ORIGINAL ARTICLE

The role of biomarkers in the early diagnosis of acute kidney injury associated with acute pancreatitis: Evidence from 582 cases

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ABSTRACT

BACKGROUND: One of the systemic complications of acute pancreatitis (AP) is acute kidney injury (AKI). AKI development in patients with AP increases mortality, morbidity, and the cost of treatment. Therefore, early diagnosis and prevention of AKI is important. The purpose of our study was to present biomarkers and case management of AKI developing in patients with AP.

METHODS: The participants of this retrospective study consisted of 582 patients who were followed up with the diagnosis of AP. Atlanta classification was used for the diagnosis and the identification of severity of AP. The laboratory values of patients at the time of first application to the emergency room were recorded. Blood tests were checked 48 h/l. Their blood tests were monitored daily until the day of discharge.

RESULTS: Of the 582 patients who were admitted with the AP diagnosis, 344 were female. AKI was detected in 147 patients (25.2%) of the patients admitted with AP diagnosis. The mean age of patients developing AKI was higher than those who did not develop AKI. The albumin and calcium levels in patients developing AKI were significantly lower than the group without AKI. The C-reactive protein (CRP)/albumin and neutrophil/lymphocyte ratios were statistically significantly higher in the group with AKI than the group without AKI. The increase values in AST and ALT levels between the group with AKI and the group without AKI were not statistically significant. The mean leukocyte, CRP, procalcitonin levels, and immature granulocyte percentage (IG%) ratio were higher in patients with AKI in comparison to the patient group without AKI. The decrease in the lymphocyte, hematocrit, and platelet levels was higher in the patient group with AKI compared to the patient group without AKI. Urea and creatinine levels of the group with AKI at the time of admission were higher than the group without AKI. The clinical picture in 13 of the patients we followed up with AP diagnosis was mortal.

CONCLUSION: The values of hematocrit, platelet, leukocyte, lymphocyte, albumin, CRP, CRP/albumin ratio, neutrophil/lymphocyte ration, IG%, procalcitonin, urea, and creatinine that were examined at the time of hospital admission can be useful biomarkers in predicting the development of AKI in patients with AP. In addition, accompanying diseases and age are among the factors affecting AKI development.

Keywords: Acute kidney injury; acute pancreatitis; immature granulocyte ratio; procalcitonin.

INTRODUCTION

The course of acute pancreatitis (AP), defined as the inflammation of pancreas, is generally mild and shows fast clinical improvement with fluid support, relief of symptoms such as pain and nausea, and early oral nutrition. However, it becomes life threatening in 20–30% of the patients, and its mortality can go up to 15%.[1] The most important determinant factor of morbidity and mortality in AP is the local and systemic complications that may develop. Fluid accumulation, pancreas

Cite this article as: Uğurlu ET, Tercan M. The role of biomarkers in the early diagnosis of acute kidney injury associated with acute pancreatitis: Evidence from 582 cases. Ulus Travma Acil Cerrahi Derg 2023;29:81-93.

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Ulus Travma Acil Cerrahi Derg 2023;29(1):81-93 DOI: 10.14744/tjtes.2022.60879 Submitted: 05.09.2022 Revised: 15.11.2022 Accepted: 06.12.2022

necrosis, pseudocyst, and pancreas abscess are among the local complications. Shock, kidney failure, respiratory failure, and cardiac and metabolic complications are among the systemic complications.[2] Acute kidney injury (AKI) is seen in about 15% of the patients with AP.[3,4] The development of AKI has been reported to be up to 69% in severe AP.[5] The development of AKI in patients with AP significantly increases the length of hospital stay, mortality, and the cost of treatment.[6] The ratio of AKI development can go up to 69% depending on the severity of AP.[5] Therefore, early diagnosis of AKI, start of aggressive treatment, and the admission of the patient to the intensive care unit without delay are of great importance. The markers related to the early diagnosis of AKI, which is one of the most significant systemic complications in AP, have not been well-defined. Although the creatinine values at the time of admission are a marker that is used frequently in determining kidney injury, its sensitivity is reported to be low in the early diagnosis of AKI. AKI development in patients with AP significantly increases the length of hospital stay, the ratio of treatment in intensive care unit, mortality, and the cost of treatment. Thus, prediction of AKI with clinical findings and biomarkers, early initiation of aggressive treatment, and admission of the patient to the intensive care unit without delay when needed are of great importance in preventing permanent damage and reducing mortality. The predictors of AKI development and the markers for early prediction of kidney injury in patients with AP have not been well-defined. Although the creatinine values at the time of first admission of patients are a frequently used marker in detecting kidney injury, its sensitivity is reported to be low in the early diagnosis of AKI. Acute inflammatory reactions in AP, which is an inflammatory disease, cause significant tissue damage in the pancreatic tissue and additionally lead to systemic inflammatory response syndrome (SIRS), which disrupts the function of organs, multiple organ dysfunctions, and ultimately death.[7] Biochemical biomarkers with high sensitivity which can assess the etiology, diagnosis, prognosis, and particularly severe complication development rapidly, easily, and more specifically are needed.[8]

In this study, we investigated the role and effectiveness of biochemical and hematological biomarkers in predicting the development of AKI in patients with AP. Thus, we presented our experiences and knowledge that can be useful in treating and monitoring patients with AP who are followed up in clinics.

MATERIALS AND METHODS

Before this retrospective study, an ethical committee approval was obtained. A total of 582 patients who were followed up with the diagnosis of AP in the General Surgery Clinic at the Mehmet Akif İnan Training and Research Hospital between June 2019 and April 2022 were included in the study. As our clinic accepts pancreatobiliary system patients from four cities in addition to our city, the number of patients with AP is high.

The exclusion criteria of the study included chemotherapy patients, patients using steroids, patients who were pregnant and under the age of 18, dialysis patients, liver failure, hospital stay shorter than 72 h, and patients with incorrect or insufficient information on their patient files and hospital database.

The confirmation of AP diagnosis was performed based on characteristic abdominal pain, serum amylase and/or lipase 3 or more times above the normal upper threshold, and AP findings in computed tomography, magnetic resonance, or abdominal ultrasonography.

The information on patients' age, gender, hematological and biochemical blood test results at the time of hospital admission and during their follow-up, radiological imaging examination reports, information on accompanying diseases, pancreatitis etiology, information on AKI diagnosis and mortality, duration of hospital stay, and the number of patients in the intensive care unit were obtained from patient files and hospital database.

Revised Atlanta classification was used to define the severity of pancreatitis in this series. Severe AP was defined as permanent organ failure with one or more organ involvement.[9]

All the information of the AP patients who developed AKI and who did not develop AKI in this study were compiled. When the records were examined retrospectively, the values and/or ratios of some hematological and biochemical biomarkers examined in blood samples taken at the time of hospital admission of patients who developed clinical and laboratory AKI after AP were compared with those who did not develop AKI. The significance of the differences was revealed. Thus, we reported results on whether the laboratory values at the time of admission were effective, can predict and guide in the development of AKI. In addition, we examined the effect of patient demographics and accompanying diseases on the development of AKI.

The patients hemogram, C-reactive protein (CRP), procalcitonin, immature granulocyte percentage (IG%), albumin, CRP/albumin urea, creatinine, calcium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), amylase, and lipase values were recorded. Creatinine values of all patients were checked daily, and the AKI diagnosis was confirmed with the creatinine values. Creatinine values of the patients were recorded until the day of discharge.

Urea and creatinine were examined in the blood samples taken from patients at the time of admission to diagnose and predict AKI. KDIGO criteria were used in the diagnosis, identification of severity, and staging of AKI. An increase of ≥0.3 mg/dL in serum creatinine within 48 h was defined as AKI. A 1.5–1.9-fold increase in basal creatinine level or ≥0.3 mg/dl increase was evaluated as Stage 1 AKI, a 2–2.9-fold increase as Stage 2 AKI, while a 3-fold increase in basal creatinine level or ≥4.0 mg/dl or initiation of renal replacement treatment was evaluated as Stage 3 AKI.[10]

Statistical Analysis

The data analysis was carried out using the Statistical Package for the Social Sciences (SPSS®) software, version 15.0 (IBM® Corp., Armonk, NY, USA). All values were expressed as mean±-standard deviation or number (percentage). The data were compared between subgroups using ANOVA (SPSS software, version 15). P<0.05 was considered statistically significant.

RESULTS

Among the 582 patients with AP who were followed up and treated, 344 (59.1%) were female, and the mean age was 57.9±21.05 in females and 58.06±17.34 in males. The most frequent cause of AP in 478 (82.1%) patients was gallstone. AKI was detected in 147 (25.2%) of the patients who were admitted to the hospital with the diagnosis of AP.

When the patients were examined according to the Revised Atlanta classification, the patients who developed AKI were the patients in the severe and moderate AP categories. AKI was seen in severe (22.4%) and moderate (76.8%) AP. The mean age of patients developing AKI was 66.74±19.397, while the mean age was 55.54±19.055 in patients who did not develop AKI. This age difference was statistically significant (p<0.0001) (Fig. 1a, b).

The mean length of stay at the clinic of the patients with AKI was 14 days. In this patient group, 54 (94.7%) patients were treated in the intensive care unit. The length of stay at the clinic of the patients without AKI was 7 days, and 33 (6.2%) patients in this group were treated in the intensive care unit. When the two groups were compared, a significant difference was found in length of hospital stay and the number of patients treated in the intensive care unit (p<0.0001) (p<0.001) (Table 1).

Seventy-four (50.3%) patients in the group with AKI were previously diagnosed with hypertension. This figure was 138 (31.7%) in the group without AKI.

The glucose values of 58 (39.4%) patients in the AKI group were above 180 mg/dl. Fifty-six of these patients were previously diagnosed with diabetes mellitus. The glucose levels of 100 (22.9%) patients in the group without AKI were above 180 mg/dl.

Table 1. The comparison of demographic data, etiology, and the length of hospital stay between the groups

	AKI -	AKI +	p
Number of patients, n (%)	435 (74.7)	147 (25.2)	
Gender, n (%)			
Female	311 (71.4)	112 (76)	
Male	124 (28.5)	35 (23)	
Median age (years)	55.54±19.055	66.74±19.397	0.0001
Length of hospital stay (day)	7	14	0.001
Intensive care unit, n (%)	33 (6.2)	54 (94.7)	0.001
Etiology, n (%)			
Biliary	425 (97.7)	56 (98.6)	
Non-biliary	7 (0.6)	–	
ERCP	3 (0.57)	2 (1.36)	

ERCP: Endoscopic retrograde cholangio pancreatogrphy; AKI: Acute kidney injury.

Blood tests performed during the admission process of the patients hospitalized with the diagnosis of AP showed that the albumin and calcium levels were significantly lower in the patients with AKI than the patients without AKI, and the difference was statistically significant (Fig. 2a, b, Fig. 3a, b).

No statistically significant difference was found in the amylase and lipase values between the patients with and without AKI. Similarly, there was no statistically significant difference in the AST and ALT levels between the patients with and without AKI (Fig. 4a, b, Fig. 5a, b, Fig. 6a, b, Fig. 7a, b).

When the hemogram parameters of the patients with and without AKI were examined, it was found that the leukocyte count and neutrophil/lymphocyte ratio were significantly high in the patients with AKI, while the lymphocyte count and hematocrit

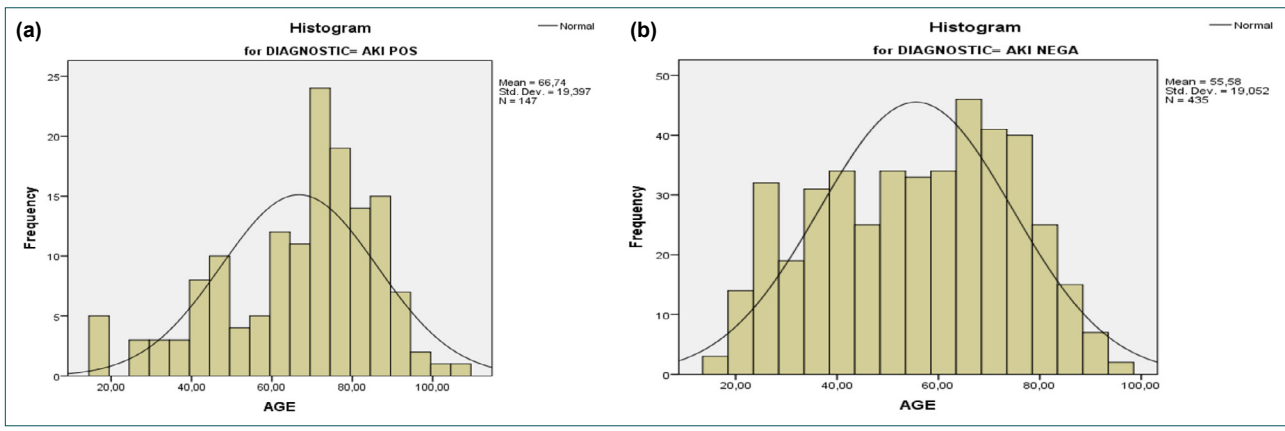

Figure 1. (a) Frequency of age in patients with acute kidney injury (AKI), **(b)** frequency of age in patients without AKI.

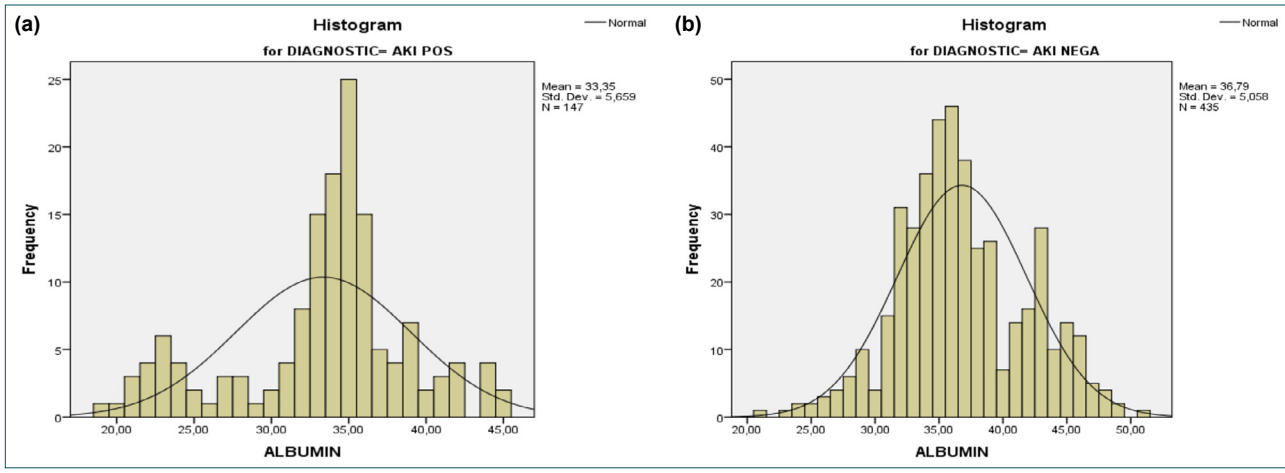

Figure 2. (a) Frequency of albumin in patients with acute kidney injury (AKI), **(b)** frequency of albumin in patients without AKI.

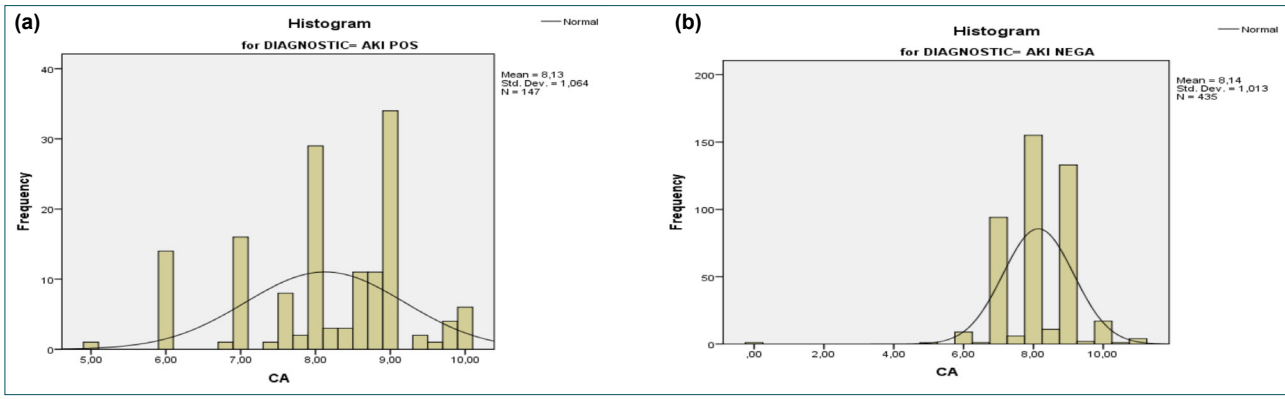

Figure 3. (a) Frequency of calcium in patients with acute kidney injury (AKI), **(b)** frequency of calcium in patients without AKI.

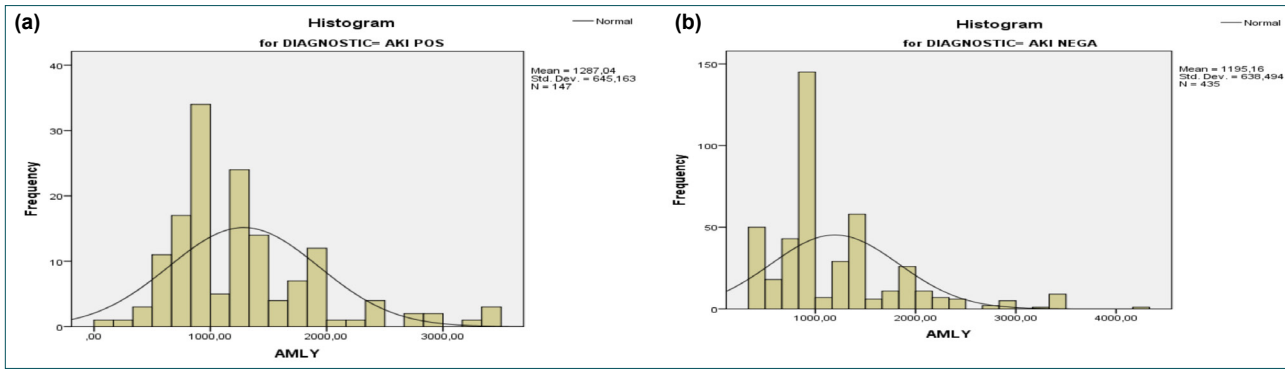

Figure 4. (a) Frequency of amylase in patients with acute kidney injury (AKI), **(b)** frequency of amylase in patients without AKI.

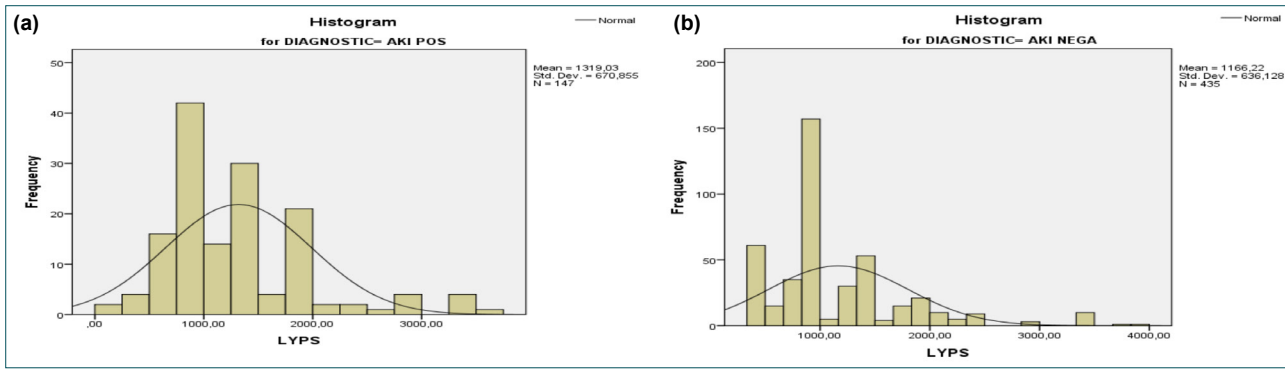

Figure 5. (a) Frequency of lipase in patients with acute kidney injury (AKI) **(b)** frequency of lipase in patients without AKI.

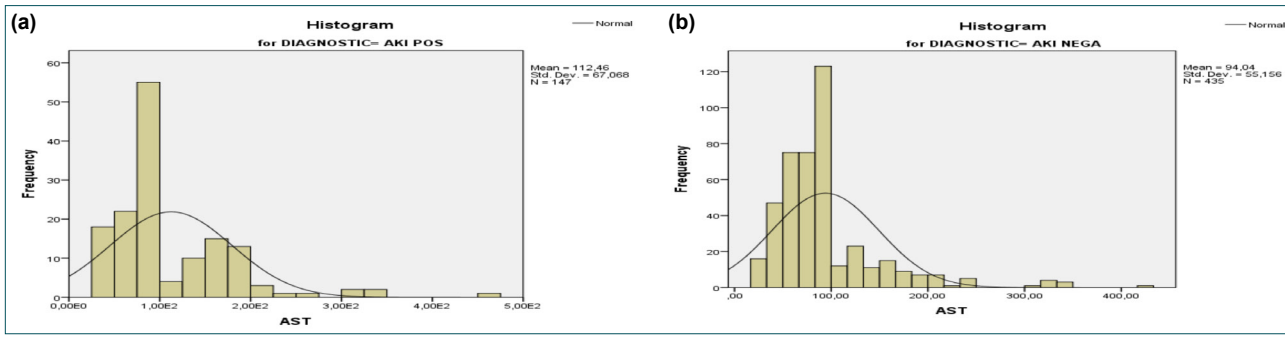

Figure 6. (a) Frequency of aspartate aminotransferase (AST) in patients with acute kidney injury (AKI) **(b)** frequency of AST in patients without AKI.

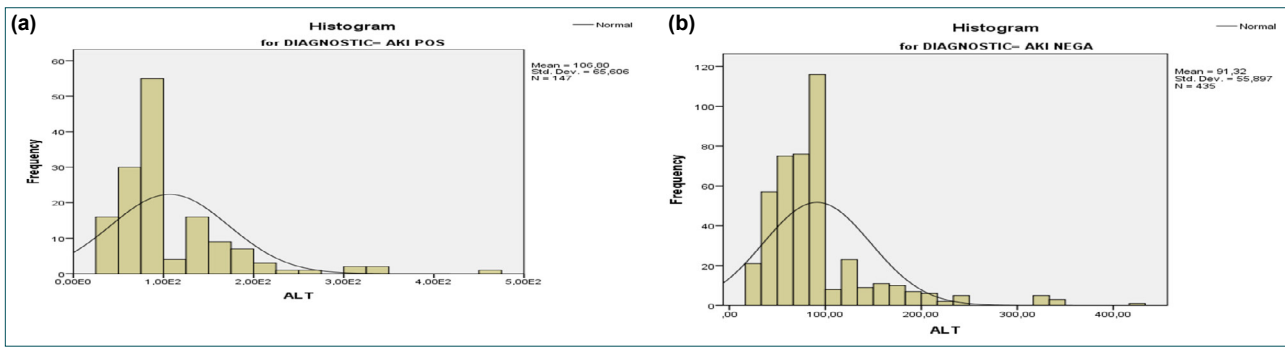

Figure 7. (a) Frequency of alanine aminotransferase (ALT) in patients with acute kidney injury (AKI), **(b)** frequency of ALT in patients without AKI.

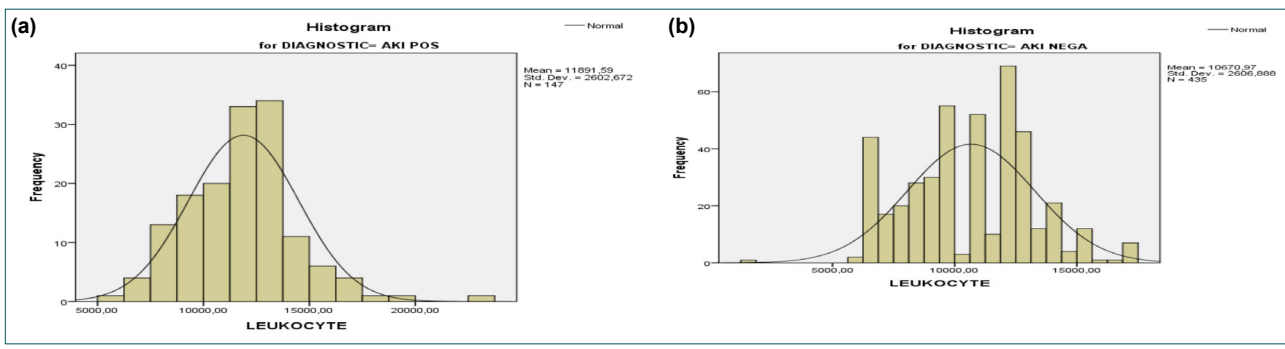

Figure 8. (a) Frequency of leukocytes in patients with acute kidney injury (AKI), **(b)** frequency of leukocytes in patients without AKI.

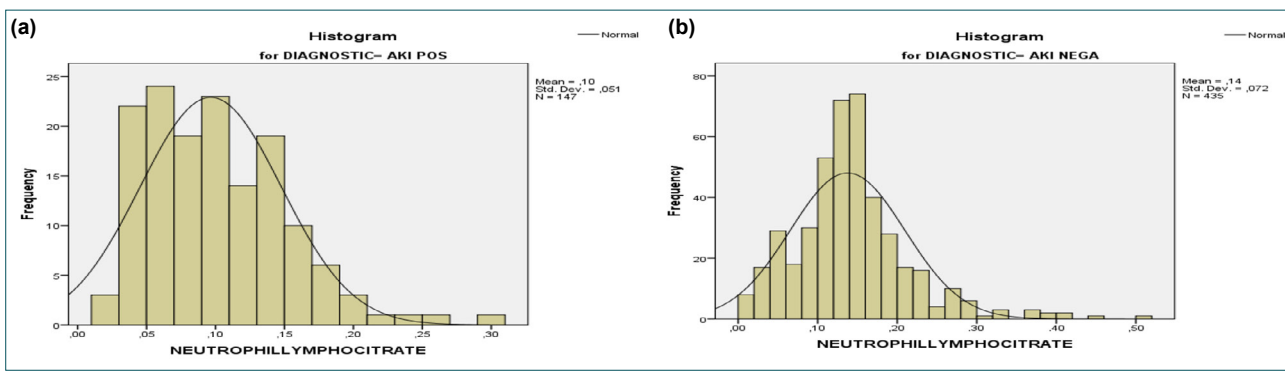

Figure 9. (a) Frequency of neutrophil-lymphocyte rate in patients with acute kidney injury (AKI), **(b)** Frequency of neutrophil-lymphocyte rate in patients without AKI.

values were significantly lower compared to the patient group without AKI. The low levels of platelets in the group with AKI were significant in comparison to the group without AKI (Fig. 8a, b, Fig. 9a, b, Fig. 10a, b, Fig. 11a, b, Fig. 12a, b).

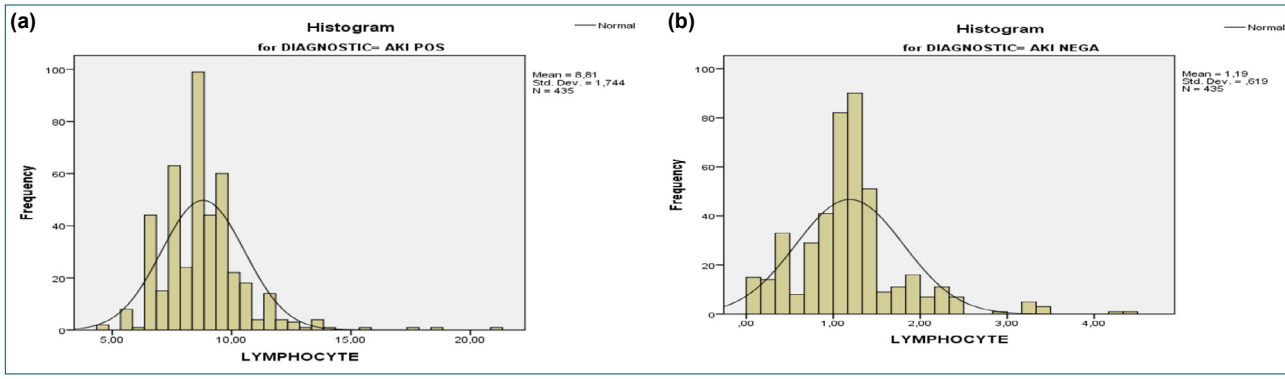

Figure 10. (a) Frequency of lymphocyte in patients with acute kidney injury (AKI), **(b)** frequency of lymphocyte in patients without AKI.

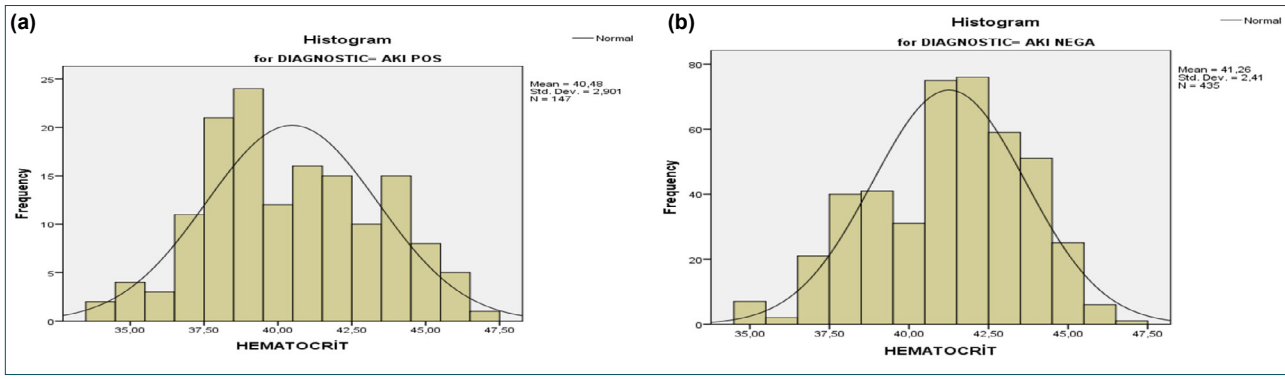

Figure 11. (a) Frequency of hematocrits in patients with acute kidney injury (AKI), **(b)** frequency of hematocrits in patients without AKI.

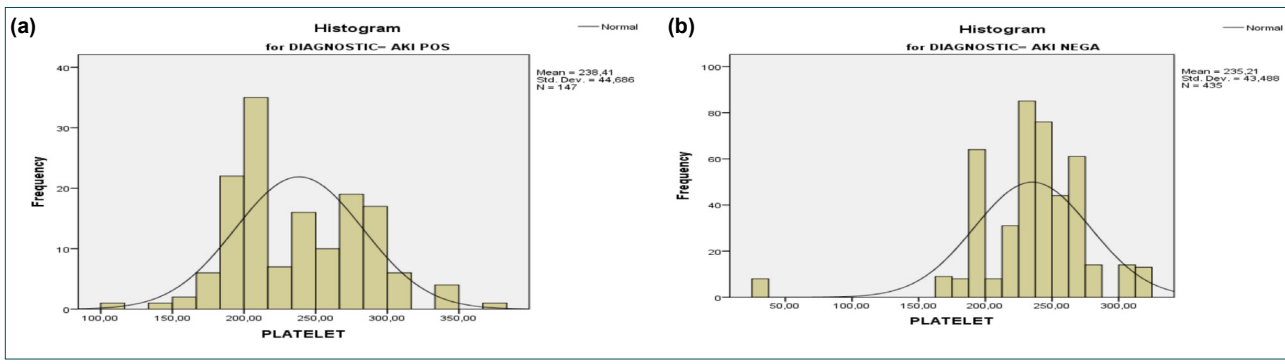

Figure 12. (a) Frequency of platelet in patients with acute kidney injury (AKI), **(b)** frequency of platelet in patients without AKI.

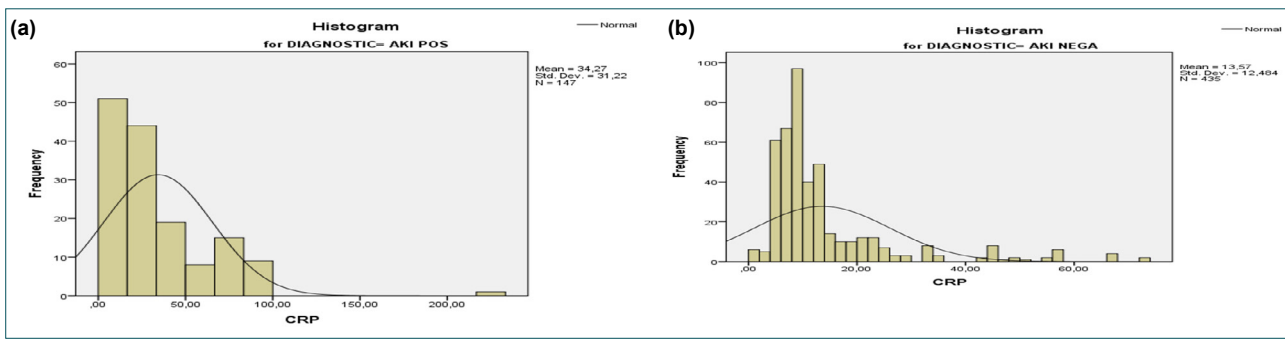

Figure 13. (a) Frequency of C-reactive protein (CRP) in patients with acute kidney injury (AKI) **(b)** frequency of CRP in patients without AKI.

CRP, IG%, and procalcitonin values, which are used as markers in inflammatory reactions, were found significantly high in the blood test results of the patients with AKI due to AP in comparison to the patients without AKI (Fig. 13a, b, Fig. 14a, b, Fig. 15a, b, Figs. 16–18). The high ratio of CRP/albumin in patients with AKI was statistically significant in

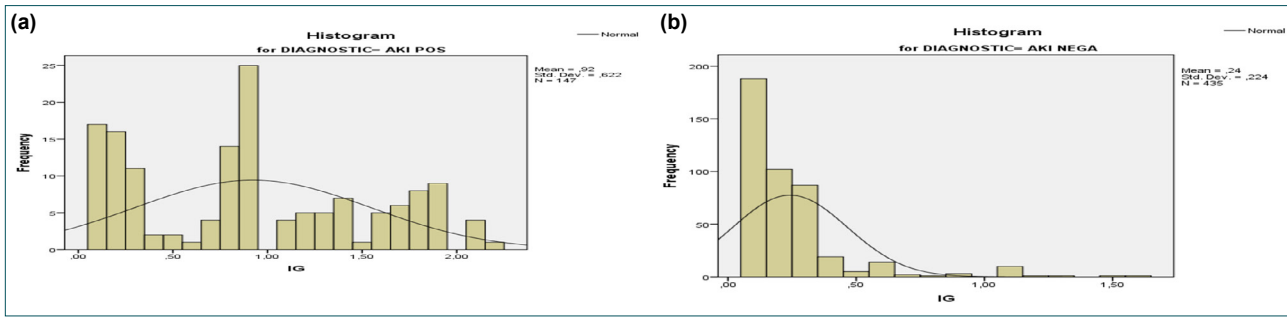

Figure 14. (a) Frequency of immature granulocyte ratio in patients with acute kidney injury (AKI), **(a)** frequency of immature granulocyte ratio in patients without AKI.

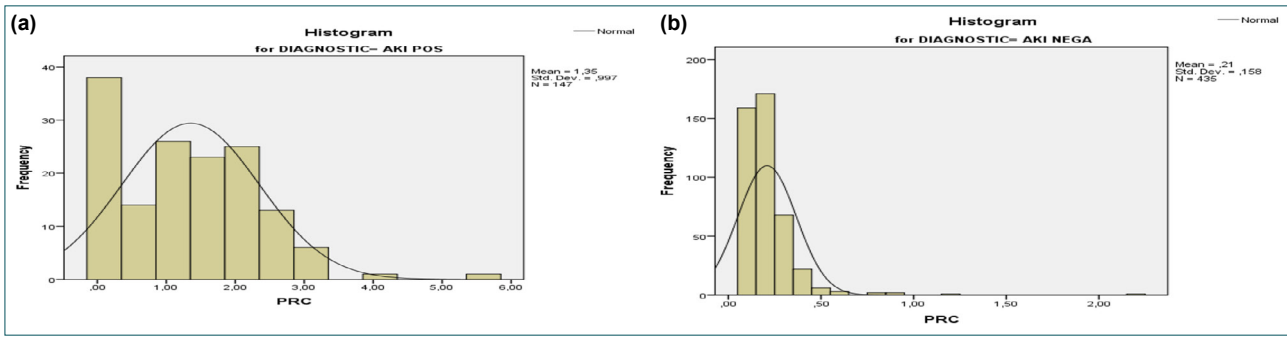

Figure 15. (a) Frequency of procalcitonin in patients with acute kidney injury (AKI) **(b)** frequency of procalcitonin in patients without AKI.

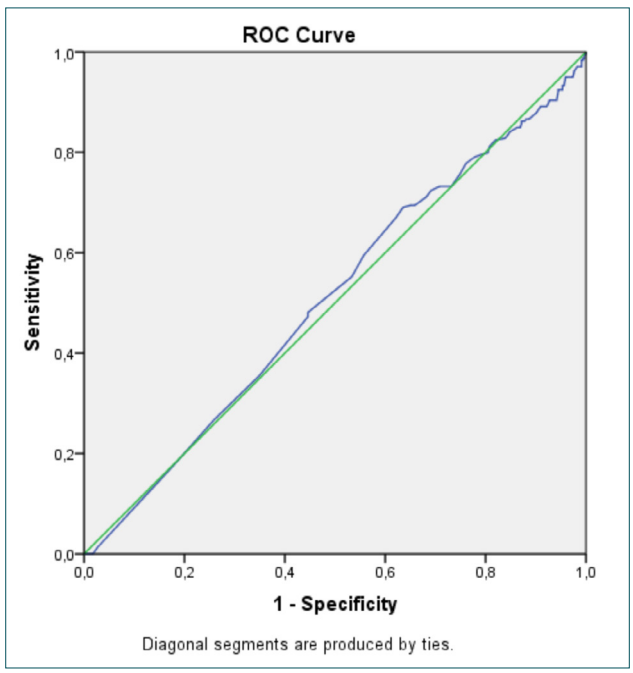

Figure 16. ROC graph for C-reactive protein value.

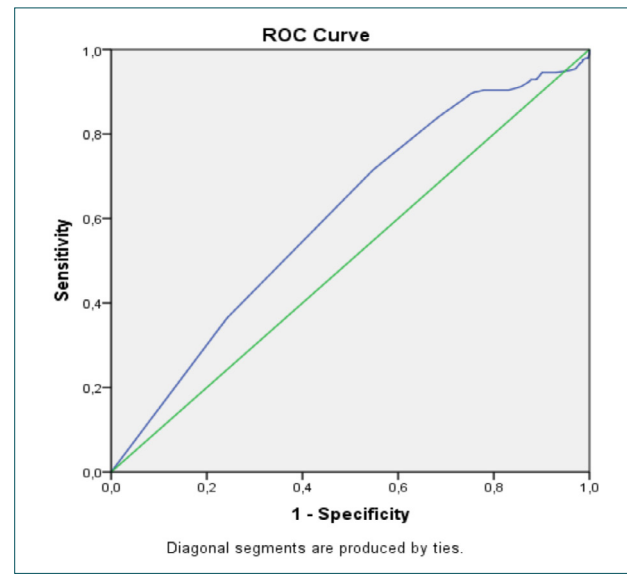

Figure 17. ROC graph for procalcitonin value.

patients without AKI (Fig. 19a, b). The urea and creatinine values of the patients who developed AKI at the time of admission were statistically significantly higher than the patients who did not develop AKI (Fig. 20a, b, Fig. 21a, b). Stage 1 AKI was reported in 88 (59.8%) and Stage 2 AKI was reported in 25 (17%) of the 147 patients who developed AKI among the 582 patients who were hospitalized, followed up, and treated for AP. Twenty-three (15.6%) patients were diagnosed with Stage 3 AKI and 15 of these patients received hemodialysis. Clinical mortality was observed in 13 of the patients who were followed up with the diagnosis of AP and 11 of these patients were in the group who developed AKI. When mortality was examined by stages, mortality was observed in one patient in Stage 1 AKI group, in six patients in Stage 2 AKI group, and in three patients in Stage 3 AKI group. The values and statistical results of hematological and biochemical biomarkers are presented in Table 2.

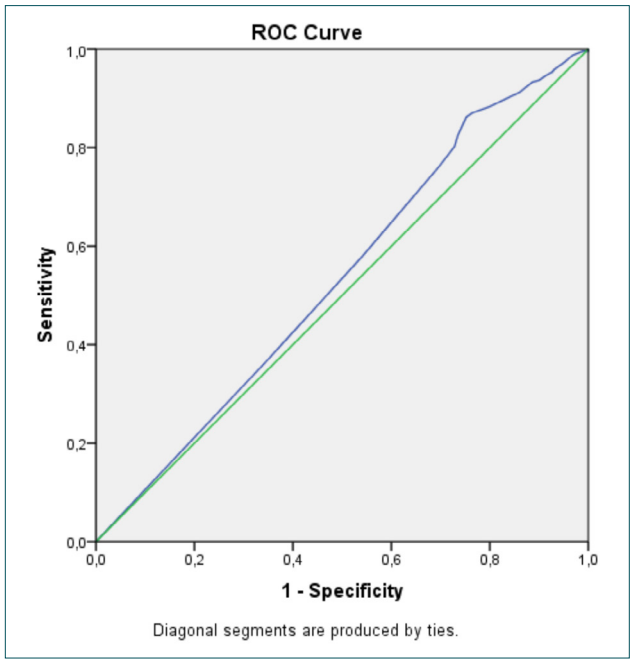

Figure 18. ROC graph for immature granulocyte ratio.

DISCUSSION

The shortcoming of AP scoring systems is that they provide information within 48–72 h at the earliest in predicting the development of complications and determining the prognosis. In our study, we presented the data that could determine AKI, which is one of the systemic complications affecting morbidity and mortality the most in AP, in the early period before becoming permanent.

Systemic complications of AP can be summarized as follows:

- Hypovolemia, shock
- Acute respiratory distress syndrome, pleural effusion, atelectasis, hypoxemia
- Acute kidney failure, azotemia
- Disseminated intravascular coagulation, vascular thrombosis
- Hypoalbuminemia, hypocalcemia, hyperglycemia, metabolic acidosis
- Stress ulcer, gastric varicose, pseudoaneurysm
- Other: Peripheral fat necrosis, encephalopathy.

The hyperinflammatory process in AP stimulates the cytokine system resulting in systemic inflammatory response (SIRS). With persistent and resistant continuation of SIRS, dysfunctions occur in one or more of the vital organs. Organ failure, which can be seen as acute respiratory failure, shock, and kidney failure, improves within 48 h in moderate AP, while it can last longer than 48 h in patients with severe AP.

As one of the AP complications, AKI increases morbidity and mortality significantly, which is why it is of great importance to diagnose AKI early.

In this study, we tried to provide evidence for the effectiveness of biochemical and hematological markers that can be

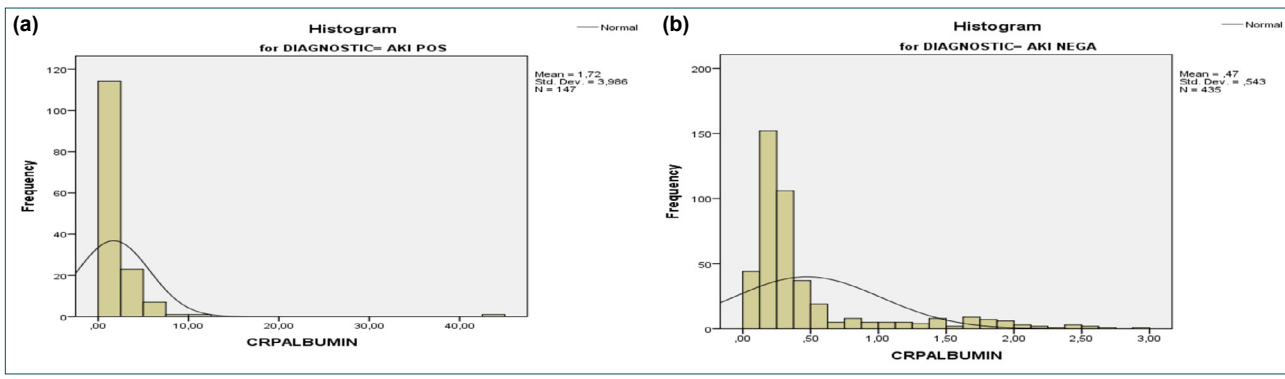

Figure 19. (a) Frequency of C-reactive protein (CRP)-albumin ratioin patients with acute kidney injury (AKI). **(b)** Frequency of CRP-albumin ratioin patients without AKI.

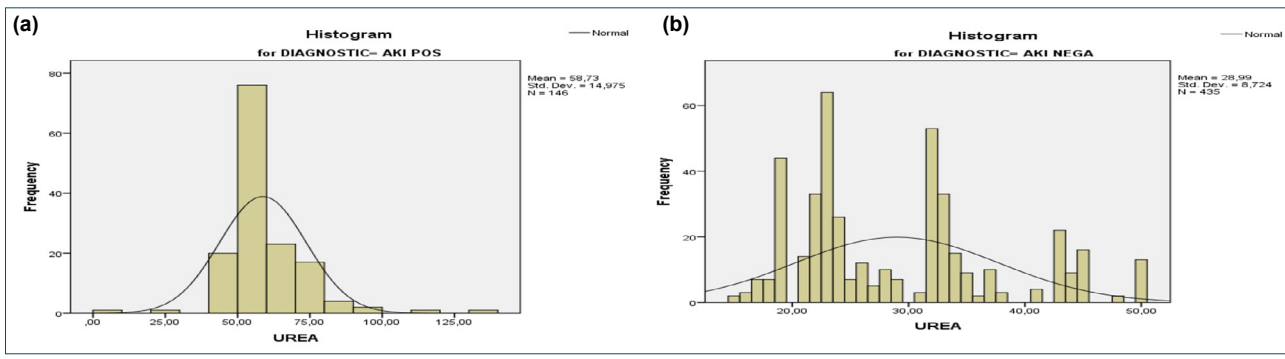

Figure 20. (a) Frequency of urea in patients with acute kidney injury (AKI). **(b)** Frequency of urea in patients without AKI.

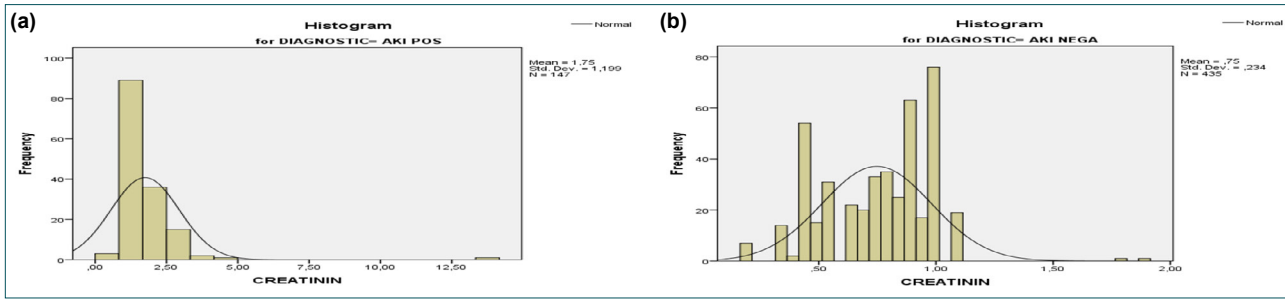

Figure 21. (a) Frequency of creatinine in patients with acute kidney injury (AKI). **(b)** Frequency of creatinine in patients without AKI.

used in the early diagnosis and detection of AKI, which is one of the systemic complications of AP, through the experiences and the data obtained from our large patient series, and provide guidance in the early diagnosis and taking necessary precautions in similar cases.

The lack and the ineffectiveness of scoring systems are still controversial in several aspects. The most important aspect is that they cannot provide information regarding the severity of the disease, prognosis, and predicting complications before 48 h. In addition, scoring systems cannot be calculated again while the AP continues, which creates problems in prognosis and early detection of complications.

Determining the severity of AP with scoring systems is important in predicting prognosis and complications. In this study, based on the Revised Atlanta classification, AKI was observed in patients with severe (22.4%) and moderate (76.8%) AP.

In our study, we attempted to present data that can predict AKI, which is one of the systemic complications affecting morbidity and mortality the most in AP, earlier than 48 h. In addition, in this study, the daily monitoring of biomarkers can be performed, and the prognosis of AKI can be monitored during the course of the disease. We believe that the values of the parameters we kept track of during the admission of the patients are very effective and important in terms of predicting AKI that could develop later. About 2–10% of mortality in AP occur as a result of complications.[11] Severe AP increases the risk of complication and, therefore, the mortality.[12] Rapid diagnosis of AP can be performed with clinical findings and biomarkers. It is of great importance to

Table 2. Hematological and biochemical biomarkers

Criterion	Group without AKI (n=435)	Group with AKI (n=147)	p
	Mean±SD	Mean±SD	
Leucocyte	10670±2606.888	11891±2602.672	0.000
Lymphocyte	1.08±0.371	1.18±0.619	0.001
Neutrophil/Lymphocyte Ratio	%14±0.72	98%±0.51	0.014
Platelet	238.41±43.488	235.21±44.686	0.002
Htc	41.6±2.41	40.47±2.901	0.001
CRP	13.56±12.484	34.27±31.22	0.0001
Procalcitonin	0.20±0.158	1.35±0.997	0.0001
IG%	0.24±0.224	0.92±0.662	0.0001
Albumin	36.79±5.058	33.35±5.659	0.0001
CRP/Albumin	0.47±5.058	1.72±5.659	0.001
AST	94.04±5.058	112.46±5.659	0.1
ALT	91.32±5.058	106±5.659	0.105
Ca	8.16±5.058	8.12±5.659	0.0000
Amylase	1195±638,494	1287±645.163	0.1
Lipase	1166±636.128	1319±670.855	0.12
Urea	28.99±8.724	58.73±14.975	0.0001
Creatinine	0.74±0.234	1.75±1.199	0.0001

AKI: Acute kidney injury; Htc: Haematocrit; CRP: C-reactive protein; IG%: Immature granulocyte; AST: Aspartate aminotransferase; ALT: Alanine aminotransfarase; Ca: Calcium; SD: Standard deviation.

start the treatment as early as possible and to take precautions for the early prediction and prevention of potential complications. In the diagnosis and follow-up, inflammatory or infection biomarkers such as serum albumin, amylase, lipase, ALT, AST, bilirubin, CRP, and procalcitonin are used together with routine hemogram and biochemical tests.[13] Age, comorbidities, and the severity of AP are among the factors affecting the clinical course of AP. Kidney failure (23% acute kidney failure, 80% proteinuria, 88% oliguria, and renal vein thrombosis) is one of the most important systemic complications of AP.[14] In a study, it was reported that the patients who developed AKI were at an advanced age, and the length of hospital stay and intensive care unit stay were significantly longer in patients with AKI than the patients who did not develop AKI.[6] In the same study, while hypertension was observed significantly more frequent, the two groups were reported to have similar results in terms of diabetes mellitus. In this study, the mean age of patients with AKI was significantly higher than the patients without AKI. We are of the opinion that the age factor plays a role in the development of AKI in AP. The length of hospital stay was significantly longer in the group with AKI.

The mean glucose and blood pressure values were reported as higher in the patient group with AKI compared to the patient group without AKI. Hypertension and diabetes history were observed more in patients with AKI. While alcohol takes the lead in the etiology of AP in Western countries, the presence of biliary stones in 53.8% of patients is the leading cause in Türkiye.[15] In our study, the most frequent cause of AP was gallstones in 478 patients (82.1%), which is higher than what is reported in the literature. Dysfunctions occurring in organs within 72 h cause mortality to increase up to 42%. The most important factor is that SIRS and organ failure are persistent and resistant to treatment. With the organ functions returning to normal, mortality rates decrease to 0%.[16] In several studies, no significant difference was reported in amylase and lipase values between the group with AKI and the group without AKI. In our study, there was no statistical difference in amylase and lipase values between the group with AKI and the group without AKI. It was observed that the amylase and lipase values did not have any prognostic effects for the development of AKI.

In a study conducted with 186 patients by Biyik et al., the AST, ALT, and glucose levels were significantly higher in the group with AKI, while the albumin and calcium values were significantly low in the same group. However, in our study, the difference in the serum ALT and AST values between the group with AKI and the group without AKI was not significant, which is why it was not considered as a prognostic marker.

A serum calcium value of <8 mg/dl can indicate poor prognosis in AP. Hyperglycemia is observed in 20% of the cases while hyperbilirubinemia is seen in 25%. Hypocalcemia and hyperglycemia are significant in predicting systemic complications. Based on the Atlanta criteria, having a calcium level of 7.5 mg/dl or below has a predictive value for systemic complications. In this study, the calcium levels in blood samples obtained during admission of patients with AKI were significantly low compared to the group without AKI. We are of the opinion that low level of calcium is significant and guiding in terms of early detection of AKI development.

White blood cells play an important role in the inflammatory process. Activation of leukocytes with inflammatory reactions in AP and the cytokine storm that initiates the inflammatory process is also responsible for the initiation of SIRS, which is responsible for single or multiple organ dysfunction, as well as local inflammatory injury and necrosis in the pancreas.[17] Neutrophil activation occurs as a result of the release of cytokines (such as complement activation, adhesion molecule expression, alveolar macrophage activation, and TNF-α), which are considered to be responsible for inflammatory reactions. The factor triggering the SIRS development is the resistant cytokine cycle which stimulates or inhibits each other as a result of the release of other mediators by TNF-α. SIRS developing as a result of this cytokine storm is responsible for increased injury in kidneys, pancreas, and other organs.[18] Studies were conducted focusing on the effects of neutrophils and lymphocytes in AKI development in AP. Neutrophil accumulation has been clearly demonstrated in ischemia and reperfusion injury caused by vascular damage in the kidney due to SIRS.[19,20] Decrease in neutrophil prevents AKI. Jeon et al.[21] found that the high level of NLR (neutrophil/lymphocyte ratio) was significant for AP-associated local damage, severity of pancreatitis, and systemic complications. One of the factors that are effective in AKI associated with AP is T-lymphocyte infiltration. T-lymphocyte density is typical both in the beginning and the advanced period of the inflammatory process. This increases kidney injury and stimulates the regeneration process after ischemia associated damage.[22] The activation of leukocytes and the variability of release of cytokines, which trigger inflammatory reactions, with negative and/or positive feedback are effective in SIRS formation, and thus, local and distant organ damage. When the hematological table was examined, the leukocyte count in the blood tests performed at the time of admission in patients with AKI was significantly high, which is consistent with the literature. It was thought that the leukocyte count could be a routine, simple, and low-cost marker that can be used to predict the AKI development. In patients with AKI, the low lymphocyte ratio and the decrease in the hematocrit and platelet values were statistically significant compared to patients without AKI, which suggested that it could be an early indicator for AKI development. At the same time, in line with the literature, the neutrophil/lymphocyte ratio in our study was significantly high in patients with AKI, which was prognostically significant. Procalcitonin is one of the most important biomarkers for diagnosis and prediction of prognosis in sepsis. It is also one of the factors

confirming diagnosis for bacterial infections. It is an important indicator for determining the prognosis and severity of AP early, and to diagnose the necrosis of infected pancreas.[23] Studies have shown that procalcitonin is an important prognostic factor in sepsis and AP, which is an inflammatory process.[24] It has been demonstrated in large study groups that procalcitonin is more effective in indicating the local damage and severity of pancreatitis and the risk of systemic organ damage when compared to other inflammatory markers.[25] It has been reported to play a role in determining the severity and prognosis of AP and in predicting the local damage and systemic organ failure. In a study conducted by Rau et al.,[26] procalcitonin and CRP values were compared, and procalcitonin was found to be a more valuable marker in early diagnosis and prognosis. High CRP level is a nonspecific, effective biomarker in determining the CRP inflammation. CRP measurement is a simple but important criterion in detecting inflammation and infection, and monitoring of clinical course.[27] It has been shown that CRP levels and disease severity are associated in predicting the AP prognosis, and that it can be effective and guiding in predicting local damage and systemic organ damage.[28] In this study, inflammatory markers, procalcitonin and CRP values, were found to be significantly higher in patients with AKI than those without AKI. High CRP and procalcitonin levels were thought to be useful in predicting AKI development.

Serum albumin level is a parameter of Imrie criteria. This scoring is recommended as it provides more concise results than Ranson scoring with its 56–85% sensitivity in severity assessment of both alcohol associated and biliary pancreatitis. An albumin level of <3.2 mg/dl within the first 48 h is an indicator of severe AP.[29]

The albumin levels at admission of patients with AKI were statistically significantly lower than those without AKI in this study. We are of the opinion that low albumin level is an indicator in predicting AKI, as in monitoring the severity of AP, and that the significantly high CRP/albumin ratio of patients with AKI should be evaluated in predicting AKI. The relationship between AP and IG% was examined and the relationship between the disease severity and IG% was investigated in a limited number of studies. IG% is a low-cost biomarker that can be performed easily in complete blood count. Recent studies have shown that the IG% increases in the early stages of inflammation much earlier than the routinely used values such as CRP and white blood cell. In recent publications, it has been determined that the IG% which is performed at the time of admission in AP is associated with the severity of the disease.[30] The role of biomarkers in the early period development of AP systemic (AKI, cardiac, cerebral, lung edema, etc.) and local complications is still being investigated. IG%, which is one of these markers, has been reported to increase at the onset of inflammation. It was observed in our study that the IG% ratio examined in the blood samples at admission was significantly higher in patients with AKI than patients without AKI. We are of the opinion that examining IG% ratios can be useful and guiding in the early detection of AKI development as in monitoring the AP severity and detecting local pancreas damage. It has been stated that the increase in urea in the first 24 h or high urea levels at the time of admission is closely related to mortality, and the increase in serum creatinine value in the first 48 h is useful in predicting AKI and the severity of local damage to the pancreas.[31]

Monitoring patients over 60 years of age with creatinine levels over 1.8 mg/dl would be appropriate.[32] In the course of AP, intensive care treatment may be required depending on the severity and the condition of complications.[33]

Stage 1 AKI was reported in 88 (59.8%) of the 147 patients who developed AKI among the 582 patients who were hospitalized, monitored, and treated for AP. Stage 2 AKI was reported in 25 (17%) patients, 23 (15.6%) patients were diagnosed with Stage 3 AKI, and 15 of those patients received hemodialysis. The urea and creatinine levels of patients with AKI at the time of admission were statistically significantly higher than the patients without AKI. We believe that the elevation in serum urea and creatinine levels is important and guiding in the early detection of AKI development. The most important limitation of this study is its retrospective nature. Another limitation is the increase in the sensitivity and selectivity of the results due to the fact that it is a high-volume series in a clinic that accepts patients from many centers.

Conclusion

All clinical and laboratory data show that AP is an inflammatory disease and a process. Local and systemic severe complications may occur in the course of this disease. AKI is one of the most frequent and important systemic complications. The results obtained in this study showed that biomarkers are important and effective in the early detection and prevention of AKI, and early initiation of treatment in terms of preventing permanent kidney injury and/or mortality. We obtained statistical results that were consistent with the literature, as well as results that were not. We believe that future studies conducted with larger series in more experienced centers will be provided guidance.

Ethics Committee Approval: This study was approved by the Harran University Clinical Research Ethics Committee (Date: 25.07.2022, Decision No: HRÜ/22.14.23).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: E.T.U.; Design: M.T.; Supervision: E.T.U., M.T.; Resource: E.T.U.; Materials: E.T.U.; Data: M.T.; Analysis: E.T.U.; Literature search: M.T.; Writing: E.T.U., M.T.; Critical revision: E.T.U., M.T.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Akut pankreatit ile ilişkili akut böbrek hasarının erken tanısında biyobelirteçlerin rolü: 582 olgudandan kanıtlar

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AMAÇ: Akut pankreatitin (AP) sistemik komplikasyonlarından biri akut böbrek hasarıdır (ABH). Akut pankreatitli hastalarda ABH gelişimi mortalite, morbidite ve tedavi maliyetini artırmaktadır. Bu nedenle ABH'nIn erken teşhisi ve önlenmesi önemlidir. Çalışmamızın amacı, AP'li hastalarda gelişen ABH'nin biyobelirteçlerini ve olgu yönetimini sunmaktır.

GEREÇ VE YÖNTEM: Bu geriye dönük çalışmanın katılımcılarını akut pankreatit tanısı ile takip edilen 582 hasta oluşturdu. Akut pankreatitin tanısında ve şiddetinin belirlenmesinde Atlanta sınıflaması kullanıldı. Hastaların acil servise ilk başvuru anındaki laboratuvar değerleri kaydedildi. Kırk sekiz saat sonra kan testleri yapıldı. Kan testleri taburcu oldukları güne kadar günlük olarak izlendi.

BULGULAR: Akut pankreatit tanısı ile başvuran 582 hastanın 344'ü kadındı. AP tanısı ile başvuran hastaların 147'sinde (%25.2) ABH saptandı. ABH gelişen hastaların ortalama yaşı, ABH gelişmeyenlere göre daha yüksekti. ABH gelişen hastalarda albümin ve kalsiyum düzeyleri ABH olmayan gruba göre anlamlı derecede düşüktü. ABH olan grupta, ABH olmayan gruba göre CRP/albümin ve nötrofil/lenfosit oranları istatistiksel olarak anlamlı derecede yüksekti. ABH olan grup ile ABH olmayan grup arasında AST ve ALT düzeylerindeki artış değerleri istatistiksel olarak anlamlı değildi. ABH olan hastalarda, AKI'si olmayan hasta grubuna göre ortalama lökosit, CRP, prokalsitonin düzeyleri ve % IG oranı daha yüksekti. ABH olan hasta grubunda, AKI olmayan hasta grubuna göre lenfosit, hematokrit ve trombosit düzeylerindeki azalma daha yüksekti. ABH olan grubun başvuru sırasındaki üre ve kreatinin düzeyleri, ABH olmayan gruba göre daha yüksekti. AP tanısı ile takip ettiğimiz hastaların 13'ünde klinik tablo ölümle sonlandı.

TARTIŞMA: Akut pankreatitli hastalarda hastaneye yatış anında bakılan hematokrit, trombosit, lökosit, lenfosit, albümin, CRP, CRP/albümin oranı, nötrofil/lenfosit oranı, IG%, prokalsitonin, üre, kreatinin değerleri ABH gelişimini öngörmede faydalı biyobelirteçler olabilir. Ayrıca eşlik eden hastalıklar ve yaş da ABH gelişimini etkileyen faktörler arasındadır.

Anahtar sözcükler: Akut böbrek hasarı; akut pankreatit; immatur granulosit oranı; prokalsitonin.

Ulus Travma Acil Cerrahi Derg 2023;29(1):81-93 doi: 10.14744/tjtes.2022.60879