



Does Serum Bilirubin Level Provide Information about Mortality in the Emergency Clinic?

Serum Bilirubin Düzeyi Acil Serviste Mortalite Hakkında Bilgi Sağlar Mı?

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Abstract

Aim: As the elderly population grows, so does the number of geriatric patients admitted to emergency departments. This highlights the need for new, accessible markers to assess mortality. This study investigates serum bilirubin as a potential marker.

Material and Method: This retrospective study included 240 patients over 65 years old who presented to a university hospital emergency department over 3 months. Patients with trauma, liver or biliary tract diseases, or using hepatotoxic drugs were excluded.

Results: Of the patients, 178 survived and 62 died within 30 days. Significant differences were observed between the two groups in direct bilirubin, age, albumin, lactate, BUN, and creatinine levels ($p<0.05$). Logistic regression analysis showed BUN and lactate as independent predictors of mortality.

Conclusion: Bilirubin levels, in addition to established markers like BUN and lactate, may be helpful in evaluating mortality risk in geriatric patients presenting to emergency departments.

Keywords: Direct bilirubin, creatinine, emergency department, geriatrics, mortality

Öz

Amaç: Yaşlı nüfusun artmasıyla birlikte acil servislere başvuran geriatric hasta sayısı da artmaktadır. Bu durum, mortaliteyi değerlendirmede kullanılabilecek yeni ve erişilebilir belirteçlere olan ihtiyacı ortaya koymaktadır. Bu çalışmada serum bilirubinün potansiyel bir belirteç olarak değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Bu retrospektif çalışmaya, üç aylık süre içerisinde bir üniversite hastanesinin acil servisine başvuran 65 yaş ve üzeri 240 hasta dahil edilmiştir. Travma öyküsü olanlar, karaciğer veya safra yolu hastalığı bulunanlar ya da hepatotoksik ilaç kullanan hastalar çalışma dışı bırakılmıştır.

Bulgular: Hastaların 178'i sağ kalmış, 62'si ise 30 gün içinde hayatını kaybetmiştir. Sağ kalanlar ile kaybedilen hastalar arasında direkt bilirubin, yaş, albümin, laktat, kan üre nitrojeni (BUN) ve kreatinin düzeyleri açısından anlamlı farklılık saptanmıştır ($p<0,05$). Lojistik regresyon analizinde BUN ve laktat mortalitenin bağımsız belirleyicileri olarak bulunmuştur.

Sonuç: BUN ve laktat gibi yerleşik belirteçlere ek olarak, bilirubin düzeyleri de acil servise başvuran geriatric hastalarda mortalite riskinin değerlendirilmesinde yararlı olabilir.

Anahtar Kelimeler: Direkt bilirubin, kreatinin, acil servis, geriatri, mortalite



INTRODUCTION

Aging is an irreversible condition in which people undergo various biological, physiological, social and psychological changes throughout their lives. The last period of this process is defined as old age. The World Health Organization considers the end of 64 years and the beginning of 65 years as the limit of old age.^[1] Geriatric individuals make up about 8.5% of the world's population and this is expected to increase to about 17% by 2050.^[2] With the increase in the geriatric population in the world, the number of geriatric patients applying for health services is also increasing. Therefore, the care and comprehensive assessment of these patients becomes important. Thus, new and easily accessible markers are needed to assess the mortality of geriatric patients admitted to the emergency department. We think that one of these parameters is serum bilirubin levels. Bilirubin is a major tetrapyrrole, bile pigment and heme catabolite and a biomarker associated with disease resistance and several biological functions.^[3] Biliverdin is formed by the metabolism of Heme, the prosthetic group of hemoglobin, myoglobin and cytochromes. Bilirubin is also produced by the breakdown of biliverdin by biliverdin reductase, a cytosolic enzyme. However, studies have shown that high bilirubin concentrations can cause inflammation, apoptosis and oxidative stress and reduce cell survival.^[4] In the literature, it is seen that when bilirubin reaches high concentrations, it actively participates in the disease process and may induce cell lysis of erythrocytes.^[5] Therefore, total bilirubin, especially UCB, plays a major medical and economic role as a biomarker in the risk assessment of cardiovascular disease, stroke, cancer and all-cause mortality. Because the prevalence of these diseases is increasing very rapidly worldwide.^[3] In the literature, there are studies showing that bilirubin increase predicts mortality. For instance, a study reported that higher serum total values within physiologic limits were significantly associated with mortality regardless of the cause.^[6] Despite all this information, it is not known whether mortality can be predicted by bilirubin levels in geriatric patients. In this study, we aimed to investigate the effect of bilirubin levels at admission on 30-day mortality in geriatric patients admitted to the emergency department.

MATERIAL AND METHOD

Study Design

This retrospective study included 240 patients aged ≥ 65 years admitted to the Emergency Department of Erzurum City Hospital, a tertiary university hospital with a daily admission of approximately 1000 patients, in January, February and March 2023. The local ethics committee approved the study (The protocol number assigned by the ethics committee is 2023/05-56 and the date of approval by the ethics committee is 13.09.2023), which was conducted in accordance with the WMA Declaration of Helsinki, 1964, and later revisions. Patients under 65 years of age, trauma patients, patients

with cirrhosis, known liver and biliary tract diseases, patients taking hepatotoxic drugs and patients with incomplete data collection forms were excluded (**Figure 1**).

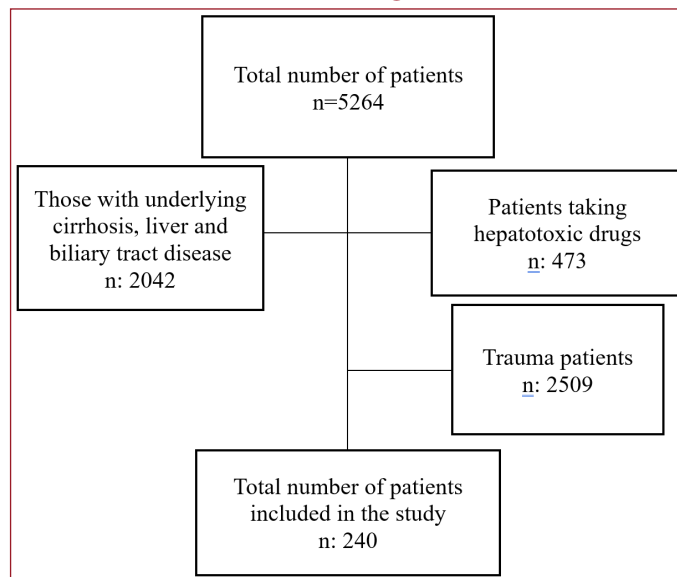


Figure 1. Number of Patients and Flow Chart

Data Collection Form

A data collection form was created for the study. Age, gender, comorbid diseases, and the complaint at presentation to the emergency department were added to this form. Vital signs such as blood pressure, pulse rate, saturation, respiratory rate and temperature were also included in the form. The laboratory reference ranges of our hospital were 0-1.2 mg/dl for total bilirubin, 0-0.3 mg/dl for direct bilirubin, and 0-1.1 mg/dl for indirect bilirubin. Bilirubin levels studied with the Atellica IM 1300 Analyzer device in the biochemistry laboratory of our hospital were retrospectively scanned from the Hospital Information Management System (HIMS) and added to the data collection form. The dates of death of the patients included in the study were obtained from HIMS and added to the data collection form.

Statistical Analysis

The SPSS 22.0 package program was used for statistical data analyses. Descriptive statistics were used for normally distributed variables of continuous variables as mean \pm standard deviation, while numerical parameters without normal distribution were shown with median (minimum-maximum). Categorical variables were represented by numbers and percentages. Continuous numerical variables were checked by the Kolmogorov-Smirnov Test to determine the normality of distribution. In the comparison of the two groups, those with normal distribution were performed with the T-test, and those with abnormal distribution were performed with the Mann Whitney U test. In comparison of categorical variables, Fisher's exact test and Chi-square test were used according to their suitability. Multivariate analysis was performed to determine the determinants of parameters associated with death. $p < 0.05$ was considered significant in all analyses.

RESULTS

Of the 240 geriatric patients aged ≥ 65 years, 111 (46.25%) were male and 129 (53.75%) were female. When the follow-up files of the patients were analyzed, 178 survived and 62 of them died. In addition, demographic data of the patients are presented in **Table 1** in detail.

In addition, another finding of the study was that BUN levels were much higher in the mortality group (42 mg/dL in the non-mortality group and 23 mg/dL in the mortality group) and there was a highly significant P value (<0.001). When two groups of living and deceased patients were compared, the mean creatinine value was found to be 1.06 mg/dl in the living group and 1.2 mg/dl in the deceased group, and it was found that the increase in creatinine was statistically significant in indicating mortality ($p: 0.005$). In another finding of our study, serum albumin levels were found to be 37.9 ± 4.930 in the mortality group and 40.5 ± 5.474 in the living group, and were significantly lower in the mortality group ($P < 0.001$) (**Table 1**).

Table 1. Biochemical And Demographic Data

Variables	Non-mortality group (n: 178)	Mortality group (n: 62)	P
Age (year)	76.2 \pm 7.18	78.2 \pm 8.62	0.039
Gender			
Male	83	28	0.883
Female	95	34	
Blood Parameters			
BUN, mg/dL	23 (7-117)	42 (15-150)	<0.001
Creatinine, mg/dL	1.06 (0.37-6.90)	1.2 (0.30-4.48)	0.005
Sodium, mEq/L	138 (127-159)	137 (125-163)	0.662
CK, U/L	79 (15-629)	65 (15-450)	0.501
Fibrinogen, mg	439.1 \pm 157.950	461.4 \pm 153.071	0.398
GFR (ml/minute)	63.2 \pm 27.4	52.4 \pm 29.9	0.010
ALT, U/L	20 (9-85)	24 (9-263)	0.179
AST, U/L	29 (11-288)	29 (11-186)	0.480
INR	1.15 (0.92-4.51)	1.24 (0.95-6.37)	0.067
D-Dimer, μ g/mL	1335 (110-6050)	1352 (370-35200)	0.211
Potassium, mmol	4.39 \pm 0.618	4.27 \pm 0.853	0.250
Calcium, mg/dL	9.01 \pm 0.739	8.99 \pm 0.727	0.874
Magnesium, mg/dL	1.79 \pm 0.376	1.88 \pm 0.442	0.104
Albumin, g/dl	40.5 \pm 5.474	37.9 \pm 4.930	<0.001

BUN, blood urea nitrogen; GFR, glomerular filtration rate; CK, creatine kinase; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase

In the study, the mean value of direct bilirubin was found to be 0.5 mg/dl in the deceased group and 0.3 mg/dl in the living group and it was found that the increase in direct bilirubin was statistically significant in showing mortality in geriatric patients ($p: 0.030$). In another finding in the study, lactate value was found to be 2.24 ± 0.983 in the living group and 2.63 ± 1.260 in the deceased group and it was found that lactate increase was significant in showing mortality in geriatric patients ($p: 0.019$) (**Table 2**).

Table 2. Bilirubin And Blood Gas Data

Variables	Non-mortality group (n:178)	Mortality group (n: 62)	P
HCO ₃ ,mEq/L	22.4 \pm 0.983	21.5 \pm 4.15	0.079
Total bilirubin, mg/dl	0.92 \pm 0.543	0.97 \pm 0.672	0.575
Indirect bilirubin, mg/dl	0.59 \pm 0.334	0.54 \pm 0.344	0.353
Direct bilirubin, mg/dl	0.30 (0.1-1.6)	0.5 (0.1-2.3)	0.030
pH	7.36 (7.02-7.54)	7.37 (6.80-7.52)	0.781
Lactate, mmol/L	2.24 \pm 0.983	2.63 \pm 1.260	0.019

Table 3. Multivariate Logistic Regression Analysis

	P	EXP(B)	95%CI
BUN, mg/dL	0.001	1.043	(1.018-1.069)
Creatinine, mg/dL	0.269	0.669	(0.328-1.365)
Direct Bilirubin, mg/dL	0.127	0.515	(0.220-1.207)
HCO ₃ , mEq/L	0.056	1.153	(0.997-1.333)
Lactate, mmol/L	0.038	1.598	(1.025-2.489)

The parameters with <0.5 were included in the table

DISCUSSION

According to the main finding of this study, the mean value of direct bilirubin was higher in the deceased group than in the living group and it was determined that the increase in direct bilirubin was significant in indicating mortality in geriatric patients. In the literature, there are few studies examining the relationship between direct bilirubin and mortality, but there is no study showing that direct bilirubin indicates mortality in geriatric patients. Studies have mostly examined the relationship between total bilirubin and mortality. However, in our study, no significant correlation was found between total bilirubin and mortality, whereas direct bilirubin was found to predict mortality significantly in geriatric patients. In a study of older adults, cardiovascular diseases (CVD) were found to be the most common cause of elevated total bilirubin, excluding liver and biliary tract pathologies. In the same study, total bilirubin levels of ≥ 0.8 mg/dl were reported to indicate CVD-related mortality.^[7] The effects of bilirubin on mortality have been found in various epidemiologic studies. In 2001, a retrospective study in Belgium investigated bilirubin levels in more than 11,000 men and women and found a significant negative association between bilirubin levels and all-cause and cancer-related mortality in men.^[8] In another study, high serum bilirubin levels were found to be associated with a high mortality rate in patients with jaundice.^[9] In addition, in another study conducted on patients receiving peritoneal dialysis, it was reported that total bilirubin level was significant in indicating all-cause mortality.^[10] Franchini et al. reported that in some cases high bilirubin levels can have toxic effects, so direct bilirubin is more of a toxic waste than a potential antioxidant. Furthermore, another study conducted on middle-aged and elderly Chinese found that direct bilirubin was independently related to coronary heart disease risk and associated mortality.^[11] In another study, it was reported that total bilirubin level was associated with

mortality in patients receiving hemodialysis for a long time, but further studies are needed to investigate the effect of unconjugated or conjugated bilirubin on mortality.^[12] In a study of patients with acute coronary syndrome (ACS), elevated direct bilirubin levels were found to be an independent predictor of mortality in patients followed for an average of 6.5 years.^[13] In another study, it was reported that high direct bilirubin levels were significantly associated with all-cause mortality in patients with heart failure.^[14] Another study in patients with idiopathic pulmonary arterial hypertension (IPAH) found that direct bilirubin increase was an independent risk factor for mortality in IPAH.^[15] Another study found that direct bilirubin levels were associated with an increased risk of MACE in ACS.^[16]

According to the findings obtained in the study, the mean BUN value was higher in the deceased group compared to the living group and it was determined that BUN increase significantly predicted mortality in geriatric patients regardless of the cause. A study in the literature found that high BUN levels were a predictor of in-hospital mortality in geriatric patients admitted to the emergency department, similar to our study.^[17] In another study conducted by Pan et al. high BUN level was found to be an independent predictor of mortality in geriatric patients admitted to the emergency department and hospitalized in the intensive care unit.^[18] It has been shown that the result we found in our study is similar to the literature.

According to another finding in this study, the mean creatinine value in the deceased group was higher than the mean creatinine value in the living group, and it was determined that creatinine increase significantly predicted mortality in geriatric patients. When the studies carried out are examined, it is seen that similar results are found with our study. When we examined the literature, in one study, creatinine value was found to be higher in patients who were hospitalized in the intensive care unit and then died.^[19] Similar to our study, in another study, in geriatric patients hospitalized in the intensive care unit, creatinine values were found to be significantly higher in the deceased group.

In another finding in this study, GFR was found to be lower in the deceased group compared to the living group and low GFR was significantly predictive of mortality in geriatric patients. When we look at the literature, it has been shown in a study similar to our study that low eGFR is associated with in-hospital mortality in geriatric patients admitted to the emergency department.^[20]

In the study, it was detected that the mean albumin value was lower in the deceased group compared to the living group and it was determined that low albumin significantly predicted mortality in geriatric patients. Malnutrition is a major health problem among older people. Serum albumin levels are an important parameter used to assess nutrition in older adults. In addition, albumin is a negative

acute phase reactant and its level decreases secondary to inflammation in the presence of critical illness.^[21] In another study, low albumin levels were observed to be an important risk factor in geriatric elderly patients in nursing homes.^[22] In another study, it was reported that albumin levels below 3.5 g/dL traditionally indicate hypoalbuminemia and are associated with mortality.^[23]

In another finding we obtained in the study, lactate value was found to be lower in the living group than in the deceased group, and lactate increase was found to be significant in showing mortality in geriatric patients. When the literature is examined, it is seen that the studies support our study. In a study, lactate was found to be an important parameter in showing in-hospital mortality in patients diagnosed with sepsis.^[24] According to another study conducted on adult patients hospitalized in the intensive care unit, lactate elevation is associated with increased in-hospital mortality regardless of the cause.^[25]

Limitations

Our study is a retrospective and single-centre study and needs to be supported by prospective and multicenter studies with a larger number of patients.

CONCLUSIONS

According to the main finding of our study, we think that direct bilirubin levels at the time of admission to the emergency department may be a parameter that can be used to predict in-hospital mortality in geriatric patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Erzurum Faculty of Medicine Scientific Research Ethics Committee (Date: 13.09.2023, Decision no: 2023/05-56).

Informed Consent: Written informed consent was obtained from all participants prior to enrollment in the study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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