

**Abstract**

**Objectives:** Urinary system infections are one of the common causes of admission to the emergency department. And in this patient group, the distinction between upper and lower urinary tract is important in patient follow-up and treatment. The aim of this study is to investigate the usability of CAR and BAR values in the differentiation of lower and upper urinary tract infections in urinary tract infections presenting to the emergency department. Our secondary aim is to investigate the mortality predictive power of CAR and BAR values in urinary tract infections admitted to the emergency department.

**Material and Methods:** The study was planned as a retrospective observational. Patients diagnosed with urinary system infection in the emergency department were included in the study. Patient information was collected over the existing hospital data recording system and used for statistical analysis. The patients were divided into 2 groups as lower and upper urinary tract infections, and the usability of CAR and BAR values in this division was calculated.

**Results:** A total of 41 patients were included in the study and 17 of them were women. The mean age of all patients was calculated as  $70.66 \pm 14.47$  years. While 32 of the patients were lower urinary tract infections, 9 of them were upper urinary tract infections. 8 patients resulted in mortality. It was found that CAR and BAR values were not statistically significant in estimating mortality with the distinction of upper and lower urinary tract.

**Conclusion:** CAR and BAR values are not successful markers that can be used to differentiate the lower and upper urinary tract infection.

**Keywords:** BUN/albumin ratio, CRP/Albumin, urinary tract infections

**Özet**

**Amaç:** Üriner sistem enfeksiyonları acil servise sık başvuru sebeplerinden bir tanesidir ve bu hasta grubunda alt ile üst üriner sistem ayırımı hasta takip ve tedavisinde önem arz etmektedir. Bu çalışmanın amacı acil servise başvuran üriner sistem enfeksiyonlarında alt ve üst üriner sistem enfeksiyonu ayırımında CRP/Albumin oranı (CAR) ve BUN/Albumin oranı (BAR) değerlerinin kullanılabilirliğini araştırmaktır. İkincil amacımız ise acil servise başvuran üriner sistem enfeksiyonlarında CAR ve BAR değerinin mortalite tahmin gücünü araştırmaktır.

**Gereç ve Yöntemler:** Çalışma retrospektif gözlemsel olarak planlanmıştır. Acil serviste üriner sistem enfeksiyonu tanısı konulan hastalar çalışmaya dahil edilmiştir. Hasta bilgileri mevcut hastane veri kayıt sistemi üzerinden toplanıp istatistiksel analiz için kullanılmıştır. Hastalar alt ve üst üriner sistem enfeksiyonları olarak 2 gruba ayrılmış ve bu ayırimda CAR ve BAR değerlerinin kullanılabilirliği hesaplanmıştır.

**Bulgular:** Çalışmaya toplam 41 hasta dahil edilmiş olup 17 tanesi kadındır. Tüm hastaların yaş ortalaması  $70,66 \pm 14,47$  olarak hesaplanmıştır. Hastalardan 32 tanesi alt üriner sistem enfeksiyonu iken 9 tanesi üst üriner sistem enfeksiyonudur. 8 hasta mortalite ile sonuçlanmıştır. CAR ve BAR değerlerinin alt ve üst üriner sistem ayırımı ile mortalite tahmininde istatistiksel anlamlı belirteçler olmadığı bulunmuştur.

**Sonuç:** CAR ve BAR değerleri alt ve üst üriner sistem enfeksiyonu ayırımında kullanılabilir başarıyla belirteçler değildir.

**Anahtar kelimeler:** BUN/Albumin oranı, CRP/Albumin oranı, üriner sistem enfeksiyonları

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## INTRODUCTION

Urinary tract infections (UTIs) are one of the most common bacterial infections. Considering the human anatomy, it is expected to be among the most common bacterial infections. UTIs account for 0.9% of all outpatient admissions in the US and represent the source of approximately 40% of patients presenting to emergency departments with septic shock (1).

UTIs include acute pyelonephritis (APN) or upper urinary tract infection (UUTI) and lower urinary tract infections (LUTI) involving the lower urinary system, mainly cystitis (2). There is a relationship between the localization of the infection and the severity of the disease and additional diseases that may occur (3). Particular attention should be paid to APN as it causes end-stage renal failure due to scar formation in the kidneys and consequently high blood pressure and renal parenchymal involvement (2). Therefore, it is important to determine the localization of the infection.

Urinary symptoms in cystitis are limited to the bladder, but upper duct involvement can also be seen. Frequent urination, urgency, and dysuria are the most common symptoms in premenopausal women. Postmenopausal women, the elderly, and children may present with fatigue, nocturia, incontinence, or foul-smelling urine (4). In pyelonephritis, urinary symptoms may or may not be present; The patient may present with fever and chills, back pain, nausea, and vomiting. The incidence of pyelonephritis is much lower than cystitis (59,0/10.000 in women and 12,6/10.000 in men), but the patterns are very similar by age and sex [5]. The effectiveness of the CRP/Albumin ratio in distinguishing between UUTI and LUTI has been studied in children, but there are no similar studies in adults (6).

Biomarkers such as C-reactive protein (CRP), albumin, and blood urea nitrogen (BUN) have been observed to be prominent in predicting the severity of various diseases in recent studies. Since CRP and Albumin are acute-phase reactants, they have proven to be successful indicators of mortality in different diseases such as acute myocardial infarction, pancreatitis, and chronic obstructive pulmonary disease (7). According to a review examining studies in which CRP differentiates UUTI and LUTI, the overall sensitivity and specificity were respectively 94% and 39% at a cut-off value of 2 mg/dl (8). However, the low specificity alone showed that it was insufficient to make this distinction. Serum albumin is a negative, acute-phase reactant. In critical care, the degree of hypoalbuminemia is associated with infection-induced inflammation. Similarly, the CRP albumin ratio (CAR) is associated with the severity of infection in sepsis [9]. Recent studies have emphasized that the BUN/albumin ratio (BAR) is also a sensitive marker in determining morbidity and mortality and that it has a strong correlation with mortality, espe-

cially in the elderly population, in patients with pneumonia, and in patients without renal failure (6).

The combination of these parameters may be more sensitive and useful for predicting APN in UUTI. In this study, we aimed to investigate the relationship between CRP/Albumin and BUN/Albumin ratio and UUTI and LUTI and their possible predictive role in the differential diagnosis of these two UTI types.

## MATERIAL METHOD

### Study Design:

This observational retrospective study was conducted with patients diagnosed with urinary tract infection who applied to the emergency department of a tertiary care university hospital between July 1, 2022, and July 1, 2023. Forty-one cases who presented to the emergency department with signs and symptoms of urinary tract infection were analyzed. Besides demographic data, comorbid factors, type of urinary infection (upper/lower), BUN/Albumin ratio (BAR), CRP/Albumin ratio (CAR), and hospitalization rate were evaluated by retrospectively and observationally examining hospital records. Patients were categorized as Lower and Upper urinary tract infections. Both groups were compared with each other.

### Patients and Setting:

Cases over the age of 18 who applied to the emergency department with symptoms of urinary system infection and were diagnosed with urinary system infection were included in the study. Cases under the age of 18 who presented with the same symptoms but were accompanied by other focal infections, and cases without any of the BUN, CRP, and albumin values were excluded from the study. In addition, chronic diseases that increase BUN value, such as renal failure and decrease albumin value such as malignancies, were excluded from the study. Patients whose information could not be reached and whose laboratory data were missing were also excluded from the study.

### Data Collection:

The data of the patients included in the study were accessed through the hospital information system and the vital parameters, demographic data, and laboratory test results of the patients were recorded in the patient forms created to be used in the statistical analysis. The outcomes of the patients admitted to the service and intensive care units for the treatment of urinary system infection were noted as exitus or discharge. The BUN/Albumin and CRP/Albumin ratios of the two groups, which were classified as lower and upper urinary tract infections, were compared with each other.

### Statistical Analysis:

Data were evaluated in the statistical package programs IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA) and MedCalc® Statistical Software version 19.6 (MedCalc Software Ltd, Ostend, Belgium). Descriptive statistics were given as number of units (n), percentage (%), mean and standard deviation. The homogeneity of the variances, which is one of the prerequisites of the parametric tests, was checked with the "Levene" test. Normality assumption was checked with the "Shapiro-Wilk" test. When it is desired to evaluate the differences between the two groups, "Student's t Test" if the parametric test prerequisites are met; If not, the "Mann Whitney-U test" was used. The performances of age, WBC, CRP, BUN, creatinine, albumin BUN/Albumin, CRP/Albumin measurement parameters in predicting the urinary system and mortality groups were evaluated with Receiver Operating Characteristic (ROC) curve analyses. A value of  $p < 0.05$  was considered statistically significant.

### RESULTS

A total of 41 patients were included in the study and 17 of them were female. The mean age of all patients was calculated as  $70.66 \pm 14.47$  years. Dysuria and flank pain were the most common complaints of admission to the emergency department. While 32 (78.05) of the patients had lower urinary tract infections, 9 (21.95) had upper urinary tract infections. While 26 of the patients resulted in hospitalization in the ward and 3 in the intensive care unit, 12 patients were discharged from the emergency department. It was observed that 8 (19.51) patients resulted in mortality. Descriptive statistics of the variables are presented in Table 1.

**Table1:** Descriptive Statistics of Variables

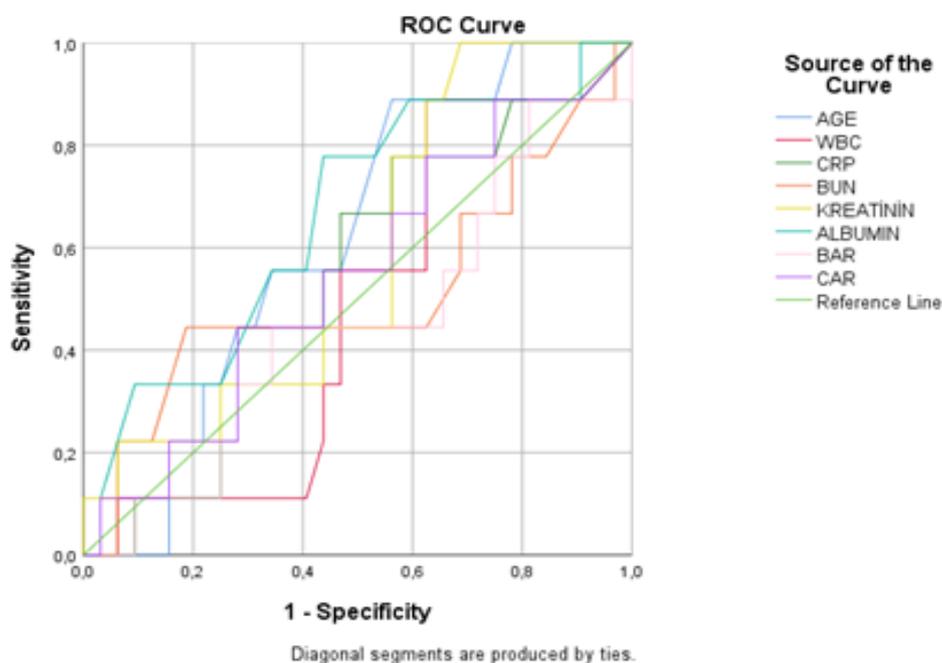
		Statistics
<b>Age</b>		70,66±14,47
<b>Gender</b>	Female	17 (41,46)
	Male	24 (58,54)
<b>Arrival complaint</b>	Fever	3 (7,32)
	Dysuria	10 (24,39)
	Pollakiuria	3 (7,32)
	Urgency	5 (12,2)
	Polyuria	1 (2,44)
	Side Pain	10 (24,39)
	Lack of Oral Intake	5 (12,2)
	Change of Consciousness	2 (4,88)
	Other	2 (4,88)
	<b>CVAT</b>	No
Yes		9 (21,95)
<b>SPT</b>	No	20 (48,78)
	Yes	21 (51,22)
<b>DM</b>	Yes	10 (100)
<b>CAD</b>	Yes	9 (100)
<b>CHF</b>	Yes	8 (100)
<b>HT</b>	Yes	9 (100)
<b>CRF</b>	Yes	5 (100)
<b>BPH</b>	Yes	5 (100)
<b>Urinary Stone</b>	Yes	1 (100)
<b>CVD</b>	Yes	3 (100)
<b>History of hospitalization in the last 3 months</b>	No	30 (73,17)
	Yes	11 (26,83)
<b>History of intervention in the hospital in the last 3 months</b>	No	29 (70,73)
	Yes	12 (29,27)

<b>Foley catheter</b>	No	20 (48,78)
	Yes	21 (51,22)
<b>CIC</b>	No	39 (95,12)
	Yes	2 (4,88)
<b>Nephrostomy</b>	No	38 (92,68)
	Yes	3 (7,32)
<b>Septic shock at the time of arrival</b>	No	38 (92,68)
	Yes	3 (7,32)
<b>Blurring of Consciousness</b>	No	36 (87,8)
	Yes	5 (12,2)
<b>Pyelonephritis</b>	No	32 (78,05)
	Yes	9 (21,95)
<b>Systit</b>	No	9 (21,95)
	Yes	32 (78,05)
<b>Urinary Tract</b>	lower urinary tract inf	32 (78,05)
	upper urinary tract inf	9 (21,95)
<b>WBC</b>		9,51±5,38
<b>CRP</b>		67,5±77,06
<b>BUN</b>		35,02±21,66
<b>CREATININE</b>		4,52±16,15
<b>ALBUMIN</b>		31,7±6,7
<b>BUN/ALB</b>		1,25±1,07
<b>CRP/ALB</b>		2,42±3,54
<b>Mortality</b>	No	33 (80,49)
	Yes	8 (19,51)
<b>Outcome</b>	Service	26 (63,41)
	ICU	3 (7,32)
	Discharged	12 (29,27)
<b>Total</b>		41 (100)

According to Table 2, the highest area under the curve (AUC) value belongs to ALBUMIN and the lowest AUC value belongs to BUN parameter. However, these parameters are not statistically significant in separating the urinary system groups.

**Table 2:** Age, WBC, CRP, BUN, CREATININ, ALBUMIN, BUN/ALB, CRP/ALB Measurements and Cutoff Scores, AUC Value, Sensitivity, Selectivity and Statistical Significance by urinary system groups.

Test Result Variables	Cutoff	AUC	Std. Error	p	Asymptotic 95% Confidence Interval		Sensitivity	Specificity
					Lower Bound	Upper Bound		
Age	>67	0,618	0,094	0,210	0,453	0,765	88,9	43,7
WBC	$\leq 10,7$	0,521	0,103	0,834	0,359	0,679	88,9	40,6
CRP	>14	0,545	0,108	0,675	0,382	0,701	77,8	43,7
BUN	>55	0,510	0,132	0,936	0,350	0,670	44,4	81,2
CRE	>0,93	0,585	0,103	0,410	0,421	0,737	100,0	31,2
ALBUMIN	>31	0,660	0,107	0,134	0,495	0,800	77,8	56,3
BUN/ALB	$\leq 0,6$	0,545	0,115	0,695	0,382	0,701	55,6	65,6
CRP/ALB	>2,46	0,547	0,112	0,676	0,384	0,703	44,4	71,9

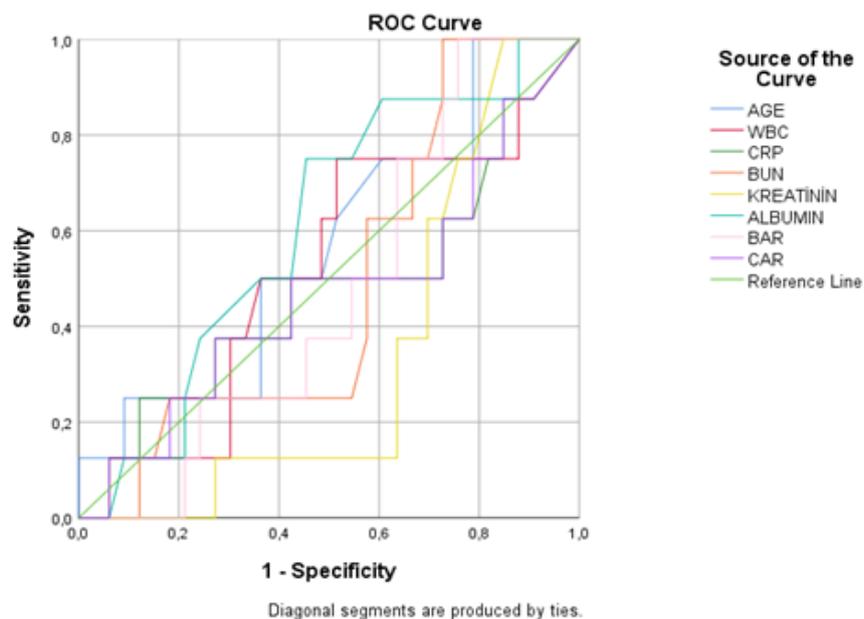


**Chart 1:** ROC Curves for Age, WBC, CRP, BUN, CREATININ, ALBUMIN, BUN/ALB, CRP/ALB Measurement parameters

According to Table 3, the highest area under the curve (AUC) value belongs to creatinine and the lowest AUC value belongs to BUN/ALB parameter. However, these parameters are not statistically significant in separating the urinary system groups.

**Table 3:** Cutoff Scores, AUC Value, Sensitivity, Selectivity, and Statistical Significance by Age, WBC, CRP, BUN, CREATININ, ALBUMIN, BUN/ALB, CRP/ALB Measurements and Mortality.

Test Result Variables	Cutoff	AUC	Std. Error	p	Asymptotic 95% Confidence Interval		Sensitivity	Specificity
					Lower Bound	Upper Bound		
Age	>58	0,568	0,116	0,555	0,404	0,722	100,0	21,2
WBC	>8,62	0,519	0,120	0,874	0,358	0,677	75,0	48,5
CRP	≤8,8	0,527	0,132	0,840	0,365	0,684	50,0	72,7
BUN	≤31	0,513	0,106	0,900	0,352	0,672	75,0	54,5
CRE	≤1,31	0,665	0,090	0,069	0,500	0,804	87,5	63,6
ALBUMIN	>31	0,606	0,106	0,318	0,441	0,755	75,0	54,5
BUN/ALB	>0,375	0,473	0,099	0,789	0,316	0,635	100,0	24,2
CRP/ALB	≤0,275	0,532	0,129	0,802	0,370	0,689	50,0	72,7



**Chart 2:** ROC Curves for Age, WBC, CRP, BUN, CREATININ, ALBUMIN, BUN/ALB, CRP/ALB Measurement parameters.

## DISCUSSION

Differentiating acute pyelonephritis from cystitis is important and necessary in many respects. It is one of the leading UTIs that need to be diagnosed and treated as soon as possible due to serious complications such as pyelonephritis, kidney failure, and hypertension. Also, a longer duration of antibiotic therapy is required in pyelonephritis and is often treated with hospitalization. As in many patient groups, it is important to distinguish between LUTI and UUTI in the emergency department, as these patients are frequently diagnosed in emergency services. Unfortunately, there are no laboratory parameters to distinguish these diagnoses easily. It is obvious that there is a need for simple, fast, non-invasive, and easier methods that will strengthen our hands and speed us up in the emergency department.

Various studies have previously been conducted to differentiate pyelonephritis from cystitis, and in a similar systemic review, the accuracy of the prediction of procalcitonin was found to be heterogeneous (10). In another review, 24 studies investigating CRP, procalcitonin, and erythrocyte sedimentation rate (ESR) in differentiating pyelonephritis and cystitis were examined and these tests were found to be sensitive but not very specific. In the same study, 13 studies with 1638 participants, in which CRP was examined, were analyzed and the summary sensitivity was found to be 0,94 and the summary specificity to be 0,39 (11). The CRP/Albumin ratio for estimating UTI localization has not been previously studied in the adult population. However, CRP/Albumin ratio was studied by Güneş H. et al. in the differentiation of LUTI and UUTI in the pediatric patient population, and it was found that a CAR value above 12,65 was significant with 53% sensitivity and 97% specificity in differentiating UUTI (6). In our study, it was concluded in the ROC analysis that the CAR value was not a usable parameter in the differentiation of UTIs and LUTS. While this was consistent with previous reviews, it was different in the study of Güneş H. et al. (6,10,11). The reasons for this may be related to the different age groups of the study population, as well as the increase in comorbid conditions with age.

It has been reported in previous studies that the CAR value is a good predictor of mortality in critically ill patients admitted to the emergency department, patients diagnosed with malignancy, and sepsis (12,13,14). In the study of Park JE et al., it was found that CRP/albumin ratio values of 34.3 and above were significantly associated with higher 28-day mortality rates (12). Ranzani OT et al. investigated the power of CAR value to predict 90-day mortality in sepsis patients and found that it could predict mortality in patients with 8.7 and above (13). In the meta-analysis of Xu HJ et al. investigating the prognostic value in malignancies, it was concluded

that CAR can be used in the evaluation of the prognosis of human malignancies (14). In our study, it was concluded that the CAR value is not a useful predictor of mortality. This can be explained by the difference in the patient population, the fact that our hospital is in the 3rd level, and therefore the number of patients with high comorbidities is higher.

BAR value calculated using BUN and albumin has been reported to be closely related to mortality and morbidity in previous studies (6,15). However, a study conducted on patients with urinary system infections could not be reached in our scans. It has been estimated that the BUN value, which is one of the parameters of the BAR value, is directly related to the function of the kidneys and therefore will be affected by urinary tract infections. In our study, it was found that the BAR value was not effective in differentiating the upper and lower urinary tracts in urinary tract infections.

BAR value is accepted as an independent and powerful marker for predicting mortality and severity of disease in current studies. In their study, Ugajin et al. stated that it is significant in estimating in-hospital mortality in community-acquired pneumonia and in determining the severity of pneumonia (16). Dundar et al. analyzed patients over 65 years of age who applied to the emergency department and compared BUN, albumin, and eGFR levels with BUN/albumin ratio; He wrote that the risk of hospitalization is higher in patients with increased BAR and that it correlates better with other laboratory parameters studied in the emergency department in determining the severity of the disease. Dundar et al. calculated the OR value for BAR as 2,82 (15). Küçükceran et al., on the other hand, stated that the OR value of BAR in predicting in-hospital mortality in patients with COVID-19 pneumonia in the emergency department is 10,48. In the study, an AUC value of 0,809, sensitivity of 87,5%, specificity of 59,9%, and a cut-off value of 3,9 mg/g were found for BAR (17). In our study, however, no statistically significant relationship was found between BAR value and mortality. This may be due to the fact that our hospital is a 3rd level hospital that accepts the most complex cases in the region. In addition, the small number of our patients may have limited the relationship between mortality and BAR value.

## LIMITATIONS

The most significant limitation of this study is that it is single centered and has a low number of patients. In addition, the presence of very complex cases due to the fact that it was performed in a 3<sup>rd</sup> stage training and research hospital stands out as a limiting factor. In complicated cases such as sepsis and multiple infections, an elevated BAR value may not be attributed to a clear cause.

## CONCLUSION

In our study, it was concluded that CAR and BAR values are not significant parameters that can be used in the differentiation of upper and lower urinary tract infections in urinary tract infection patients admitted to the emergency department. In addition, CAR and BAR values were not associated with mortality in urinary tract infection patients admitted to the emergency department.

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