The value of serum NGAL in determination of dialysis indication
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Abstract
Objective: To investigate if Neutrophil Gelatinase-associated Lipocalin can be used or not as a biochemical marker to determine the indications for emergency dialysis treatment.
Methods: The study was conducted at the Emergency Department of Numune Taraining and Research Hospital, Ankara, Turkey, in 2012, and comprised 60 patients who had uraemic symptoms and abnormal laboratory tests, including elevated potassium, blood urea nitrogen, and creatinine level or lowered pH and bicarbonate. They were divided into 2 equal groups as those having indication for dialysis (Group 1) and those not having such indications (Group 2). Relevant values, including that of Neutrophil Gelatinase-associated Lipocalin, were compared between the two groups. To assess the utility of Neutrophil Gelatinase-associated Lipocalin measurements at varying cut-off values to predict indications for dialysis, a conventional receiver operating characteristic curve was generated and the area under the curve was calculated. P<0.05 was considered statistically significant.
Results: The mean age of the 30 patients in Group 1 was 68.29±16.9 years, while in Group 2 it was 66.47±14.2 years (p<0.65). The mean Neutrophil Gelatinase-associated Lipocalin level was 817.65±334.76ng/mL in Group 1 and 398.97±202.42ng/mL in Group 2 (p<0.001). The best cut-off level for Neutrophil Gelatinase-associated Lipocalin to predict emergency haemodialysis indication was 615ng/mL with a sensitivity of 82% and a specificity of 80%, and the areas under curve was 0.84.
Conclusion: Serum Neutrophil Gelatinase-associated Lipocalin level may be a determining parameter for indication of emergency haemodialysis.
Keywords: Emergency, Dialysis, NGAL. (JPMA 64: 739; 2014)
and urine soon after acute renal injury. NGAL has the advantages of being an early, sensitive and non-invasive biomarker for acute renal injury.18

In this study, we aimed to investigate if we can use NGAL as a biochemical marker to determine the indications for emergency dialysis treatment or not.

 Patients and Methods
The study was conducted at the Emergency Department of Numune Training and Research Hospital, Ankara, Turkey, in 2012 after approval by the institutional ethics committee. Written informed consent was also obtained from the patients or the attendants in case patients were unconscious. Patients over 18 years of age with uraemic symptoms, including nausea, vomiting, altered consciousness, and willing to participate in the study were included, while those who did not meet the criteria were excluded.

A total of 60 patients represented the final study sample. Blood samples were drawn for the measurement of pH, HCO₃, BUN, creatinine, potassium, and NGAL at presentation. Thirty patients having indications for emergency dialysis were determined as Group 1, and 30 patients not having indications for emergency dialysis as Group 2. Serum NGAL levels were studied with a bedside kit (Triage NGAL test, Biosite, USA).

Serum pH, BUN, creatinine, K, HCO₃ and NGAL values were compared between the two groups.

Descriptive statistics were expressed as frequency and percentage, and mean ± standard deviation (SD). Normality of data distribution was tested with Kolmogorov-Smirnov test. X² test was used to compare categorical variables. Student’s t test was used for the comparison of continuous variables between the groups because distribution of data was normal. To assess the utility of NGAL measurements at varying cut-off values to predict dialysis indication, a conventional receiver operating characteristic (ROC) curve was generated and the area under curve (AUC) was calculated. The statistical analysis was performed using SPSS version 18.00 and p<0.05 was considered statistically significant.

Results
The characteristics of the 60 patients in the study were noted at the outset and there was no significant difference between the groups with respect to gender (p>0.05) and age (p>0.05).

In terms of laboratory findings, there was a significant difference between the groups for BUN, creatinine, K, and blood pH, HCO₃ levels (p<0.05) (Table).

<table>
<thead>
<tr>
<th>Table-1: Demographic, clinical and laboratory characteristics.</th>
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<tbody>
<tr>
<td><strong>Group 1 (mean±SD)</strong></td>
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<tr>
<td>------------------------</td>
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<tr>
<td>Ngal (ng/mL)</td>
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<td>pH</td>
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<td>Urea (mg/dL)</td>
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<td>Age (year)</td>
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<td>Gender (M/F)</td>
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NGAL: Neutrophil Gelatinase-associated Lipocalin.
HCO₃: Bicarbonate.

Discussion
The definitive therapy for CKD is renal transplantation.
Dialysis therapy, on the other hand, is only a temporary solution until a definitive therapy has been constituted. Emergency dialysis is life-saving under some circumstances.19

BUN or serum creatinine levels are elevated in renal failure. However, further tests are needed to distinguish between acute and chronic renal failure. A previously increased BUN, a previously increased and long-term stable serum creatinine level, and an abnormal urinalysis are supportive for CKD.14 Among them, creatinine is the most commonly used laboratory parameter in clinical practice. Although it is widely used in clinical practice, it has some potential disadvantages: it is affected by several factors such as age and gender, and it is unable to reflect acute renal injury as early as desired.20 First of all, renal functions are needed to be impaired more than 50% for an elevation in serum creatinine level to occur. Moreover, serum creatinine does not reflect renal function accurately until a stable renal condition has been reached, which requires several days.21 Serum creatinine value is a poor indicator for acute renal injury.22 In our study, serum BUN and creatinine levels were higher in both groups (Table). There was a significant difference between two groups in terms of serum BUN or creatinine levels (p<0.05). A serum pH level below 7.1 is another emergency dialysis indication.12,13 Subjects in both groups in our study had acidic blood pHs (Table). There was a significant difference between the two groups (p<0.05). A serum K level greater than 7 mEq/dL constitutes another indication for emergency dialysis.12 Subjects in Group 1 had a higher potassium level (Table). There was a significant difference between the two groups (p<0.05). A serum HCO3 level below 11 mEq/dL is another emergency dialysis indication.12,13 There was a significant difference between the two groups (p<0.05) in our study.

NGAL is a marker of active tubular pathology.23,24 Serum NGAL level is arguably the most promising novel biomarker for detection of AKI.24 The reasons for NGAL increase in AKI are acute tubular injury and NGAL secretion from neutrophils, macrophages, and other immune cells as an acute phase reactant.15 There is growing literature suggesting that NGAL is also a marker of kidney disease and severity in CKD.23 It has been shown that tubulo-interstitial injury occurs in almost all forms of CKD and serum NGAL increases as a result of this insult.24 A study found that NGAL is a potential early marker for impaired kidney function/kidney injury.25

A study in patients with AKI in ICUs detected that NGAL levels were elevated 10-fold in plasma and 100-fold in urine secondary to sepsis, ischaemia and nephrotoxins. Both urine and plasma levels were found to be correlated with serum creatinine levels.16 A prospective study reported that acute renal injury developed in 28% of the children who underwent cardiopulmonary bypass where serum creatinine levels were elevated 1-3 days after the surgery. However, NGAL levels were elevated 10-fold and it was detected in urine and plasma within 2-6 hours after the surgery. It was concluded that both urine and plasma levels of NGAL are strong, independent markers for acute renal injury.26

One study suggested that serum NGAL levels can be used as a marker for initiation of renal replacement therapy (RRT) in critical care patients.27 Others reported that serum NGAL level is a potential early, sensitive marker of kidney impairment/injury.28 and that serum NGAL levels were higher in haemodialysis patients compared to the control subjects.29 In the current study, NGAL values were elevated in both groups. However, when NGAL values were considered, a statistically significant difference was detected between the two groups (p<0.05). An ROC analysis was performed to ascertain the effectiveness of serum NGAL in determination of emergency dialysis indication. The sensitivity and specificity of a cut-off level of 615ng/mL were 82% and 80%, respectively.

Conclusion
Serum NGAL level may determine the indication of emergency dialysis which can be life-saving.

References