Assessment of the Prognostic Effect of Blood Urea Nitrogen to Serum Albumin Ratio in Patients with Fournier's Gangrene in a Referral Center

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Purpose: To assess the prognostic effect of blood urea nitrogen to serum albumin ratio in patients with Fournier's gangrene (FG) in a referral center.

Materials and Methods: Patients with FG were admitted and enrolled consecutively in this study from March 2008 to April 2020. Statistical analysis was done to evaluate the differences between the two groups and to identify the best cutoff value to predict mortality and the need for intensive care.

Results: Of all 114 patients, 46 patients (40.35%) died in the course of hospitalization and 40 entered the study. No variable manifested a notable difference except for the BUN to albumin ratio, which was significantly different (*P*-value = 0.045). The ratio of BUN to albumin was not associated with any other variables and was independently a predictor of death in FG patients.

Conclusion: The ratio of BUN to albumin was significantly different among deceased and survived patients with FG. Therefore, more studies with a larger sample size are still needed to access this parameter properly.

Keywords: blood urea nitrogen; Fournier's gangrene; intensive care unit; mortality; prognosis

INTRODUCTION

Fournier's gangrene disease (FG), caused by a combination of aerobic and anaerobic organisms, is a life-threatening disease in which perineal and scrotal infections, followed by proliferation in the fascia, lead to soft tissue necrosis. The mortality risk is usually 20 to 40 %, but in some studies, it has been reported even at 88 %[(1)].

FG mainly affects men through the third and sixth decade of their life though it may occur in all age groups, even women and infants[(2)]. The average age of involvement is 50.9 years, and the disease ratio in men to women is 10 to 1[(3)]. The mortality rate is higher in patients with delayed hospitalization, patients with diabetes mellitus, and those initially presented with sepsis[(4)].

Risk factors for FG include diabetes, alcoholism, medications, immunodeficiency, malignancies, kidney failure, and liver failure[(5)]. Female gender is also a risk factor for death in patients with FG, which is due to the increased prevalence of inflammation in the retroperitoneal space and the abdominal cavity on account of anatomical causes[(6)].

The optimal outcome of FG treatment is based on rapid diagnosis, debridement of all necrotic tissues, and extensive antimicrobial experimental treatment, usually combined with antibiotics affecting aerobic and anaerobic bacteria. Prevention of uroseptic shock is mandatory with the treatment of local infections[(7)].

The prognostic role of the ratio of blood urea nitrogen (BUN) to albumin in diseases such as hospital-acquired pneumonia and community-acquired pneumonia and non-small lung cancer has been proven. In this way, with increasing the ratio of BUN to albumin, the risk of mortality and the need for ICU, and the length of hospital stay will increase as well[(8-11)]. Given that no study has been performed on patients with FG, the current study could play a potentially beneficial role in reducing the mortality of FG patients.

MATERIALS AND METHODS

Patients with FG were consecutively admitted and enrolled to Shohada-e-Tajrish Hospital (Tehran, Iran) from March 2008 to April 2020 in the study. The Ethics Committee of the hospital permitted us to review the patients' medical data. The patients' health records were de-identified. The research terms included Fournier's gangrene (FG), soft tissue infection, and necrotizing fasciitis.

Patients' gender, age, comorbidities (diabetes mellitus, cerebrovascular accidents, malignancies, urinary incontinence, and so on), laboratory data, duration of hospital stay, and final disease outcomes were included in

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Table 1. Baseline characteristics of enrolled patients

	Minimum	Maximum	Mean	Std. Deviation
Age	25	87	62.58	14.360
Days of admission	3	62	16.95	12.140
Hemoglobin	7.1	15.6	10.6	2.07
Platelet (×1000)	28	461	216.6	107.3
White blood cells (×1000)	0.32	57	17.2	11.6
Albumin1	.50	4.07	2.57	0.56
BUN	8	110	42.8	25.8
Estimated sedimentation rate	2	92	43.5	26.3
C-reactive protein	4	181	70.25	46.3
AST	6	75	31.37	17.45
ALT	4	146	24.74	27.12
Alkaline phosphatase	90	2364	338.96	455.41
BUN to albumin ratio	2.86	51.49	17.16	10.34

BUN:Blood Urea Nitrogen; AST:Aspartate Aminotransferase; ALT:Alanine aminotransferase

the medical data. Disease diagnosis was based on the symptoms of pain, erythema, ulcers, swelling, crepitus, necrosis, purulent discharge, and later confirmations with the tissue inspection in the operating room. Patients were excluded from the study if they had been hospitalized 90 days prior to the study. They were also excluded if they were chronically immunosuppressed (such as chemotherapy, human immunodeficiency virus infection, therapy with more than 20 mg prednisone or equivalent, and other immunosuppressive therapies) or if they had advanced liver disease or end-stage renal disease.

The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.SRC.REC.1399.005), and informed consent was obtained from all patients according to the hospital's guidelines. Some patients had missing data, so they were excluded. As mentioned, among 114 patients, 40 patients were enrolled in the study.

Results were expressed as mean ± SD frequency and confidence interval (CI). The normality of data was determined with the Shapiro-Wilk test. The nonparametric Mann-Whitney U test was applied for continuous variables and the Chi-Square test for categorical variables. Variables significantly associated with mortal¬ity or need for intensive care at the 0.20 level in univariate analysis were considered in a multivariate backward analysis. Analysis of a receiver-operating characteristic (ROC) curve was performed to identify the best cut-off value to predict mortality and the need for intensive care. A probability value less than 0.05 was considered to be statistically significant.

RESULTS

During the study period, a total of 114 FG patients were admitted; of these, 40 patients entered the study and 74 patients were excluded. The average age of the patients was 62.58 ± 14.36 years, and the mean value of hospitalization days was 16.95 ± 12.14. Among 114 patients, 46 (40.35%) died in the course of hospitalization. Patient charac¬teristics are shown in **Table** 1.

The subjects were divided into two groups (deceased and surviving), and the variables were studied in both. None of the variables showed a significant difference, except for the ratio of BUN to albumin. The comparison of variables in the two groups is given in **Table 2**.

According to the data, the ratio of BUN to albumin was not correlated with any of the other variables and was independently a predictor of death in FG patients. ROC curve was used to determine the optimal cut-off value of the BUN to albumin ratio.

The value of 12.71 was determined with 79% sensitivity and 62% specificity. The ROC curve for predicting mortality by the BUN to albumin ratio is depicted in Figure 1.

[The Odds Ratio is 6.13 (1.17 – 32.10) and the Relative Risk is 2.86 (1.08 – 7.58); AUC = 0.690 (0.522 – 0.858) (*P*-Value = 0.040)]

No significant relationship was observed between the ratio of BUN to albumin and the number of hospitalization days (P = 0.48) by the Spearman Correlation test. Although patients who needed hospitalization in the ICU had a higher BUN to albumin ratio (18.90 ± 11.04

Table 2. Comparison of characteristics between deceased and surviving patients

	Deceased (n = 20)	Surviving (n = 20)	*P* value
Age	66.45 ± 10.097	58.70 ± 17.02	0.88
Days of admission	18.45 ± 14.136	15.45 ± 9.897	0.44
Hemoglobin	10.12 ± 2.209	11.2 ± 1.836	0.1
Platelet (×1000)	206.1 ± 108.1	226.5 ± 108.3	0.55
White blood cells (×1000)	16.9 ± 13.5	17.5 ± 9.6	0.87
Estimated sedimentation rate	42.8 ± 29.2	44.3 ± 24.9	0.91
C-reactive protein	75.7 ± 54.3	64.7 ± 39.7	0.65
AST	35.3 ± 17.9	26.5 ± 16.3	0.2
ALT	30.2 ± 33.9	17.9 ± 13.5	0.25
Alkaline phosphatase	382 ± 577.4	288.7 ± 268.8	0.61
BUN to albumin ratio	20.4 ± 10.5	13.9 ± 9.3	0.045

BUN, Blood Urea Nitrogen; AST, Aspartate Aminotransferase; ALT, Alanine aminotransferase

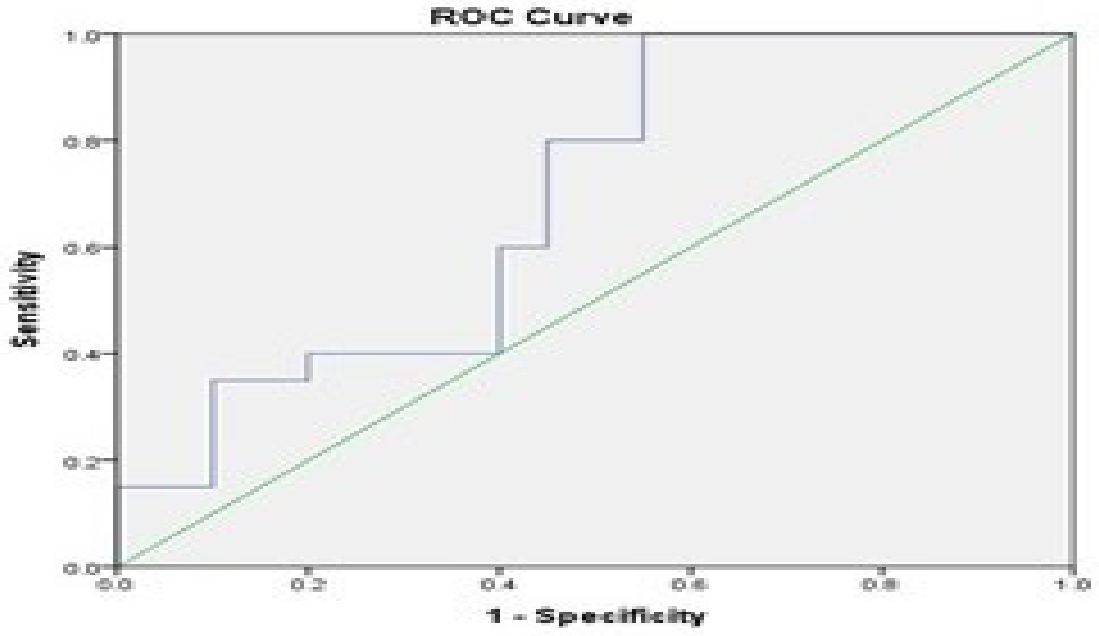

Figure 1. Analysis of ROC curve for predicting mortality

vs. 15.23 ± 9.42), this difference was not significant (*P* = 0.26).

DISCUSSION

FG is an uncommon disease; 110 cases of FG or necrotizing fasciitis admitted to our hospital for 10 years were reviewed, and finally, 40 patients were enrolled in the current study. Due to its progressive nature, the disease mortality rate remains high (43–53%) despite intensive care treatment and advances in medical therapy[8,9]. The overall mortality rate in the present study was 40.35% (46 of 114 patients). The mean age of survivors was 58.70 ± 17 years old, and deceased patients had a mean age of 66.45 ± 10 years old which was not statistically significant. Some studies showed similar findings[4,12,13], whilst others showed contradictory results[2,7,8,14].

Many factors have been reported that predispose patients to the development of FG, with diabetes mellitus (DM), chronic renal failure (CRF), and malignancy as the main ones. For example, Tuncel et al.[13] found an association between DM and poor prognosis; however, Corcoran et al. reported no similar relationship in their study[15]. In the present study, 24 (60%) patients had a positive past medical history of DM, which was not significant between survivors and deceased patients.

No consensus is available on clinical variables for predicting poor outcomes in FG[13]. FGSI was developed to facilitate the prediction of the outcomes in FG patients. Laor et al. found an FGSI score of > 9 that consisted of 75% death probability, while a score of ≤ 9 was associated with 78% survival probability[16]. This threshold for predicting mortality in patients has been confirmed in other studies[3,11].

Recent studies have evaluated the ratio of BUN to albumin in predicting the prognosis of diseases. Feng et al.[8] studied its role on hospital-acquired pneumonia, while in three studies[9-11], community-acquired pneumonia was the main disease to be evaluated. Moreover, Kos[17] and Gundpatil[18] assessed the BUN/albumin on non-small lung cancer and non-chronic kidney diseases, respectively. In this way, the risk of mortality, the need for ICU admission, and the length of hospital stay will increase with increasing the BUN to albumin ratio. In the current study, the ratio of BUN to albumin was significantly higher among deceased patients in comparison to the survived ones. Despite the variations seen in the need for ICU admission and the length of hospital stay, the differences were not significant.

There are several indexes used for Fournier gangrene prognosis like Fournier's Gangrene Severity Index (FGSI), Uludag Fournier Gangrene Severity Index (UFGSI), Age-Adjusted Charlson Comorbidity Index (ACCI), Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score, the Combined Urology and Plastics Index (CUPI) and neutrophil–lymphocyte ratio (NLR) and surgical APGAR (sAPGAR). According to the studies, the UFGSI does not seem to be more powerful than FGSI. In daily routine, we suggest applying ACCI because it is more easily calculated, generally applicable, and well-validated. UFGSI has the most sensitivity rate (85%) and sAPGAR has the lowest sensitivity rate (55%). However, sAPGAR has the most specificity rate (91%) and UFGSI has the lowest specificity rate (67%).[19] In prediction for skin reconstruction in FG patients, FGSI, UFGSI, and NLR are more reliable.[20] Overall, UFGSI is the most common index for assessing FG patients. According to our results, the sensitivity of BUN/Alb is not as high as UFGSI, but it is acceptable and very useful due to the simplicity of performing tests.

According to the findings, the ratio of BUN to albumin was significantly different among the deceased and survived patients with FG. Further studies with a larger sample size are recommended to properly assess this parameter.

CONCLUSIONS

The ratio of BUN to albumin was significantly different among deceased and survived patients with FG. Therefore, more studies with a larger sample size are needed to access this parameter properly.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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