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The relationship between erectile dysfunction and blood urea nitrogen/creatinine and blood urea nitrogen/albumin ratios: A case-control study

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Introduction Blood urea nitrogen (BUN)/creatinine (Cr) and BUN/albumin ratios are used in the evaluation of many diseases that can be associated with ED. The aim of this study was to examine the relationship between ED and BUN/Cr and BUN/albumin ratios and compare them to healthy peers.

Material and methods Total of 1,664 patients diagnosed with ED between January 2020 and August 2024 were accessed and retrospectively examined. Six hundred and seventy-two male patients with IIEF-5 score below 22 and complaining of ED were included in the study. Ninety-six patients without ED complaints were selected as the control group. Control and ED groups were compared in terms of BUN/Cr and BUN/Albumin ratio values and other biochemical and hormonal parameters.

Results BUN/Cr value was calculated as 27.63 ±12.3 in the ED group and 17.52 ±5.1 in the control group (p <0.001). The AUC value of this ratio was calculated as 0.745 and its sensitivity was found to be 32% and specificity was found to be 98%. BUN/albumin ratio was calculated as 6.03 ±5.8 in the ED group and 3.54 ±1.2 in the control group (p <0.001). The AUC value of this ratio was found to be 0.718, its sensitivity was 43% and its specificity was 98%. The BUN/Cr ratio of all ED subgroups was significantly higher than control group, and BUN/albumin value was significantly higher in mild, moderate and severe groups.

Conclusions In this study, it was calculated that the risk of ED was higher in patients with BUN/Cr ratio >33.92 and BUN/albumin ratio >5.80, and both values had high specificity.

Key Words: albumin ‹› blood urea nitrogene ‹› endothelial dysfunction ‹› erectile dysfunction ‹› creatinine

INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to achieve or maintain a full erection during sexual intercourse [1]. It can be seen in 52% of men between the ages of 40 and 70, and it is estimated that approximately 322 million men will suffer from ED in the near future [2, 3]. ED is accepted as a social-psychological-physiological disorder with a complex and multifactorial etiology. Vasculogenic, psychogenic, anatomical, neurogenic, and hormonal factors play a role in the pathophysiology of ED [4]. Therefore, ED is also seen as an important examination finding. It was reported that the diagnosis of ED was a significant early indicator of the development of cardiovascular diseases and the associated mortality and morbidity rates [5]. Similarly, it was stated that diabetes mellitus, atherosclerosis, hypertension, and ischemic events had common pathophysiological processes with ED [6]. For this reason, diagnosing ED in the early period could not only contribute positively to the sex life of the patient but also provide important insights into his systemic diseases [7]. In the diagnosis of ED, the International Index of Erectile Function – 5 (IIEF-5) is used in current practice to assess sexual

health, determine the severity of ED, and plan follow-ups. It is also difficult to access and implement ED-specific invasive or radiological assessment tests. The purpose of laboratory tests that are routinely performed is to detect potential comorbidities. Thus, there is a need for more specific and easily applicable assessments to support the diagnosis of ED. Blood urea nitrogen (BUN), creatinine (Cr), and albumin concentrations are easy-to-obtain and objective blood test results. The BUN/Cr and BUN/albumin ratios are parameters that are utilized to determine the severity and prognosis of various diseases, calculate mortality rates, and potentially offer information about inflammatory and endothelial functions [8]. For all these reasons, one may expect that they could be parameters that would provide important findings if they were found to be connected to ED. However, in the literature, no data on this issue could be encountered.

The purpose of this study was to compare the BUN/Cr and BUN/albumin ratios between patients diagnosed with ED and their healthy counterparts and identify the applicable cut-off points that can be used in the diagnosis or exclusion of ED.

MATERIAL AND METHODS

This study was carried out at the Urology clinic of Ordu University Research and Training Hospital. The data of a total of 1,664 patients who were diagnosed with ED between January 2020 and August 2024 were reached and retrospectively analyzed. The sample of the study included that data of 672 male patients who presented to our outpatient clinic, scored below 22 on IIEF-5, were 40–70 years old, and had complaints of ED. The control group included the data of 96 patients who did not have complaints of ED or scored above 22 on IIEF-5 but presented to our outpatient clinic for other reasons.

The age, height, weight, and body mass index (BMI) information of the patients was collected and compared. The laboratory tests of the patients were completed between 8 am and 10 am after a period of fasting. In the collected blood samples, fasting blood glucose, creatinine (Cr), blood urea nitrogen (BUN), albumin, total testosterone, C-reactive protein, and erythrocyte sedimentation ratio (ESR) analyses were conducted. The ratio of BUN values to Cr values (BUN/Cr) and the ratio of BUN values to albumin values (BUN/albumin) were calculated.

The International Index of Erectile Function – 5 (IIEF-5) form was used in the study to measure the severity of ED. Score between 5 and 7 were defined as severe, scores of 8–11 were defined as moderate, scores of 12–16 were defined as mild-to-moderate, and scores of 17–21 were defined as mild ED. The sample of the study excluded patients with acute or chronic renal failure, those with complications related to diabetes mellitus such as diabetic ketoacidosis and diabetic polyneuropathy, those with comorbid malignancies, neurological and neurovascular diseases, psychiatric diseases, penile diseases, a history of penile or urological surgery, Peyronie's disease, or chronic liver failure. The stages of case selection are shown in Figure 1.

Statistical analysis

The statistical analyses were conducted using SPSS 21.0 (IBM, Chicago, USA). The parameters with normal distribution are given as mean ±SD (standard deviation), while the parameters with non-normal distribution are given as median ±interquartile range (IQR). Chi-squared homogeneity tests were applied to determine whether the groups were homogeneously distributed. Independent-samples t-tests were conducted to analyze the normally distributed data, while the Mann-Whitney U and Kruskal-Wallis tests were used to analyze the non-normally distributed data. A receiver operating characteristic (ROC) curve analysis was carried out to determine cut-off points for the examined ratios. Area under the (ROC) curve (AUC) values were used to compare ratios. The effect size was measured using Cohen's (2013) criteria. The minimum sample size required for the study for $\alpha = 0.05$ and power = 0.90 in the basic intergroup and intragroup comparisons was determined using the G*Power 3.1 program.

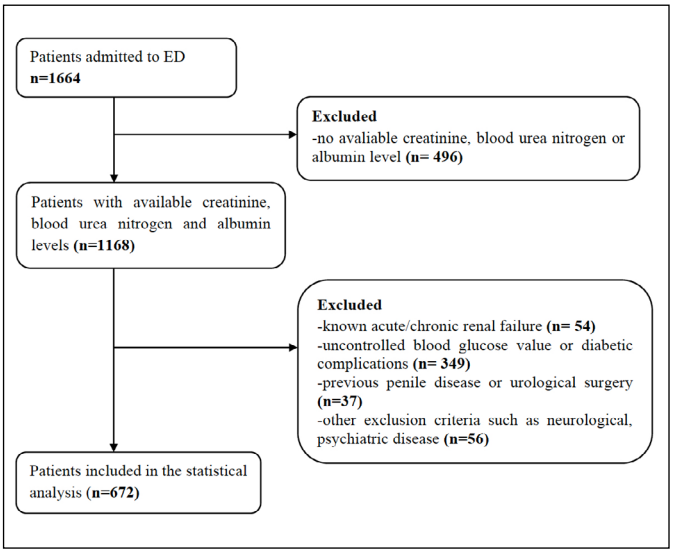


Figure 1. *The study flow chart.*

Bioethical standards

The study was approved by Ordu University Clinical Research Ethics Committee (Decision no: 2024/128).

RESULTS

The sample of the study consisted of 768 male patients, including 672 in the case group (ED group) and 96 in the control group. The data of the groups were analyzed and compared. The mean ages of the patients were 62.8 ±8.9 in the ED group and 53.6 ±10.7 in the control group (p <0.001). The mean BMI values of the patients were 29.41 ±4.16 kg/m^2 in the ED group and 27.84 ±3.65 kg/m^2 in the control group, and the difference between the ED and control groups in terms of their BMI values was not statistically significant (p = 0.098). In the comparisons of the comorbidity rates of the groups, the rate of diabetes mellitus comorbidity was 25% in the ED group and 24% in the control group, and the groups were not significantly different (p = 0.779). There was also no significant difference between the ED and control groups in terms of their dyslipidemia and cardiovascular disease comorbidity rates (p = 0.868, p = 0.054). The rate of hypertension comorbidity, on the other hand, was significantly higher in the ED group than in the control group. The distributions of the demographic characteristics and comorbidities of the patients in the two groups are presented in Table 1.

In the examinations of the biochemical parameters of the patients, the mean serum creatinine values were 0.88 ±0.13 mg/dl in the ED group and 0.91 ±0.11 mg/dl in the control group, and the groups were not significantly different. The mean BUN values of the patients were 23.97 ±10.6 mg/dl in the ED group and 15.8 ±4.41 mg/dl in the control group, and the values in the ED group were significantly higher (p <0.001). The mean albumin values of the patients were 4.44 ±0.5 g/dl in the ED group and 4.46 ±0.2 g/dl in the control group (p = 0.003). No significant difference was observed between the ED and control groups in terms of their fasting blood glucose or total testosterone levels (p = 0.162, p = 0.508). In comparison to the control group, the ED group had significantly higher CRP and ESR values (p <0.001, p = 0.016; Table 2).

The mean BUN/Cr ratios were 27.63 ±12.3 in the ED group and 17.52 ±5.1 in the control group, and the values in the ED group were significantly higher than those in the control group (p <0.001). The mean BUN/albumin ratios were 6.03 ±5.8 in the ED group and 3.54 ±1.2 in the control group, and the values in the ED group were significantly higher than those in the control group (p <0.001). The BUN/Cr and BUN/albumin ratios were evaluated by ROC analysis to determine their power to distinguish the diagnosis of ED and their prognostic performance levels. The optimum cut-off point of the BUN/Cr ratio for the diagnosis of ED was found to be 33.92, and the risk of ED was greater at values higher than this cut-off point. The AUC value for this ratio was calculated as 0.745, with a sensitivity of 32% and a specificity of 98% (Figure 2). The optimum cut-off

Table 1. *Demographic characteristics and comorbid disease of patients and control groups*

Parameter	Control (n = 96)	ED group (n = 672)	p-value[b]
Age [year][a]	53.60 ±10.97	62.08 ±8.92	<0.001**
Weight [kg][a]	81.27 ±11.18	85.45 ±11.96	0.135
Height [cm][a]	170.86 ±5.87	170.57 ±6.35	0.844
BMI [kg/m^2][a]	27.45 ±27.84	29.41 ±4.16	0.098
Comorbidities			
Diabetes mellitus	23 (24%)	168 (25%)	0.779
Hypertension	19 (20%)	228 (34%)	0.008*
Dyslipidemia	12 (%13)	81 (13%)	0.869
Cardiac disease	9 (%9)	94 (14%)	0.054

0.05 * <0.001**
[a] Data are mean ± standard deviation
[b] Mann-Whitney U test.
BMI – body mass index

Table 2. *Relationship between biochemical, and hormonal parameters in ED patient and control groups*

Parameter	Control (mean ±SD)	ED group (mean ±SD)	p-value[a]
Glucose [mg/dl]	112 ±21	113 ±26	0.162
Total testosterone [µg/l]	4.68 ±1.8	4.51 ±1.9	0.508
Creatinine [mg/dl]	0.91 ±0.11	0.88 ±0.13	0.051
BUN [mg/dl]	15.8 ±4.4	23.97 ±10.6	<0.001**
Albumin [g/dl]	4.46 ±0.22	4.44 ±54	0.003*
CRP [mg/dl]	0.38 ±0.4	3.23 ±4	<0.001**
Sedimentation [mm/h]	15.8 ±12.3	22.1 ±18	0.016*
BUN/Creatinine	17.52 ±5.1	27.63 ±12.3	<0.001**
BUN/Albumin	3.54 ±1.2	6.03 ±5.8	<0.001**

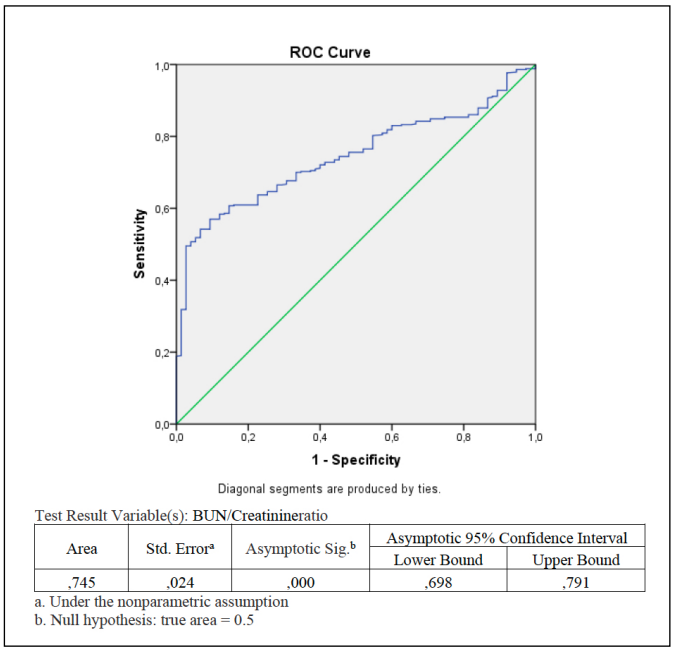
*0.05
** <0.001
[a] Mann-Whitney U test
BUN – blood urea nitrogen; CRP – C-reactive protein

point of the BUN/albumin ratio for the diagnosis of ED was found to be >5.80. The AUC value for this ratio was calculated as 0.718, with a sensitivity of 43% and a specificity of 98% (Figure 3).

DISCUSSION

In this study, BUN/Cr and BUN/albumin ratios were compared between patients diagnosed with ED and those in the control group. In comparison to the control group, both ratios were significantly higher in the ED group, and it was seen that these ratios could be significant parameters to support the diagnosis of ED ($p < 0.001$). In terms of their capacity to identify health and affected individuals, the BUN/Cr ratio (AUC = 0.745) was determined to be more successful than the BUN/albumin ratio (AUC = 0.718).

ED is among the most frequently encountered sexual dysfunctions and significantly affects the quality of life of those who are affected. The prevalence of ED increases with age, and while it affects 25.3% of men at the ages of 45–54, this rate rises to 52.2% in those over the age of 75 [9]. As vascular, hormonal, neurological, and psychological factors are seen in the development of ED, it is known that ED has common pathophysiological pathways with diseases such as diabetes mellitus, atherosclerosis, ischemic heart diseases, and hypertension [10]. Thus, the objective of the diagnosis of ED is not only to contribute positively to the sex life of the patient but also to obtain important information about his general health status. It was determined that approximately 57% of patients diagnosed with ED also had the aforementioned conditions [11]. The relative risk of cardiovascular disease development in patients diagnosed with ED was 1.47 [12]. Additionally, in studies screening oncology patients in terms of the diagnosis of ED, ED complaints were seen in more than 40% of patients [13]. Hence, ED is an important health problem because of its negative effects on physical and mental health, the decrease it causes in the quality of life of both patients and their partners, and the comorbidities it can be accompanied by [14]. Serum creatinine, BUN, and albumin values are low-cost and reliable parameters that can be easily obtained in daily practice. Serum creatinine levels can provide information about the factors that can potentially affect the mechanisms of erection such as age, race, muscle mass, and diet, as well as associated conditions [15]. While BUN is usually used along with creatinine, it is, in fact, an important parameter that is independent of creatinine. In particular, it provides important information about clinical parameters and conditions such as renal perfusion, cardiac output, endothelial dysfunction, dehydration, neurohumoral effects, and elevated sympathetic nervous system activity. In previous studies, elevated BUN levels were reported to be associated with vascular pathologies such as myocardial infarction, pneumonia, pulmonary embolism, and thrombosis, and it was an independent predictor of mortality and morbidity not connected to creatinine in criti-

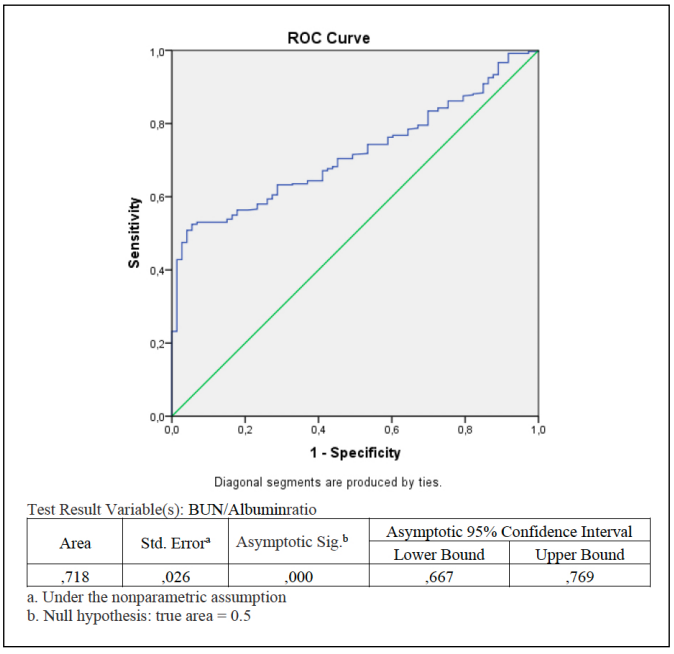


Test Result Variable(s): BUN/Creatinineratio

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,745	,024	,000	,698	,791

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

Figure 2. *BUN/creatinine ratio ROC curve.*



Test Result Variable(s): BUN/Albuminratio

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,718	,026	,000	,667	,769

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

Figure 3. *BUN/albumin ratio ROC curve.*

cal patients [16]. Albumin is a negative acute phase reactant that decreases in the presence of systemic inflammation. It is a mediator which shows both anti-inflammatory and antithrombotic effects with a negative impact on platelet activation and aggregation. It has important activities that protect the patient from ischemic events by preventing microthrombi and endothelial dysfunction. A reduction in albumin levels in the serum results in systemic hypoperfusion and a decrease in circulatory volume by lowering the plasma oncotic pressure [17, 18]. It acts as an antioxidant mechanism by scavenging free oxygen radicals in the serum at rates close to 70% [19]. Considering all these effects, serum creatinine, BUN, and albumin levels would be expected to provide valuable information in patients diagnosed with ED. In our study, it was determined that the BUN and albumin levels of the ED and control groups were significantly different from each other, while the difference between the creatinine levels of the two groups was not statistically significant. In the examinations of their mean values, it was concluded that the results did not demonstrate a substantial difference between the two groups, and they would be similar in daily practice. Hung et al. emphasized that using the ratios of these parameters to each other, rather than using them as single parameters, showed more effective results in the prediction of severity and prognosis [20]. In other studies, the BUN/Cr ratio has been used to identify dehydration, inflammatory conditions, diabetes and associated organ damage, cardiac output, conditions affecting hemodynamics, and cardiovascular diseases, as well as the associated prognosis, mortality, and morbidity rates [21, 22]. For these reasons that are common among such studies, it was thought that this ratio could be an important ratio in the diagnosis of ED. In our study, the BUN/Cr ratios in the ED group were found to be significantly higher than those in the control group ($p < 0.001$). The cut-off BUN/Cr value distinguishing the ED group from the control group was calculated as 33.92, and the sensitivity and specificity rates of this value were 32% and 98%, respectively. In the literature, the BUN/albumin ratio has been used in the context of inflammation, nutritional balance, oxidant-antioxidant balance, and endothelial events such as cardiac performance and predisposition to microthrombi [23, 24]. In this study, the BUN/albumin ratios in the ED group were significantly greater than those in the control group ($p < 0.001$). The cut-off BUN/albumin value distinguishing the ED group from the control group was calculated as 5.80, and the sensitivity and specificity rates of this value were 43% and 98%, respectively. We believe that important results were obtained in our study in terms of using these two ratios to distinguish ED cases from control patients.

In the comparisons made in this study after dividing the patients into subgroups based on their IIEF-5 scores, it was seen that 20% of the patients had mild ED, 33% had mild-to-moderate ED, 20% had moderate ED, and 27% had severe ED. The BUN/Cr and BUN/albumin ratios of these subgroups were not found to be significantly different from each other ($p = 0.855$, $p = 0.139$; Table 3). The BUN/Cr values in all ED subgroups were significantly greater than the BUN/Cr values in the control group (mild [$p < 0.001$], mild-moderate [$p = 0.001$], moderate [$p < 0.001$], and severe [$p = 0.002$]; Table 4). The BUN/Albumin values were significantly greater in the mild, moderate, and severe ED subgroups than in the control group ($p = 0.006$, $p = 0.001$, $p < 0.001$). On the other hand, while the mean value of the mild-to-moderate ED subgroup was greater than the mean value of the control group, this difference was not statistically significant ($p = 0.065$; Table 4). According to our results, we believe that both ratios can be beneficial in supporting the diagnosis of ED and distinguishing patients diagnosed with ED from those with no ED-related complaints, and they can contribute to the literature.

The limitations of this study include its single-center design, the retrospective analysis of the data,

Table 3. *Comparison of ED patient's subgroups*

Parameter	Mild (n = 132) (20%)	Mild-moderate (n = 220) (33%)	Moderate (n = 136) (20%)	Severe (n = 184) (27%)	p-value[a]
BUN/creatinine	26.29 ±10.6	24.59 ±11.4	26.01 ±10.1	26.71 ±14.9	0.855
BUN/albumin	4.93 ±2.13	4.61 ±2.43	5.1 ±2.17	5.97 ±3.21	0.139

* 0.05
** <0.001
[a] Kruskal Wallis test
BUN – blood urea nitrogen

Table 4. *Comparison of subgroups of ED patients with the control group*

	Groups	Ort+-sd	p-value[a]
BUN/creatinine	Mild (n = 132)	26.29 ±10.6	<0.001**
	Control (n = 96)	17.52 ±5.1	
	Mild-moderate (n = 220)	24.59 ±11.4	0.001*
	Control (n = 96)	17.52 ±5.1	
	Moderate (n = 136)	26.01 ±10.1	<0.001**
	Control (n = 96)	17.52 ±5.1	
	Severe (n = 184)	26.71 ±14.9	0.002*
	Control (n = 96)	17.52 ±5.1	
BUN/albumin	Mild (n = 132)	4.93 ±2.13	0.006*
	Control (n = 96)	3.54 ±1.2	
	Mild-moderate (n = 220)	4.61 ±2.43	0.065
	Control (n = 96)	3.54 ±1.2	
	Moderate (n = 136)	5.1 ±2.17	0.001*
	Control (n = 96)	3.54 ±1.2	
	Severe (n = 184)	5.97 ±3.21	<0.001**
	Control (n = 96)	3.54 ±1.2	

*0.05
** <0.001**
[a] Mann-Whitney U test
BUN – blood urea nitrogen

and our inability to conduct penile Doppler ultrasound scans because the procedure is invasive and has potential ethical problems.

CONCLUSIONS

In this study, it was determined that patients with BUN/Cr ratios of >33.92 and BUN/albumin ratios of >5.80 were at a higher risk of ED. Both these values had high rates of specificity. As these are parameters that are easily applicable and reliable in routine practice, they can have an important place in the diagnosis of ED. Hence, we believe that this study can guide further studies on the subject. There is a need for comprehensive, large-scale, and multi-center studies on this issue.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

This research received no external funding.

ETHICS APPROVAL STATEMENT

The study was approved by Ordu University Clinical Research Ethics Committee (Decision no: 2024/128).

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