated appendicitis group, 80 in the complicated appendicitis group, and 184 in the control group. C-reactive protein (CRP) level, white blood cell (WBC) count, absolute neutrophil count (ANC), MPV, PC, and MPV/PC ratio were compared between the groups and their discriminatory power were assessed by receiver operating characteristic (ROC) curve analysis. Correlations between the laboratory markers were identified with Spearman rank correlation test. Results with p<0.05 were considered statistically significant.

Results: CRP, WBC, and ANC levels differed significantly between the groups (p<0.001 in all pairwise comparisons). There was a negative correlation between MPV and PC (r=-0.434, p<0.001). Median MPV was 8.3 femtoliter (fL) in the control and 7.9 fL in the complicated appendicitis group (p=0.041). Both PC and MPV/PC ratio were able to distinguish cases of complicated appendicitis from healthy controls (p=0.003 and p=0.002, respectively) and from cases of uncomplicated appendicitis (p=0.010 and p=0.045, respectively). Areas under the ROC curve for CRP, WBC, ANC, MPV, PC, and MPV/PC ratio were 0.921, 0.951, 0.973, 0.606, 0.569, and 0.591, respectively.

Conclusion: According to the results of our study, MPV/PC ratio can be used in addition to conventional markers to help emergency department physicians discriminate cases of complicated appendicitis.

PP-10

Matrix selection for measurement of zinc levels

Sema Kardesler, Fatma Demet Arslan, Inanc Karakoyun, Banu Isbilen Basok, Ayfer Colak

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

Objectives: Zinc (Zn) measurement frequently used in the diagnosis of a few conditions such as growth retardation, immunodeficiency, infertility, neurological disorder, and acrodermatitis enteropathica. The serum matrix is the most preferred one to determine Zn levels due to the ease of analysis with other tests and cost-effectiveness of blood collection tubes to obtain serum. The Clinical and Laboratory Standards Institute's guideline, "Control of Preanalytical Change in Trace Element Determination-C38-A" recommends using specifically designed tubes for trace element measurements. In our study, we aimed to compare serum and plasma Zn results for accurate and reliable Zn measurement in plain tubes with clot activator and gel and in heparin-free tubes, which specifically produced for trace element analysis.

Materials and Methods: Twenty-seven randomly selected patients were included in the study. Blood samples were taken simultaneously from patients to tubes with clot activator and gel (SST) (SST II Advance, Vacutainer, Becton Dickinson and Company, USA) as well as trace element tubes with sodium heparin (NH) (NH Trace Elements Sodium Heparin, Vacuette, Greiner Bio-One GmbH, Austria). After the centrifugation process, serum and plasma Zn levels analyzed by colorimetric method using an autoanalyzer. Bias between serum and plasma Zn levels evaluated according to the allowable bias criterion based on biological variation and regression analysis performed.

Results: The mean and standard deviation of serum and plasma Zn levels were 49.0±11.5 µg/dL and 46.4±12.0 µg/dL, respectively, and a statistically significant difference determined (p=0.012) in between. Besides, the bias between serum and plasma was 6.8%, which was above the allowable bias (3.3%) considered as clinically significant. No systematic or random errors detected.

Conclusion: When selecting a blood collection tube for trace element analysis, the differences due to the structure of the tube and the matrix effect should be considered carefully.

PP-11

Evaluation of Troponin I on the RADIOMETER AQT 90 FLEX Poc testing

Melek Alan[1], Mujgan Ercan Karadag[1], Nihayet Bayraktar[1], Yakup Arga[2], Huseyin Akcali[2]

[1]Department of Biochemistry, Harran University Faculty of Medicine, Sanliurfa, Turkey

[2]Department of Cardiology, Harran University Faculty of Medicine, Sanliurfa, Turkey

Objectives: Troponin I (TnI) is the biochemical marker of choice for assessing patients presenting to the Emergency Department with cardiac symptoms. Given the urgent nature of such requests, a rapid turn-around-time (TAT) is an important prerequisite for troponin assays and one which makes point-of-care testing attractive to clinician. The Radiometer AQT90 FLEX is a point-of-care (POC) immunoassay analyzer intended for the quantitative determination of cardiac tests on whole-blood samples. We aimed to investigate the concordance of TnI between the Radiometer AQT90 FLEX device with the Siemens AdviaCentaur XP.

Materials and Methods: A total of 73 patients with chest pain were included in the study. Plasma samples were analyzed for TnI on the AQT90 FLEX and serum samples were analyzed for TnI on the Advia Centaur XP devices. Cut-off values were>0.023 ng/mLfor AQT90 FLEX and>0.06 ng/MI for Advia Centaur XP.

Results: 59 samples resulted positive and 14 samples resulted negative on Advia Centaur XP device. There were 57 positive and 16 negative results on AQT90 FLEX device.

Conclusion: AQT90 FLEX and Advia Centaur XP showed good correlation in terms of Troponin I results. AQT90 FLEX can be stated preferable for Troponin I tests as a POC device.

PP-12

Comparison of procalcitonin results in two different autoanalyzers

Pinar Eker

Department of Central Lab2, Istanbul Provincial Health Directorate Chairman of Public Hospital Services-2, Istanbul, Turkey

Objectives: The accurate and precise measurement of Procalcitonin (PCT) is crucial for emergency diagnosis. The Snibe Maglumi 4000P device which is used at the Central Laboratory for some specific proteins and hormones was planned to undergo a performance evaluation due to the fact that it contains the procalcitonin test in its menu and therefore could be an alternative to the currently existing device.

Materials and Methods: In this study, for the procalcitonin test, Snibe Maglumi 4000P, Biomerieux Vidas3 autoanalyzers and CLSI EP09-A3 standard were used to evaluate bias on the basis of patient samples and repeatability tests were performed. The tests were carried out simultaneously by Snibe Maglumi 4000P device located in the central laboratory and the Biomerieux Vidas3 device which was physically neighboring located in the Fatih Sultan Mehmet Education and Research Hospital. In the study, 100 leftover samples from patients that were admitted to the İstanbul Fatih Sultan Mehmet Education and Research Hospital were used after these samples were anonymized..Maglumi and Vidas3 devices' within run and between days repeatability were tested with two level controls and patient sample pool.

Results: Within run and between days repeatability results tested using control serums were found 3.1% (level 1), 0.9% (level 2); 5.8% (level 1), 4.9% (level 2) respectively. Within run and between days repeatability results using patient sample pool were found 1.41% and 0.04% respectively. The regression equality between results for the PCT was determined as y=0.893x+0.056 and the value of R^2 was determined as 0.987.

Conclusion: As a result, the procalcitonin results for Maglumi 4000P were found to be compatible with the results obtained from the Biomerieux Vidas3 device which is currently being used. The results obtained from the Maglumi 4000P device were approved to be suitable for use with clinical evaluation and monitoring.

PP-13

The effect of allowing to clot of blood samples for different periods on high sensitive troponin I levels

Nalan Gokalp, Nejla Baris, Fatma Demet Arslan, Banu Isbilen Basok

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

Objectives: False positivity of troponins, which are the most important biochemical tests in the diagnosis and prognosis of acute myocardial infarction, may cause unnecessary hospitalization and/or invasive interventions. Since we observed false-positive high sensitivity troponin I (hsTnI) in 4 patients whose results were incompatible with the clinical condition within two months and no problems detected due to analyzer or reagent, it aimed to evaluate the effect of allowing to clot for different periods in a pilot study.

Materials and Methods: hsTnI levels during the follow-up of 4 patients at 3-hour intervals were decreased as follows: 325 to 0.1, 135 to 2.2, 85 to 9.1 ng/L, and 1136 to 3.1 (reference range: 0-17 ng/L). The analytical phase was checked and confirmed through some studies, including system check (water and electrical system), calibration, internal and external quality control data, daily patient results, and precision studies. 24 patients (F/M:11/13) aged 25-85 years who admitted with non-cardiac symptoms were randomly selected. The blood samples were collected into plain tubes with gel (Isotherm-UnilabLab.Malz.Co.Ltd.,Turkey). Tubes were stand to clot in room temperature for 5 and 30 minutes and their sera were separated. hsTnI levels were analyzed with a DxI 800 analyzer (Beckman Coulter Inc.,USA).

Results: No visible fibrin presence detected in the serum samples. hsTnI levels were 3.85±5.00 and 4.65±5.00 ng/L for 5 and 30 minutes, respectively. It was observed that allowing to clot the samples before the centrifugation did not cause any significant differenceS (p=0.053).

Conclusion: Several studies have highlighted the false-positive hsTnI/TnI and underlying causes such as fibrin, heterophilic antibody, carry-over, alkaline phosphatase or bilirubin presence, hemolysis, or lipemia, etc. In general, the recommended time to clot is approximately 30 minutes, and below that undesirable microfibrin particles may form. Although no effect detected in our limited study, more comprehensive studies still needed.

PP-14

Can Ionized calcium level calculated by zeisler method be an alternative to direct Ionized calcium measurement?

Erdem Cokluk[1], Fatima Betul Tuncer[1], Mehmet Ramazan Sekeroglu[1], Sezen Irmak Gozukara[2], Mehmet Ozdin[2]

[1]Department of Medical Biochemistry, Sakarya University, Faculty of Medicine, Sakarya, Turkey

[2]Department of Medical Biochemistry, Sakarya University, Faculty of Medicine, Training and Research Hospital, Sakarya, Turkey

Objectives: To investigate whether the ionized calcium levels calculated by Zeisler Method can be an alternative to each other by comparing the ionized calcium values measured with blood gas device.

Materials and Methods: In this study, serum total calcium and venous blood gas ionized calcium levels of 388 same patients were evaluated retrospectively last 1 year (April 2018-April 2019). Total calcium levels measured by autoanalyser were calculated by Zeisler method and converted to ionized calcium levels. The mean and standard deviations of the calcium levels measured by both methods and the differences between the two methods were calculated by discriminating both total and gender. Correlation analysis was performed. Linear regression graph was drawn between two methods. In addition, Blant-Altman analysis was performed in Excel Program.

Results: The mean blood gas ionized calcium (KGiCa) levels were found to be 1.164±0.20 mmol/l, while the ionized calcium level (ZMiCa) calculated from the serum total calcium by Zeisler Method was 0.99±0.16 mmol/l. The difference between the two methods (KGiCa - ZMiCa) was 0.17±0.22 mmol/l. The linear regression equation between the two methods was found to be for r^2=0.90 was Zeisler iCa=0.71X blood gas iCa+0.304. Blood gas ionized calcium levels were 8.91%;% Bias, 7.60%; Total CV% and 21.44; % TAH.

Conclusion: We think that it is more appropriate to use direct measurement method for ionized calcium. However, if ionized calcium is calculated by Zeisler Method, we think that it is appropriate to evaluate the mean difference between the two methods we found in this study by considering the regression equation and the total permissible error intervals calculated for ionized calcium.

PP-15

Assessment of attitude for pregraduate medical biochemistry education: the sample of Sakarya University Faculty of Medicine

Erdem Cokluk[1], Fatima Betul Tuncer[1], Mehmet Ramazan Sekeroglu[1], Selin Tunali Cokluk[2]

[1]Department of Medical Biochemistry, Sakarya University, Faculty of Medicine, Sakarya, Turkey

[2]Department of Office of Research, Sakarya Provincial Health Directorate Public Health Services, Sakarya, Turkey

Objectives: Measuring the learning and development levels of students and evaluating their satisfaction during learning are considered as the main elements of education. In this study we planned to find out how the medical biochemistry course in our faculty is perceived by the preclinical students.

Materials and Methods: The population of the study consisted of 439 students, term I-II-III (D-I, D-II, D-III). When stratified sample selection is made according to classes, 76 students from D-I, 70 students from D-II and 60 students from D-III. A total of 279 students were surveyed by using face to face questioning technique. The questionnaire consisted of a total of 31 questions, 20 of which belong to the "Attitude Scale for Undergraduate Medical Biochemistry Education" and 11 questions of sociodemographic characteristics. 9 for the importance (A1), 7 for the interest (A2) and 4 for the satisfaction (A3). The total score of the questionnaire was 100.

Results: The questionnaire was applied to 140 female,139 male students. Of the 279 students, 106 were educated in D-I, 99 in D-II, and 74 in D-III. The scores of D-I, D-II and D-III students were 63.52±12.56, 58.11±13.62, 69.09±11.00, respectively. When the total and sub-group scores were compared by classes, there was a significant difference between A1, A3 and total score between D-I and II, A1 score between D-I and III, and A1, A2, A3 and total score between D-II and III ($p<0.05$).

Conclusion: It may increase the interest and satisfaction of referring to the clinic of diseases. In addition, this study will be useful in identifying and eliminating existing deficiencies related to medical biochemistry course, developing new educational strategies and increasing orientation towards post-graduate medical biochemistry education.

PP-16

Instrument verification and its importance for the medical laboratories

Selin Onur, Banu Isbilen Basok, Umit Bozkurt, Fatma Demet Arslan

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

Objectives: The affirmation of a measurement performance before analysis at newly introduced instrument in clinical laboratories is called verification. The Clinical and Laboratory Standards Institute (CLSI) EP15-A2 guideline includes verification protocols of the manufacturer performance's targets. The method verification is not mandatory as stated in The Health Quality Standards version5 and the procedure isn't widespread in our country. Our aim is to remind the importance of verification up to the manufacturer's targets before establishing an instrument through our experiences.

Materials and Methods: As the verification protocol for each established system in to our laboratory, the precision of ASO, RF, IgM, IgA, IgG, IgE, C3, and C4 tests that performed with nephelometric method on Siemens BNII was calculated for two levels of ASO and RF, three levels of Ig's, C3, and C4 tests by using commercial internal quality control sera in accordance with EP15-A2 and evaluated according to the precision limits specified in the package insert.

Results: Since RF and IgE within the limits, CVs of the ASO (2 levels), IgM (high), IgA (low-high), IgG (medium), C3 (low), and C4 (3levels) exceed the manufacturer's total CV targets. The issue evaluated together with the manufacturer's technical staff. Since no problems were detected in the within-run CVs, electrical infrastructure questioned and strengthened. After grounding and maintenance, the CVs% of mentioned tests achieved the manufacturer's goals. While there was a significant difference between median values of ASO (2 levels), IgM (high), IgA (low-high), and C4 (low-normal) before and after grounding, there was no difference for C3 (low) and C4 (high). After grounding, only IgG (high) between-run CV% was detected above the target.

Conclusion: Manufacturers determine instrument performance under optimum conditions. However, the laboratory infrastructure where the device installed may not always have the optimum conditions. Before accepting an instrument, its verification can improve the patient safety and increase cost effectiveness by reducing unnecessary repetitions through detecting such electrical problem and hence improving precision.

PP-17

Evaluation of periodic maintenance of routine biochemistry instrument using precision studies

Veli Iyilikci[1], Selin Onur[1], Osman Erguder[2], Banu Isbilen Basok[1]

[1]Department of Medical Biochemistry, University of Health Sciences Tepecik Training and Research Hospital, Izmir, Turkey

[2]Beckman Coulter Inc., Izmir, Turkey

Objectives: Periodic maintenance of the analyzer is very important in terms of the operability and lifetime of the analyzer, concurrently it can directly affect the test measurements. Although the maintenance's scope and its timetable are regularly determined and proceed by the manufacturer, it's important that laboratory professionals evaluate the possible effects of maintenance, thereby test results. We aim to emphasize the impact and importance of maintenance by evaluating the change of data between before and after the periodic maintenance by using internal quality control data.

Materials and Methods: During each 20 days before and after 6-months of scheduled periodic maintenance, using by two levels (low-high) commercial internal quality control (Beckman Coulter Inc, USA) in two separate autoanalyzers of the same brand and model (analyzer A and B; AU5800, Beckman Coulter Inc, USA) CV% of these parameters -creatinine, glucose, total bilirubin, alanine aminotransferase (ALT), and potassium (K)- were calculated. Each CV% was evaluated according to the CV% limit based on biological variation. Statistical analyses were performed with Excel 2016 and SPSS 25.0.

Results: While all tests except creatinine were within the limits, analyzer A (level 2) and analyzer B(both levels) were out of limits in creatinine before maintenance and were improved with maintenance. After maintenance, creatinine (both devices/levels), glucose (analyzer B/both levels), and K (both devices/levels) CVs% decreased, also total bilirubin (both devices/levels) and ALT (both devices/levels) CVs% increased. Significant differences were found in creatinine (level 2), ALT (level 2), and K (level 2) between medians before and after maintenance at analyzer A.

Conclusion: Scheduled periodic maintenance of the analyzer is especially important for creatinine measurement and also positively affects potassium analysis. Therefore, we believe that it is important to perform comprehensive periodic maintenance in analyzers, where these two parameters are studied within a maximum of 6 months or even shorter periods.

PP-18

Plasma levels of P-Selectin, and beta-thromboglobulin and platelet indices in patient with prediabetes

Nesibe Esra Yasar[1], Dildar Konukoglu[2]

[1]Department of Medical Biochemistry, Ministry of Health, Kars Harakani Public Hospital, Kars, Turkey

[2]Department of Medical Biochemistry, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey

Objectives: Platelets play an important role in the atherogenesis and thrombus formation. The changes in platelet morphology and function have been occurred in inflammatory and vascular diseases. We aimed to evaluate the relationship between plasma p-selectin and beta-thromboglobulin levels and platelet indices in prediabetic individuals in this study.

Materials and Methods: According to American Diabetes Association criteria; subjects were grouped as control (n=31) and prediabetics (n=103) who had impaired fasting glucose (IFG, n=60), impaired glucose tolerance (IGT, n=14) or IFG+IGT (n=29) based on oral glucose tolerance test results. Platelet count, mean platelet volume, platelet distribution width and plateletcrit were determined by impedance method; P-selectin and beta-thromboglobulin levels were determined by enzyme-linked immunosorbent assay in blood samples taken after a follow-up 10-12 hours fasting. Differences between study groups were tested for significance by independent samples t-test. The Analysis of variance test was used for multiple-group comparison. Pearson analysis was used for the correlations. p value of <0.05 was considered as statistically significant.

Results: In control and prediabetic groups, there was no significant different for platelet counts, indices, and plasma P-selectin levels. There was no significant difference between the prediabetic subgroups and the control group for these parameters. Plasma beta-thromboglobulin levels were significantly higher in the prediabetic group than in the control group ($p<0.001$). Beta-thromboglobulin levels were significantly higher

in the prediabetic subgroups compared to the control group (p<0.001 for IFG, p<0.05 for IGT and IFG+IGT). There was no significant difference in beta-thromboglobulin levels among prediabetic subgroups.

Conclusion: Our results suggest that granule activation has begun without the platelet size affected and platelet indices have not changed in the prediabetic stage.

PP-19

Immunomodulatory effects of breast cancer-derived exosome mimetic nanovesicles

Mustafa Oztatlici[1], Alper Tunga Ozdemir[2], Mahmut Kemal Ozbilgin[1], Rabia Bilge Ozgul Ozdemir[3], Hilmi Orhan[4]

[1]Department of Histology and Embryology, Manisa Celal Bayar University, Faculty of Medicine, Manisa, Turkey

[2]Department of Medical Biochemistry, Merkezefendi State Hospital, Manisa, Turkey

[3]Department of Immunology and Allergy, Manisa City Hospital, Manisa, Turkey

[4]Department of Pharmaceutical Toxicology, Ege University, Faculty of Pharmacy, Izmir, Turkey

Objectives: In spite of significant progress has been made in the treatment of breast cancer, some cases may resistant to all treatment approaches. The cancer immunotherapy is the alternative approach for treatment of these resistant cases, but sometimes it may not be beneficial. Extracellular vesicles, such as exosomes, are emerging as novel cell-cell communication mediators in physiological and pathological scenarios. Exosomes may play an important role in shaping the tumor microenvironment by delivering tumor derived cellular components to the immune cells.Tumor cells can produce large quantities of exosomes. However, large amounts of cells and conditioned media are required to isolate these exosomes. Therefore, alternative methods to generation a large quantity of homogeneous exosomes carrying specific cargoes are of great interest. Exosome-mimetic nanovesicles (NVs) with more than a 100-fold greater yield than exosomes have been shown to deliver information to recipient cells, and properties of these NVa are similar to natural exosomes.

Materials and Methods: In this study we investigated immunomodulatory effects of MDA-MB-231 cells-derived NVs on $CD4^+$ Jurkat cells. NVs were prepared by serial extrusions of cells through polycarbonate membranes and characterized with CD9 and CD63 exosomal surface proteins by using ExoFACS kit. After administration of 5, 10 and 50 µg/mL NV to the Jurkat cells, mRNA changes of IFN-g, T-bet, IL-10 and FoxP3 molecular were measured by qRT-PCR technique.

Results: We have found that a significant increase in expression of IFN-γ and T-bet but significant decrease in IL-10 and FoxP3.

Conclusion: According to our findings, NVs isolated from MDA-MB-231 cells can activate pro-inflammatory pathways in Jurkat cells and inhibit anti-inflammatory pathways. These findings suggest that tumor-derived NVs may induce anti-tumor effect in CD4 Jurkat cells. However, in order to reach a more accurate judgment, prospective studies should perform by using the immune cells of healthy donors.

PP-20

Investigation of anti-inflammatory lipid mediators in patients with rheumatoid arthritis

Rabia Bilge Ozgul Ozdemir[1], Ozgul Soysal Gunduz[2], Alper Tunga Ozdemir[3], Ozgur Akgul[4]

[1]Department of Immunology and Allergy, Manisa City Hospital, Manisa, Turkey

[2]Department of Internal Medicine, Manisa Celal Bayar University, Faculty of Medicine, Division of Rheumatology, Manisa, Turkey

[3]Department of Medical Biochemistry, Merkezefendi State Hospital, Manisa, Turkey

[4]Department of Physical Therapy and Rehabilitation, Manisa Celal Bayar University, Faculty of Medicine, Division of Rheumatology, Manisa, Turkey

Objectives: In a healthy organism, inflammation needs to be resolved following the elimination of the pathogen causing the activation of the immune response. At this stage, leukotrienes, which are arachidonic acid (AA) metabolites, are enzymatically modified to strong suppressor molecules lipoxins and resolvins. The aim of this study was to investigate the relationship between AA metabolites which involved in the resolution of joint inflammation in rheumatoid arthritis (RA) and the immune system. For this purpose, we measured the LXA4, RvD1, RvE1, IL-6, IL-8, IL-17a, IL-22 and CCL2 serum levels of RA patients that newly diagnosed (ND, n=10), treated for 5 years (RA-5, n=15), treated for more than 5 years (RA-5+, n=15) and healthy control subjects (HC, n=15) by using ELISA and Luminex methods.

Materials and Methods: According to disease duration, the IL-6 levels of RA-5+ group were significantly higher than other groups. IL-22 levels of the HC group were significantly higher than the ND and RA-5 groups. The CCL2 levels of the RA-5+ group were significantly higher than the RA-5 group. There was not any significant difference for the IL-8, IL-10 and IL-17a levels. When we compared lipid metabolites between groups, we observed that LXA4, RvD1 and RvE1 levels of the HC group were significantly higher than the other groups.

Results: In our findings, there was an association between disease duration over 5 years and CCL2 levels that cause chemotactic effect for lymphocytes, and IL-6 elevations which play an important role in differentiation of naive T cells into Th17 cells. For LXA4, RvD1 and RvE1 levels, we detected that a significant decrease regardless of disease duration.

Conclusion: Our study indicated that the duration of the disease may adversely affect the underlying autoimmune pathology, and that lipid metabolites involved in the resolution of inflammation may be a potential diagnostic and therapeutic target.

PP-21

Evaluation of laboratory performance criteria by CLIA 2019, CLIA 1988, Riqas and Turkey

Ozlem Cakir Madenci, Zeynep Yildiz, Ozlem Hurmeydan, Asuman Orcun, Nihal Yucel, Lale Koroglu Dagdelen

Department of Clinical Biochemistry, Istanbul Kartal Doctor Lutfi Kirdar Training and Research Hospitali Istanbul, Turkey

Objectives: Allowable total error (TEa) is an analytical quality specification setting acceptable limits for a single test result. It is used for sigma metric evaluation which shows test performance and description of control rules and measurement numbers according to the performance. The total error of a test (TE) should not exceed the TEa as well.

In our study, we aimed to assess our laboratory performance for 19 biochemistry tests according to new Clinical Laboratory Improvement

Amendments (CLIA) 2019, CLIA 1988, Riqas Randox International Quality Assessment (Riqas) and also international Turkey criteria which were published at 13.10.2016 with circular number 95966436. We calculated sigma values (σ) and aimed to evaluate our laboratory analytical performance with four different criteria.

Materials and Methods: This study was undertaken in Dr Lütfi Kırdar Kartal Education and Training Hospital biochemistry laboratory at a period from January to December 2018 on Beckman AU5800 analyser (Beckman Coulter, Inc., Brea, USA).

TEa values were derived from 1988 and 2019 CLIA, Riqas and Turkey criteria and sigma metrics were calculated from the standard sigma equation, Σ(σ)=(TEa-bias)/CV. CV's were calculated from the Bio-Rad Internal Quality Controls of both normal and abnormal levels and bias from the Bio-Rad External Quality Assurance Scheme. Total error was calculated from the equation Total error=%Bias+1.65%CV.

Results: Albumin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, total bilirubin, high density lipoprotein cholesterol, Lactate Dehydrogenase, magnesium, total protein and triglyceride showed >3 σ with all approaches while there was no test σ≤3 according to Turkey criteria.Chloride, total cholesterol and urea showed σ≤3 according to CLIA 1988, CLIA 2019 and Riqas and amylase, creatine kinase, iron, glucose and creatinine showed σ ≤ 3 for Riqas and CLIA 2019.

Conclusion: Different TEa values cause different six sigma quality values and decisions in clinical laboratory practice.

PP-22

The effect of hemolysis on routine coagulation tests

Aysegul Ozgenc, Dildar Konukoglu

Department of Medical Biochemistry, Istanbul University- Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey

Objectives: Hemolysis is the most prevalent preanalytical error. The aim of this study is to evaluate the influence of hemolysis on routine coagulation tests.

Materials and Methods: Blood samples were collected in 6 vacuum tubes containing 3.2% sodium citrate (Vacuette Greiner Bio-One) from a healthy volunteer by vacutainer technique. Each tube was labeled as H0, H1, H2, H3, H4 and H5. H0 was kept non-hemolysed sample. Incremental hemolysis was artificially created in five aliquots (H1, H2, H3, H4 and H5) by aspiration of anticoagulated blood (1 time, 3 times, 5 times, 7 times and 9 times, respectively) through insulin needle (26 Gauge). All tubes were centrifuged for 5 minutes at 3500 rpm. After centrifugation; aPTT, PT, and fibrinogen parameters were performed on Sysmex CS-2500 analyzer and hemolysis index (HI) was performed on Roche Cobas 6000-C501 analyzer. Each sample was analyzed twice and the results were averaged. % Bias was calculated for other tubes according to H0 (Desirable bias: For PT:±2%, for aPTT:±2.3%, for fibrinogen: ±4.8%).

Results: HI was determined in the range of 4-421. On visual inspection of samples, hemolysis was noticed beginning from H2 tube (HI:91). % Bias values were compared with desirable bias values. HI> 90 for PT, HI>300 for aPTT and HI>400 for fibrinogen were found to exceed the desirable bias values.

Conclusion: As the severity of hemolysis causing biological and analytical interference on coagulation test increases, the effect of the interference increases, too. The effect of hemolysis was detected earlier in PT compared to other parameters. HI should be examined before coagulation analysis in the samples of emergency departments where these tests are important and hemolysis is more common. The explanation that alerts the clinician for parameters that may be affected should be indicated in the report.

PP-23

The lipemia effect on coagulation tests

Melek Karasu, Aysegul Ozgenc, Dildar Konukoglu

Department of Medical Biochemistry, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey

Objectives: In our study we aimed to investigate the changes in frequently analyzed coagulation tests probably caused by lipemia which is one of the interference factors in pre-analytic phase of clinical laboratories' analytical process.

Materials and Methods: ½, 1/4, 1/8, 1/16, 1/32, 1/64, 1/128 and 1/256 serial dilutions of %10 oliclinomel parenteral lipid emulsion (Baxter Oliclinomel N4-550 Emulsion, India) were prepared and 1 mL of each dilution was transfered to tubes. Each 1 mL of a plasma pool consisted of randomly selected sixteen blood were added onto lipid emulsion contented tubes and mixed.1 mL of reactive diluent was added to control plasma which was separated. PT, aPTT, INR, fibrinogen and D-dimer levels of lipemic samples processed in Sysmex® CS-2500 twice. Mean was calculated. Triglyceride (TG) concentration and lipemia index (LI) processed in respectively Cobas® 8000 and Roche Cobas® 6000 C501.Bias was calculated and compared to desirable bias (%) values (PT:±2, aPTT:±2.3, fibrinogen:±4.8, D-dimer:±8.82)

Results: In order of the control sample to the most lipemic sample TG levels were found in a range of 54 -4644 mg/dL and LI levels were found in a range of 7 -2350. The analyzer failed to give any results of PT, aPTT and fibrinogen at LI >600 (TG>1400 mg/dL) and D-dimer' at LI>1200 (TG>2565 mg/dL). Calculated bias(%) levels were out of desirable bias range for PT at LI: 300, for aPTT at LI: 50 and for fibrinogen at LI: 150 while for D-dimer at LI:1200.

Conclusion: It was concluded that lipemia especially at high LI levels leads to unreliable test results of PT,aPTT and fibrinogen by effecting laboratory analysis methods besides it must be taken into consideration while evaluating the samples given in nonfasting period or given by dislipidemic patients.

PP-24

Rate of inappropriate HbA1c test orders over 1-year period

Merve Sena Odabasi

Department of Biochemistry, Sisli Hamidiye Etfal Research and Training Hospital, Istanbul, Turkey

Objectives: Diabetes mellitus is a chronic disease with high prevalence and Hemoglobin A1c (HbA1c) is used for its monitoring. There are many opinions in terms of the frequency of optimal test request interval. Turkish Ministry of Health has issued a procedure to reduce the number of unnecessary tests required and to maintain test requests cost-effectively. According to this procedure Hba1c should not be requested before 60 days. In this study it assessed the frequency of inappropriate Hba1c testing.

Materials and Methods: Hba1c test requests between 01.08.2018-01.08.2019 were examined. Requests made within 60 days after the previous test were identified as inappropriate test requests. Based on the time interval between HbA1c requests, it was determined which clinics made more inappropriate test requests.

Results: Of the 89855 samples, for 6041 samples the test request time was less than 60 days while for 2750 samples the test request time was less than 30 days. 15% of the tests requested in less than 60 days belonged to inpatients and 75% to outpatients. Internal medicine outpatient department was found to be responsible the most inappropriate

test request. The percentage changes in the results were calculated for the tests requested in less than 30 days and less than 60 days.

Conclusion: Reducing unnecessary testing requirements is necessary for cost-effective use of laboratory resources. It was planned to give verbal warning to the related clinics and to make test request restrictions on the operating system.

PP-25

Comparison of becton dickinson and S-Monovette-Sarsted tubes for in vitro hemolysis

Ozlem Cakir Madenci, Ozlem Hurmeydan, Zeynep Yildiz, Asuman Orcun, Nihal Yucel, Lale Koroglu Dagdelen

Department of Clinical Biochemistry, Istanbul Kartal Doctor Lutfi Kirdar Training and Research Hospital, Istanbul, Turkey

Objectives: In vitro hemolysis is one of the most important sources of pre-analytical errors in clinical laboratories leading to erroneous results, cost increases and time loss. In this study, we aimed to evaluate the effect of different blood collection techniques on in vitro hemolysis and test results.

Materials and Methods: A total of 159 patients who were admitted to the emergency department yellow field and were bled by intravenous catheter were included in the study. Samples were taken from the same patient by the same phlebotomists who were trained by aspiration technique in Sarstedt S-Monovette® 4.9 mL serum Gel tube and vacuum filling technique in BD 5 mL Vacutainer® SST ™ II tube and transported to the laboratory by the same personnel without waiting. Blood samples were incubated for 30 minutes at room temperature and centrifuged at 1500 g for 5 minutes. Serum hemolysis index and AST, CK, Potassium and LDH tests were performed on both tubes using Beckman Coulter AU680 analyzer (Beckman Coulter, Indianapolis, IN). The effect of different blood collection techniques on serum hemolysis index and tests were investigated. Wilcoxan rank test was used to compare groups.

Results: Hemolysis was observed in 62 patients, as + in 19 patients, ++ in 28 patients, +++ and ++++ in 15 patients in BD Vacutainer® SST ™ II tube. Hemolysis rates were 38.9% and 0.63% in BD and S-Monovette tubes, respectively. Serum hemolysis index AST, CK, Potassium, LDH tests were significantly different between BD and S-Monovette tubes. A significant difference was found between the tubes in all hemolysis levels except CK test at + hemolysis level.

Conclusion: The serum hemolysis index is lower in Sarstedt S-Monovette tube samples and caused significant difference in test results. It contributes to safe sampling in emergency departments where intravenous catheter sampling is performed.

PP-26

Evaluation of analytical performance

Alev Kural, Yuksel Gulen Cicek, Sehide Baz, Soner Erdin, Mehmet Zahit Ciraci, Sebnem Tekin Neijmann, Zeynep Levend Cirakli, Nilgun Isiksacan

Department of Clinical Chemistry Laboratory, University Health of Sciences Bakırkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

Objectives: Clinical laboratories should produce reliable and accurate test results. Six sigma and total analytical error are some of the quality strategies for clinical laboratories. The aim of our study is to evaluate the analytical process performance of random routine five tests in our laboratory with six sigma and total analytical error.

Materials and Methods: Internal Quality Control (IQC) and External Quality Control (EQC) data of routine 5 tests in our laboratory were obtained 6 months retrospectively. We calculated mean, standart deviation and coefficient of variation (CV), bias values from IQC and EQC. Total analytical error and process sigma values were calculated using formula. Total error allowable (TEa) values determined CLIA and Fraser, Sigma value <3 low, 3-6 good and >6 was excellent quality.

Results: The sigma levels for five tests we determined >3 sigma values. Sigma levels of calcıum, total protein,AST and triglyceride were between 3-6. Glucose was >6. We also calculated total analytical error for five parameters. And we compared these results with Fraser (desirable limits) and CLIA levels. All analytical errors for five parameter were lover than CLIA and Fraser limits.

Conclusion: Acording to results of study, our laboratory performance for these parameters were good and sufficient. We will check all other parameters performans periodically in a year. Each laboratory should adopt its own quality strategies.

PP-27

Evaluation of serum proinflammatory cytokines, oxidative stress and some other biochemical markers in chronic viral hepatitis B and C infections

Nihayet Bayraktar[1], Mehmet Bayraktar[2], Yasemin Ersoy[3]

[1]Department of Medical Biochemistry, Nihayet Bayraktar, Harran University, Faculty of Medicine, Sanliurfa, Turkey

[2]Department of Medical Microbiology, Mehmet Bayraktar, Harran University, Faculty of Medicine, Sanliurfa, Turkey

[3]Department of Infectious Diseases, Yasemin Ersoy, İnönü University, Faculty of Medicine, Malatya, Turkey

Objectives: The aim of this study was to investigate the effects chronic viral hepatitis B&C infections on serum cytokines tumor necrosis factor-α (TNF-α), interlukin-1β, (IL-1 β) interlukin-2R (IL-2R), interlukin-6 (IL-6) and interlukin-8 (IL-8), antioxidant enzymes, lipid peroxidation and serum zinc (Zn) and copper (Cu) to find whether there is the relationship between them.

Materials and Methods: We examined a total of 78 patients (40 chronic HBV positive patients, 30 inactive HBV carriers and 8 chronic HCV positive patients) with positive clinical and serological markers of HBV and HCV infection. Thirty healthy subjects were included in the study. Cytokines (TNF-α, IL-1β, IL-2R, IL-6, IL-8), Zn and Cu concentrations were measured in serum. MDA levels in plasma, antioxidant enzymes SOD, GSH-Px, CAT activities were measured in erythrocytes.

Results: Serum cytokines (TNF-α, IL-2R, IL-6 and IL-8) levels were significantly higher when compared with HBV positive or IC patients and control group ($p<0.001$). When HCV positive patients and control group were compared, it was also found statistically significant ($p<0.001$). However, no statistically significant difference was found IL-1β ($p>0.05$). Erythrocytes SOD, GSH-Px, CAT activities and serum Zn levels were low ($p<0.001$), plasma MDA and serum Cu levels were found to be significantly increased ($p<0.05$).

Conclusion: Determining the importance of proinflammatory cytokines and antioxidants in patients infected with chronic HBV and HCV has been observed. In addition, the importance of maintaining the balance between antioxidants and trace element oxidative stress and lipid peroxidation as a result of metabolic interactions with Zn is thought to lead to an increase in Cu.

PP-28

Ischemia-modified albumin as a predictor of the disease activity in rheumatoid arthritis patients

Ayfer Colak[1], Filiz Meryem Sertpoyraz[2], Elif Merve Girgin[1], Anil Baysoy[1], Ali Taylan[3]

[1]Department of Clinical Biochemistry, Health Sciences University, Tepecik Training and Research Hospital, Izmir, Turkey

[2]Department of Physical Medicine and Rehabilitation, Health Sciences University, Tepecik Training and Research Hospital, Izmir, Turkey

[3]Department of Rheumatology, Health Sciences University, Tepecik Training and Research Hospital, Izmir, Turkey

Objectives: Rheumatoid arthritis (RA) is a chronic, progressive, autoimmune disease characterized by synovial inflammation, cartilage damage and bone erosion. Ischemia modified albumin (IMA) is a potential marker that can be used to assess atherosclerosis-related myocardial ischemia. Cardiovascular events such as myocardial infarction and stroke are frequent comorbidities in rheumatic diseases. We aimed to evaluate the relationship between disease activity and ischemia-modified albumin (IMA) in patients with RA.

Materials and Methods: This study included 74 RA patients, and 70 healthy controls. Disease activity was assessed by disease activity score of 28 joints (DAS-28). Serum IMA level was measured spectrophotometrically using the albumin cobalt binding test.

Results: The mean IMA levels in RA group and healthy controls were 0.46±0.16 ABSU and 0.39±0.10 ABSU, respectively, and the difference was statistically significant (p=0.002). Disease Activity Score of 28 joints (DAS-28) were found to be positively correlated with IMA (r=0.388, p=0.002), C C-reactive protein (CRP) (r=0.476, p<0.001), and erythrocyte sedimentation rate (ESR) (r=0.495, p<0.001) in the study group.

Conclusion: The positive correlation between DAS-28 and IMA level in patients with AR suggests that IMA can be used as a biomarker for disease activity.

PP-29

Effect of percentile value on reference intervals for lysosomal enzymes

Eser Yildirim Sozmen[1], Erhan Canbay[1], Sema Kalkan Ucar[2], Ebru Demirel Sezer[1], Mahmut Coker[2]

[1]Department of Medical Biochemistry, Ege University Faculty of Medicine, Izmir Turkey

[2]Department of Pediatric Metabolism, Ege University Faculty of Medicine, Izmir Turkey

Objectives: Lysosomal storage diseases resulting from the defects of the catabolism and/or transport of by-products of cellular turnover are characterized by the accumulation of incompletely metabolized substrates within particular cell types. The measurement of enzyme activity is still the most important diagnostic tool and for correct diagnosis the decision-making limits (cut off values) should be known.

In this retrospective study, we aimed to investigate any effect of growth (weight and height) percentiles on the reference intervals for α-glycosidase, α-galactosidase, sphingomyelinase and β-glycosidase enzyme activities in the DBS samples.

Materials and Methods: The enzyme activity results and percentile values of 150 healthy children (73 girls, 85 boys, ages between 0-12 years old) were re-evaluated. Enzyme activity measurements were made with LC MS/MS.

Results: While there was no statistical significance difference in α- and β- glycosidase activities regarding age, α-galactosidase and sphingomyelinase activity were negatively correlated with age. All enzyme activities were slightly higher in children with low percentile values compared to others. Especially in the first year of life, α-glycosidase and α- galactosidase activities were higher of children in low percentile group (<10%) than those of in high percentile group (>90%).

Conclusion: It's utmost important to define the cut off values regarding to age as well as growth percentile values for early ages.

PP-30

Artificial intelligence and robotic technology use in health from healthcare providers' perspective

Banu Isbilen Basok[1], Fatma Demet Arslan[1], Selin Onur[1], Hakan Sakaoglu[2], Gokhan Akbulut[3]

[1]Department of Medical Biochemistry, University of Health Sciences Tepecik Training and Research Hospital, Izmir, Turkey

[2]University of Health Sciences Tepecik Training and Research Hospital, Directorate of Administrative and Financial Affairs, Izmir, Turkey

[3]Department of General Surgery, Medipol University, Bagcilar Medipol Mega Hospital, Istanbul, Turkey

Objectives: The evil character of science fictions, "artificial intelligence" (AI), is now one of the important technologies in Industry 4.0 era that has led to major transformations in many sectors, including healthcare. PwC, questioned the public awareness and willingness, including the participants from Turkey about the AI and robotics use in health, and the willingness of these participants found to be 85%. Since the patients were almost ready, we aimed to evaluate the awareness and willingness of healthcare providers about AI and robotics.

Materials and Methods: During a symposium titled as "New AI-based Approaches in Medicine" which organized by our hospital on 06.12.2017, a questionnaire consisting of 12 questions in which 5 of them demographic (Table 1) was distributed as pre- and post-. Nine of the completed questionnaires excluded due to missing data and 55 questionnaires evaluated. Chi-square and McNemar-Bowker tests used for statistical analysis.

Results: Demographic data as follows: 20-60 years, female/male 31/24, all graduated(except one), average working years 16.9±10.7, and the occupation percentages for doctors, healthcare providers other than doctors, and non-medical participants percentages 54%, 11%, and 35%, respectively. 64.8% of the participants were willing similar before and after the symposium. Age (below/over 35), working years (below/over 10), and educational status(undergraduate/graduate) did not change willingness, while men willingness was significantly higher than women (p<0.001). Only 53.3% of the doctors were willing and it was lower than medical stuff's (66.7%), and non-medical participants' (78.9%) (p<0.001) willingness. Forty-five percent of participants agreed to be used only AI in laboratory/imaging services.

Conclusion: There is a growing interest in AI and robotics in health. Doctors are less willing and more cautious than other medical or non-medical occupational groups. It seems that the AI use in laboratory and imaging services considered more appropriate than surgical and medical interventions services in future.

PP-31

Evaluation of analytical performance of beckman coulter access estradiol and sensitive estradiol kits

Merve Katkat, Huseyin Yaman, Mehmet Akif Bildirici, Suleyman Caner Karahan, Sumeyye Aytekin, Asim Orem

Department of Medical Biochemistry, Karadeniz Technical University, Trabzon, Turkey

Objectives: Estradiol (E2) is a natural estrogen used to monitor ovulation status and to assess amenorrhea, infertility and menopause. Sensitive kits are being developed to improve the analytical performance of the tests and measure lower concentrations. The aim of this study is to evaluate by comparison the analytical performance of Beckman Coulter Access E2 and Sensitive E2 kits used in our laboratory.

Materials and Methods: This study was performed between May 2018-May 2019 for the E2 test measured in Beckman Coulter Unicel DxI-800 autoanalyzer (2 autoanalyzer). In our laboratory, E2 kit was used between 01.05.2018-30.11.2018 and sensitive E2 kit was used between 01.12.2018-31.05.2019. The analytical performance of the tests was evaluated with total error, process sigma values and measurement uncertainty. Paired-T test was used to compare the analytical performance of estradiol tests and $p<0.05$ was considered statistically significant.

Results: For the E2 kit in the first and second autoanalyzer 6-month calculated analytical performance values were found at level 1 control value CV%10.75;10.91, process sigma value 2.24; 2.30, measurement uncertainty 24.37; 20.99; at level 2 control value CV%8.05; 8.21, process sigma value 3.45; 3.18, measurement uncertainty 16.23; 20.81 while total error values %24.12; 22.59, respectively. Values found for the sensitive E2 kit at level 1 control value were CV%5.04; 5.64 process sigma value 5.30; 5.87, measurement uncertainty 16.75; 16.42; at level 2control value CV%4.83; 4.73, process sigma 5.66; 6.01, measurement uncertainty 8.4; 6.87 while total error values %13.25; 13.04. In the comparison between the two kits, statistically significant difference was found between total error and CV values.

Conclusion: It was observed that the total error, uncertainty of measurement and process sigma values of the sensitive E2 kit were better than the E2 kit in both autoanalyzer. This is mainly because the sensitive E2 kit has lower CV values. We think that sensitive kits should be developed for tests with high CV values and poor analytical performance.

PP-32

The relationship between cardiolipin and isocitrate dehydrogenase in post mortem tissues

Emine Firdevs Yildirim[1], Ozlem Dogan[2], Aslihan Gurbuz[2]

[1]Ankara University, Institute of Forensic Sciences, Ankara, Turkey

[2]Department of Medical Biochemistry, Ankara University, Faculty of Medicine, Ankara, Turkey

Objectives: Aim of this study is to investigate the relevance of cardiolipin and isocitrate dehydrogenase levels with manner of death (trauma, death by firearm, cardiovascular diseases) and post mortem interval (12-15h, 16-20h, over 20h) in post mortem tissue samples.

Materials and Methods: Cardiolipin and isocitrate dehydrogenase levels were determined by ELISA and statistically evaluated.

Results: In terms of manner of death and post mortem interval notable proportional difference exist when the results are not statistically significant ($p<0.05$).

Conclusion: The results of the study showed that further studies should be performed with more sample had the potential to provide usable data for the forensic sciences although the result were not statistically significant.

PP-33

Evaluation of heterophile antibody interference in clinical incompatible insulin measurement

Suleyman Caner Karahan, Mehmet Akif Bildirici, Huseyin Yaman, Merve Katkat, Yuksel Aliyazicioglu, Sumeyye Sura Ayan

Department of Medical Biochemistry, Karadeniz Technical University, Trabzon, Turkey

Objectives: Insulin and C-peptide are among the tests commonly used in the follow-up of diabetes mellitus, metabolic syndrome and related clinical conditions and are analyzed by automated immunoassay systems. Insulin results that are not consistent with clinical diagnosis are reported in some cases, such as elevated insulin levels. Heterophile antibodies are common causes of interference in immunoassay measurements.In this study, the effect of heterophile antibodies on insulin values which were found to be incompatible with the clinical diagnosis of the patient was investigated.

Materials and Methods: A 70-year-old female patient admitted to Endocrinology Clinic of our hospital was consulted laboratory because of the high insülin level (72.8 mIU/L) incompatible with the clinic. The patient's insulin measurements at different times were reported to range from 72.8 mIU/L to 279 mIU/L (Siemens Immulite 2000 XPi, healthy individual reference range <29.1 mIU/L), whereas glucose and C-peptide results were in the reference range.The patient sample was treated with polyethylene glycol (PEG) and the measurements were repeated using the heterophile antibody blocking tube (HBT) (Scantibodies Laboratory) to examine the possible interference effect on insulin value.

Results: The insulin value in the studied sample was 72 mIU/L after PEG treatment. In the sample treated with HBT, the insulin value was below the measurable lower limit (2 mIU/L) and results were confirmed by repeated three times. Endocrinology clinic physician was informed about pretreatment of serum sample and measured insulin levels. The patient's HBT pretreatment insulin measurement result, which was approved by the clinician,was reported as <2 mIU/L.

Conclusion: The presence of heterophile antibody could not be ruled out by PEG measurement. However, the insulin level measured by HBT indicates the presence of heterophile antibody in the patient. We suggest that the presence of heterophile antibody should be evaluated with PEG and HBT separately. The presence of heterophile antibody interference should not be neglected in insulin measurements incompatible with clinical diagnosis.

PP-34

Our experiences in transition from serum to plasma for Troponin I test

Ramazan Avci, Banu Isbilen Basok, Fatma Demet Arslan, Inanc Karakoyun, Ayfer Colak

Department of Biochemistry, University of Health Sciences, Tepecik Training and Research Hospital, Istanbul, Turkey

Objectives: Reducing the turn-around time (TAT) of the high-sensitivity Troponin I (hsTnI) test for acute coronary syndrome in laboratories is one of the key targets. Upon the complaints of delayed hsTnI results from the Emergency Department (ED), studies planned to reduce the TAT and the experiences reported.

Materials and Methods: In our preliminary study on using lithium heparin (LH) tubes, which not require allowing to clot and had a shorter centrifugation time, it considered that laboratories should be careful and the reference values for plasma should be confirmed when switching from serum to plasma and hence plasma samples could use after the reference interval transfer. As a result, the tested 5 mL LH tube (BD Vacutainer®Barricor LH tube) which has a mechanical separator started to use in March 2019 in the ED for hsTnI test, by excluding samples from pediatric patients. TAT statistics evaluated and the experiences after the transition represented.

Results: Since blood samples collected by injector in ED, sample rejection rates increased due to insufficient blood samples. The advantage of using plasma use was not experienced due to the simultaneous delivery of LH tubes with other ones. To obtain plasma, a separate centrifuge placed in ED lab since there was need a different centrifugation period for the LH tubes. After the transition to plasma, TAT shortened only for 6 minutes. In spite of the warnings and the training given, insufficient improvements in TAT, increased sample rejection rates and putting another tube to the intensive work program considered as negative factors.

Conclusion: Plasma hsTnI analysis did not meet the expectations and caused unwanted problems in the workflow due to physical and organizational challenges in both ED and ED laboratory. It recommended that all processes including physical conditions and personnel organization should consider when switching from serum to plasma.

PP-35

Antalya Ataturk Goverment Hospital 2019 Ozone treatment results

Ozgur Bilgin Ayoglu, Ozer Bolat, Bahar Bulut

Antalya Ataturk Goverment Hospital, Antalya, Turkey

Objectives: We wanted to share our results regarding the oxidative process markers studied in patients who received Major Autohemotherapy and Minor Ozone therapy.

Materials and Methods: 40 patients who applied to Antalya Atatürk DH GETAT outpatient clinic and received Ozone treatment. 29 (72.5%) were female and the mean age was 45.3±4.2 years. Antioxidant and oxidant levels were measured before and after treatment. These measurements were performed using Rel Assay Diagnostics ® TAS (Total Antioxidant Status) and TOS (Total Oxidant Status) kits. TAS test principle: The antioxidants in the sample turn the dark blue-green ABTS radical solution into a colorless ABTS form. The change in absorbance at 660 nm gives the total amount of antioxidant. TOS test principle: Oxidants in the sample oxidize the ferrous ion clamp, which is integrated with the ferric ion. Ferric ion forms a colored compound with chromogen in acidic environment. The darkness of the color measured in the spectrophotometer gives the total amount of oxidant molecules in the sample. Symptoms of the patients were evaluated before and after treatment with clinical scales appropriate to their pathology.

Results: The mean pre-treatment Total Antioxidant and Oxidant values were 1.43±0.30 mmol Trolox Equiv./lt and 37.30±30.51 olmol H_2O_2 Equiv./lt, respectively. Patients underwent an average of 6.3 sessions of major autohemotherapy. 100 cc blood was taken from the patients, 100 cc O3 was treated and returned to the patients. O3 doses were started with 20 gamma and increased to 40 gamma. After the treatment, control blood values were measured in all patients. Total Antioxidant and Oxidant values after treatment were 1.35±0.17 mmol Trolox Equiv./lt and 14.51±8.47 µmol H_2O_2 Equiv./lt.

Conclusion: Although antioxidant values were decreased with treatment, it was not statistically significant. There was a significant decrease in oxidant levels with treatment. Clinical symptoms were significantly improved in all patients. It was observed that ozone therapy provided clinical and laboratory improvement to the patients.

PP-36

Are monocyte/HDL, lymphocyte/monocyte and lymphocyte/neutrophil ratios prognostic or follow-up markers in ischemic cerebrovascular patients?

Selma Tekin[1], Esin Avci[2], Rukiye Nar[2], Eylem Degirmenci[1], Suleyman Demir[2], Hande Senol[3]

[1]Department of Neurology, Faculty of Medicine, Pamukkale University, Denizli, Turkey

[2]Department of Medical Biochemistry, Faculty of Medicine, Pamukkale University, Denizli, Turkey

[3]Department of Biostatistics, Faculty of Medicine, Pamukkale University, Denizli, Turkey

Objectives: We investigated the association of monocyte to high-density lipoprotein cholesterol (HDL) ratio (MHR), lymphocyte to neutrophil ratio (LNR) and lymphocyte to monocyte ratio (LMR) with prognostic value and infarct types in patients with acute ischemic cerebrovascular disease (CVD).

Materials and Methods: The study was carried out retrospectively in 223 patients, but after the exclusion criterion,150 patients with acute ischemic CVD were included to the study. The complete blood count and lipid profile were examined at the admission of the patients. Serum total cholesterol, LDL-cholesterol, HDL-cholesterol, creatinine, uric acid and ALT, AST levels were analyzed in Cobas e702 biochemistry auto-analyzer with electrochemiluminescent, complete blood counts were measured on Siemens ADVIA 2120i hematology analyzer with electrical impedence method. National Institutes of Health Stroke Scale (NIHSS) score and modified Rankin Scale (mRS) score were evaluated. After the etiological investigations and neuroimaging, infarct types were defined.The exclusion criterions were severe renal, liver, heart failure, malignancy, hematological disorder, systematic acute/chronic inflammatory/autoimmune or infectious diseases.

Results: We found that as the NIHSS score increased, LMR and LNR values decreased statistically (p=0.02, p=0.013). Additionally, statistical significant differences were determined between MHR values and mRS scores (p=0.45). According to the results of regression analysis, it was observed that the increase of MHR was statistically significant on the MRS of people with cardioembolic infarction (p=0.004, StB=0.383).

Conclusion: Our study provides, LMR and LNR values are related with the initial neurologic state, and they would be prognostic markers for the neurological deficit of acute cerebrovascular disease. MHR can be a follow-up marker for CVD and also a predictable marker especially for cardioembolic infarct type.

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