Araştırma Makalesi
Research Article

# Neutrophil/Monocyte Ratio: A new predictor of in-hospital mortality in patients with spontaneous ascites infections

NÖTROFİL/MONOSİT ORANI: SPONTAN ASSİT ENFEKSİYONLARINDA HASTANE İÇİ MORTALİTE İÇİN YENİ BİR GÖSTERGE

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**ABSTRACT**

**Objective:** To determine the clinical features and in-hospital mortality predictors of spontaneous ascites infection (SAI).

**Materials and Methods:** In this retrospective study, 496 patients with liver cirrhosis hospitalized at the gastroenterology clinic between 2015-2019 were screened. Of the 304 cases with ascites, 80 diagnosed with SAI were included in the study.

**Results:** Spontoneus ascites infections (SAI) was detected in 80 (16.1%) of 496 hospitalized patients with cirrhosis. In cirrhotic patients with SAI, the most common reason for presentation to the hospital was altered mental status, which was observed in 26 (32.5%) patients. Thirty-one (38.8%) patients were diagnosed with spontaneous bacterial peritonitis, 41 (51.2%) with culture-negative neutrocytic ascites, eight (10%) with monomicrobial non-neutrocytic bacteria ascites. In-hospital mortality was observed in 25 (31.3%) patients, and one-year mortality rate was 35% with total 28 patients. A high MELD-Na score, history of SAI, presence of hepatic encephalopathy at the time of hospitalization, and a neutrophil/monocyte ratio of >9.1 were determined as the predictors of in-hospital mortality. A neutrophil/monocyte ratio of >9.1 predicted in-hospital mortality at 72% sensitivity and 62% specificity.

**Conclusion:** Successfully predicting mortality in SAI, easily calculated by a hemogram examination, and providing inexpensive, effective and fast results, neutrophil/monocyte ratio presents as a useful marker.

**Keywords:** cirrhosis, ascites, spontaneous ascites infection, mortality, neutrophil/monocyte ratio.

**ÖZ**

**Amaç:** Bu çalışmanın amacı spontan assit enfeksiyonunun (SAI) klinik özelliklerinin ve hastane içi mortalite prediktörlerinin belirlenmesidir.

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**Gereç ve Yöntem:** Bu çalışma retrospektif bir çalışmadır. Ocak 2015-Haziran 2019 arasında Gastroenteroloji bilim dalında yatan 496 karaciğer siroz hastası taranmıştır. 304 assitli olgudan SAI saptanan 80 olgu çalışmaya dâhil edilmiştir. Hastaların demografik, klinik ve laboratuar verileri kaydedilmiştir.

**Bulgular:** Siroz tanısı ile yatan 496 olgudan 80 (%16,1)'inde SAI saptanmıştır. En sık hastaneye başvuru nedeni bilinç bulanıklığı olup, 26 hastada (%32,5) gözlenmiştir. Hastaların 31 (%38,8)'i spontan bakteriyel peritonit, 41 (%51,2)'i kültür-negatif nötrositik assit ve 8(%10)'i monomikrobiyal non-nötrositik bakterassit tanısı almıştır. Hastane içi mortalite 25 (%31,3) hastada gözlenmiş olup, bir yıllık total mortalite %35 oranında, toplam 28 hastada görülmüştür. Yüksek MELD-Na skoru, öyküde SAI, yatışta hepatik ensefalopati varlığı ve nötrofil/monosit oranının >9,1 olması hastane içi mortalite prediktörleri olarak saptanmıştır. Nötrofil/monosit oranının >9,1 olması hastane içi mortaliteyi %72 sensitivite ve %62 spesifite ile predikte etmiştir.

**Sonuç:** Nötrofil/monosit oranının, SAI'de mortaliteyi predikte etmesi, hemogram tetkikinden basit olarak hesaplanabilmesi, ucuz, efektif ve hızlı sonuç vermesi nedeniyle bir belirteç olarak kullanılabileceği düşünülmüştür.

**Anahtar Sözcükler:** siroz, assit, spontan assit enfeksiyonu, mortalite, nötrofil/monosit oranı

Ascites is one of the most common complications with which cirrhosis patients presented to hospital (1-3). Spontaneous ascites infection (SAI) is a serious condition that occurs in patients with cirrhosis and related ascites (4). Increased intestinal wall permeability, bacterial translocation, and impaired host immune system play a role in the pathogenesis of SAI (5-7). These immune changes include impaired phagocytosis, opsonization defect, and neutrophil dysfunction. Because of all these mechanisms, there is a five- to seven-fold increase in bacterial infection risk in cirrhosis cases (8).

It is known that among the cases with cirrhosis that develop ascites, 10-30% of hospitalized patients and 3.5% of outpatients have SAI. In-hospital SAI mortality varies between 20 and 40% (9, 10). Patients may present with fever (50-75%), abdominal pain (27-72%), chills (16-29%), and nausea-vomiting (8-21%), or may be asymptomatic (13%) (11). The diagnosis of SAI is made by the sampling of ascites fluid. Spontaneous bacterial peritonitis (SBP) is a prototype of SAI and is the most commonly seen form. SBP is indicated by the number of polymorphonuclear leukocytes (PML) being ≥250/mm$^3$ and the presence of organisms in culture; monomicrobial non-neutrocytic bacterascites (MNB) is defined based on the number of PML being less than 250/mm3 and the detection of a single organism in culture, and culture-negative neutrocytic ascites (CNNA) presents with a negative ascites fluid culture and a PML number of >250/mm3 (12).

Bacteria isolated from ascites fluid in patients with SBP are usually found in normal intestinal flora. Over 92% of all cases are monomicrobial; aerobic gram (-) negative bacilli are responsible for two-thirds of cases. Escherichia coli accounts for approximately half of these cases, followed by Klebsiella species and other gram (-) negative bacteria (13). Patients with SAI should be treated with empirical, broad-spectrum antibiotics immediately after peritoneal fluid sampling. Once culture results are obtained, antibiotic coverage can be extended to include specific organisms identified (13). The aim of this study was to determine the clinical features and in-hospital mortality predictors of SAI.

## MATERIALS AND METHODS

This study had a retrospective cross-sectional design. 496 cases hospitalized for cirrhosis at the Gastroenterology Department of Medical Faculty Hospital, between January 2015 and June 2019, were retrospectively screened. Of the 304 patients with ascites, those under 18 years of age, those with a history of antibiotic use within the last two weeks, those having secondary bacterial peritonitis, and those with incomplete data were excluded, and the remaining 80 patients with SAI were included in

the study. The clinical and laboratory data of the patients included in the study were obtained from electronic patient files.

For the patients included in the study, age; gender; etiology of cirrhosis; reason for presentation to the hospital; presence of esophageal variceal bleeding (EVB); history of SAI; presence of hepatic encephalopathy (HE); blood leukocyte value, neutrophil, lymphocyte, hemoglobin, monocyte, neutrophil/lymphocyte (N/L) ratio, neutrophil/monocyte (N/M) ratio, lymphocyte/monocyte (L/M) ratio, platelet, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin, albumin, creatinine, sodium (Na), international normalized ratio (INR), and C-reactive protein (CRP) measured at the time of presentation; presence of model for end-stage liver disease (MELD)-Na; Child-Turcotte-Pugh (CTP) score; presentation symptoms and findings; SBP/CNNA/MNB status according to the ascites culture results and neutrophil count; ascites total protein; ascites albumin values; and in-hospital mortality were recorded in the case report form.

SBP was defined based on a PML number of ≥250/mm$^3$ and presence of organism in culture, MNB based on a PML number of <250/mm$^3$ and presence of a single organism in culture, and CNNA based on a negative culture result for the ascites fluid taken before the use of antibiotics but the number of PML being 250/mm$^3$, in accordance with revised American Association for the Study of Liver Diseases Practice Guidelines (12). The diagnosis of liver cirrhosis was made using clinical, laboratory and imaging methods. HE was graded according to the West Heaven classification (14).

Hypotension was defined as a systolic blood pressure of <90 mmHg and/or a diastolic blood pressure <60 mmHg (15). The CTP score was calculated using the presence and degree of ascites, presence and degree of HE, total serum bilirubin and albumin levels, and prothrombin time (16). Local ethics committee approval was received for the study (19-12T/46).

IBM SPSS 20.0 software package was used for statistical analysis. The chi-square test (or Fisher's exact test) was used to analyze the relationship between categorical variables, and the Mann-Whitney U test was conducted to compare continuous variables. The Spearman test was used for the correlation analysis. A p value of <0.05 was considered statistically significant. A univariate analysis was performed to determine the predictors of mortality, and a multivariate logistic regression analysis was undertaken using the forward stepwise method (likelihood ratio) with parameters found significant in the univariate analysis.

## RESULTS

SAI was detected in 80 (16.1%) of 496 patients hospitalized with the diagnosis of liver cirrhosis. The mean age was 66.1 ± 10.8 years, and 57 (71.3%) of the cases were male. Thirty-one patients (38.8%) were diagnosed with SBP, 41 (51.2%) with CNNA, and eight (10%) with MNB. The main reason for presentation to the hospital was altered mental status in 26 (32.5%) patients, abdominal pain in 22 (27.5%), abdominal distension in nine (11.3%), fatigue in six (7.5%), shortness of breath in five (6.3%), fever in five (6.3%), oliguria in four (5%), and EVB in three (3.8%). Regarding subgroups, the most common reason for presentation was abdominal pain (n=11, 35.5%) for the SBP cases, and altered mental status for CNNA and MNB (n = 14, 34.1% and n = 4, 50%, respectively). There was no statistically significant difference between the SAI subgroups in terms of main complaint (p = 0.2). In the medical history of patients, SAI was present in 19 (23.8%) of patients, and known hepatocellular carcinoma (HSK) in 17 (21.3%). The most common three etiologies of cirrhosis were chronic hepatitis B virus (HBV) infection in 21 (26.3%) patients, alcohol in 14 (17.5%) patients, and non-alcoholic steatohepatitis (NASH) in 14 (17.5%) patients. Cirrhosis related to other etiologies constituted 31 (39.2%) of the cases.

According to the CTP classification, 41 (51.2%) cases were evaluated as Class B and 39 (48.8%) as Class C cirrhosis. During the examination undertaken at the time of hospitalization, tenderness in the abdomen was detected in 55 (68.8%) of the patients, fever in 49 (61.2%), HE in 44 (55%), and hypotension in six (7.5%). Thirty-nine patients (31 SBP and 8 MNB) (48.8%) had growth in culture in the

ascitic fluid obtained by puncture. Among the 39 patients with growth in ascitic culture, gram (+) positive and gram (-) negative bacteria were identified in 21 (53.8%) and 18 (46.2%) patients, respectively. Gram-positive bacterias were Staphylococcus spp. (n=10), Strepcoccus spp. (n=5), Enterococcus spp. (n=4), Corynebacterium spp. (n=1), Bacillus spp. (n=1) and gram-negative bacterias were Escherichia spp. (n=10), Klebsiella spp. (n=3), Acinetobacter spp. (n=2), Pseudomonase spp (n=2), and Campylobacter spp. (n=1). As initial therapy emphiric cefotaxime, 2 g intravenous every 8 hours was started according to institutional protocol. Initial therapy was continued in 43 patients (53.7%); cefotaxime was switched to carbapenems in 21 (26.2%) patients, and in 16 patients (20.1%) were added antifungal, glycopeptide and/or fluoroquinolone therapy according to the clinical course of patients. In-hospital mortality rate was found 31.3% (25/80 patients died). Three other patients died within one year and One-year mortality rate was reached 35%. The Clinical characteristics of patients are shown in Table 1.

**Table 1.** Clinical characteristics of patients**.**

| | **SBP n (%)** | **KNNA n (%)** | **MNB n (%)** | **p** |
|---|---|---|---|---|
| **Number of patients** | 31 (38.8) | 41 (51.2) | 8 (10) | |
| **Gender (male)** | 21 (67.7) | 30 (73.2) | 6 (75) | NS |
| **Age** | 63.4 ± 10.5 | 68.8 ±9.9 | 63.2 ±13.9 | NS |
| **Etiology** | | | | NS |
| HBV | 9 (29) | 12 (29.3) | 0 | |
| Alcohol | 6 (19.4) | 4 (9.8) | 4 (50) | |
| NASH | 4 (12.9) | 8 (19.6) | 2 (25) | |
| HCV | 4 (12.9) | 6 (14.6) | 0 | |
| Cryptogenic | 1 (3.2) | 5 (12.1) | 1 (12.5) | |
| Budd-Chiari Syndrome | 2 (6.5) | 2 (4.9) | 0 | |
| Autoimmune | 1 (3.2) | 2 (4.9) | 0 | |
| Others[a] | 5 (16) | 2 (4.9) | 1 (12.5) | |
| **Symptoms at admission (three most common)** | | | | NS |
| Abdominal pain | 11 (35) | 11 (26.8) | 0 (0) | |
| Confusion | 8 (25.8) | 14 (34.1) | 4 (50) | |
| Abdominal distension | 4 (12.9) | 4 (9.8) | 1 (12.5) | |
| **Physical examination findings** | | | | |
| Abdominal tenderness | 27 (87.1) | 27 (65.9) | 1 (12.5) | 0.000 |
| Fever | 27 (87.1) | 19 (47.5) | 3 (37.5) | 0.001 |
| Hepatic encephalopathy | 14 (45.2) | 23 (56.1) | 7 (87.5) | NS |
| Hypotension | 3 (9.7) | 2 (4.9) | 1 (12.5) | NS |
| **CTP Score** | | | | NS |
| CTP B | 15 (48.4) | 22 (52.6) | 4 (50) | |
| CTP C | 16 (51.6) | 19 (46.3) | 4 (50) | |
| **History of SAI** | 10 (32.3) | 7 (17.1) | 2 (25) | NS |
| **In Hospital Mortality** | 13 (41.9) | 10 (24.4) | 2 (25) | NS |

[a]:hepatitis B virus + hepatitis D virus (n:2), primary biliary cholangitis (n:2), cardiac cirrhosis (n:3), caroli disease (n:1).
SBP: Spontaneous bacterial peritonitis, CNNA: Culture-negative neutrocytic ascites, MNB: Monomicrobial nonneutrocytic bacterascites, HBV: hepatitis B virus, NASH: non-alcoholic steatohepatitis, HCV: hepatitis C virus, CTP: Child-Turcotte-Pugh, SAI: Spontaneous ascites infection, NS: Not significant.

When the SBP, CNNA and MNB groups are compared in terms of demographic and clinical features, there was a statistically significant difference between the three groups in relation to the presence of fever and tenderness in the abdomen. In paired comparisons, a statistical difference was found between SBP and CNNA, and between SBP and MNB in terms of the presence of fever on physical examination (p = 0.001). In the comparisons of tenderness in the abdomen, a statistical difference was found between the SBP and CNNA groups; SBP and MNB groups; and CNNA and MNB groups (p = 0.000). There was no significant difference between the groups for the remaining parameters. The biochemical parameters of blood and ascites are shown in Table 2. When the SBP, CNNA and MNB groups were compared in terms of blood and ascites parameters, statistically significant differences were detected in blood CRP (p = 0.047), blood lymphocyte (p = 0.049), blood N/L ratio (p = 0.002), blood N/M ratio (p = 0.002), ascites leukocyte (p = 0.000) and neutrophil (p = 0.000) levels, while there was no statistically significant difference in the remaining parameters (Table 2).

**Table 2:** Blood and ascites parameters of the patients with SAI.

| | **SBP median (min. - max.)** | **CNNA median (min. - max.)** | **MNB median (min. - max.)** | **p** |
|---|---|---|---|---|
| **Blood** | | | | |
| AST (U/L) | 45 (10-167) | 43 (12-159) | 23.5 (14-72) | NS |
| ALT (U/L) | 25 (6-79) | 22 (5-91) | 11 (9-36) | NS |
| ALP (U/L) | 108 (45-757) | 106 (41-612) | 138 (30-172) | NS |
| GGT (U/L) | 58 (6-641) | 56 (6-697) | 34 (12-165) | NS |
| T.Bilirubin (mg/dL) | 2.4 (0.2-30.5) | 2.2 (0.3-14.7) | 1.7 (0.8-7.4) | NS |
| Albumine (g/dL) | 2.6 (1.7-4.4) | 2.6 (1.9-3.7) | 2.7 (2.4-4) | NS |
| Creatinine (mg/dL) | 1.1 (0.4-4.3) | 1.1 (0.5-6.4) | 1.3 (0.7-3.1) | NS |
| Na (mEq/L) | 132 (115-143) | 134 (117-144) | 137 (127-143) | NS |
| INR | 1.6 (0.9-3.5) | 1.4 (0.9-3.2) | 1.4 (1.0-2.4) | NS |
| **CRP (mg/dL)** | 4.9 (0.2-25.3) | 5.9 (0.1-17.5) | 4.5 (1.1-23.4) | **0.047** |
| MELD-Na | 22 (6-40) | 18 (6-34) | 18 (8-36) | NS |
| Leukocyte ($10^3$/μL) | 8.9 (3.9-24.0) | 7.91(1.7-84.8) | 9.6 (3.9-15.1) | NS |
| Neutrophil ($10^3$/μL) | 6.3 (2.7-20.9) | 5.1 (1.0-71.5) | 7.63 (3.1-14.0) | NS |
| **Lymphocyte($10^3$/μL)** | 0.9 (0.2-2.8) | 0.8 (0.2-3.2) | 0.7 (0.3-1.5) | **0.049** |
| Haemoglobin (g/dL) | 10.1 (7.4-15.3) | 10.5 (7.2-13.7) | 9.3 (4.4-12.5) | NS |
| Platelet ($10^3$/μL) | 93 (34-314) | 112 (28-56) | 156.5 (63-223) | NS |
| **N/L Ratio** | 8.6 (1-29.5) | 6.6 (1.7-29.3) | 10.2 (4.5-35.9) | **0.002** |
| **N/M Ratio** | 10.8 (3.8-32.9) | 7.7 (2.5-33.5) | 10.71 (4.3-41.5) | **0.002** |
| L/M Ratio | 1.1 (0.4-6.8) | 1.2 (0.4-6.3) | 1.4 (0.3-3.1) | NS |
| **Ascites** | | | | |
| T.Protein (g/dL) | 1.6 (0.9-3.6) | 1.6 (0.6-5.9) | 1.3 (0.7-2) | NS |
| Albumine (g/dL) | 0.8 (0.1-1.7) | 0.8 (0.1-3.4) | 0.5 (0.2-0.7) | NS |
| **Leukocyte ($10^3$/μL)** | 1.9 (0.5-10) | 1.4 (0.4-2) | 0.2 (0.06-0.6) | **0.000** |
| **Neutrophil ($10^3$/μL)** | 1 (0.1-8.5) | 1.1 (0.3-18.7) | 0.04 (0.01-0.06) | **0.000** |

SAI: Spontaneous ascites infection, SBP: Spontaneous bacterial peritonitis, CNNA: Culture-negative neutrocytic ascites, MNB: Monomicrobial nonneutrocytic bacterascites AST: Aspartat aminotransferase, ALT: Alanin aminotransferase, ALP: Alkaline phosphatase, GGT: Gama glutamyl transferase, Na: Sodium, INR: International normalized ratio, CRP: C-reactive protein, MELD-Na: Model for end-stage liver disease-Na N/L: Neutrophil/lymphocyte, N/M: Neutrophil/monocyte, L/M: Lymphocyte/monocyte, NS: not significant.

Factors predicting in-hospital mortality were the history of SAI (p = 0.021) and the presence of HE (p = 0.011) and hypotension (p = 0.01) at the time of presentation. When the patients that died in hospital (n = 25) and those that were discharged (n = 55) were compared, a statistically significant difference was found in terms of the blood lymphocyte (p = 0.048), blood albumin (p = 0.021), blood creatinine (p = 0.000) and blood Na (p = 0.026) levels, CTP class (p = 0.0018), and MELD-Na (p = 0.000) scores. According to the univariate analysis, history of SAI, HE and hypotension at the time of presentation, blood lymphocyte count, blood Na level, CTP class, MELD-Na score, serum albumin, serum creatinine, serum CRP, INR, and N/L and N/M ratios were significant variables for in-hospital mortality. In the univariate analysis, although hypotension at presentation was found to be a significant factor, it was not included in the regression model because it was only detected in six patients that all died in hospital. Since the serum albumin, serum creatinine, INR and blood Na levels were also the variables of CTP class and MELD-Na scores, they were also excluded from the model. For the remaining variables found significant in the univariate analysis, a multiple logistic regression analysis was conducted using the forward stepwise likelihood ratio method, and the model was completed by the inclusion of the MELD-Na score, N/M ratio, presence of HE at presentation, and history of SAI. The results revealed that mortality was increased by a higher MELD-Na score, N/M ratio of >9.1, presence of HE, and history of SAI. In the receiver operating characteristic (ROC) curve constructed using the N/M ratio, when the cut-off value for this ratio was accepted as 9.1, this parameter had 72% sensitivity and 61.8% specificity in the prediction of in-hospital mortality. The risk factors associated with in-hospital mortality in SAI patients are shown in Table 3.

**Table 3:** Risk factors of SAI for in-hospital mortality.

| | OR | CI %95 | p |
|---|---|---|---|
| **History of SAI** | 4.095 | 1.055-15.866 | 0.042 |
| **Presence of HE** | 4.390 | 1.207-15969 | 0.025 |
| **MELD-Na Score** | 1.140 | 1.045-1.244 | 0.003 |
| **N/M Ratio (> 9.1)** | 5.614 | 1.526-20.659 | 0.009 |

OR: odds ratio, CI: confidence interval, SAI: spontaneous ascites infection, HE: hepatic encephalopathy, MELD-Na: model for end-stage liver disease-sodium, N/M: neutrophil/monocyte.

A second model for the multiple regression analysis was constructed by excluding the MELD-Na score and CTP class, and including the variables of these two parameters that were found significant in the univariate analysis; i.e., serum albumin, serum albumin, serum creatinine, INR, blood lymphocyte count, blood Na level, serum CRP, N/L ratio, N/M ratio, presence of HE at presentation, and history of SAI. The analysis was conducted with the forward stepwise likelihood ratio method. According to the results, the parameters that were found to be significant predictors of in-hospital mortality are presented in Table 3.

The factors predicting first-year mortality were the presence of HE (p = 0.030) and hypotension (p = 0.001) at presentation. When the groups that developed and did not develop mortality within one year were compared, their blood albumin (p = 0.021), creatinine (p = 0.002), Na (p = 0.035), CTP class (p = 0.020), and MELD-Na (p = 0.001) scores were found to statistically significantly differ.

## DISCUSSION

In this study, SAI was detected in 80 (26.3%) of 304 (61.2%) patients with ascites among the 496 patients hospitalized for cirrhosis. In the literature, ascites has been

reported in approximately 58% of cirrhotic cases (17). In a recent study conducted in our clinic, the rate of ascites was found to be 64% in hospitalized patients with cirrhosis (18). In our study, the incidence of ascites in cirrhotic cases was at a similar rate to the literature.

In previous studies, the incidence of SAI in patients with ascites has been reported to be between 10 and 30% (19). In a study conducted by Bor et al. in our center in 1996, SAI was detected in 28.4% of 102 patients with cirrhotic ascites (20). In the current study, we detected SAI in 16.1% of all patients with cirrhosis and 26.3% of patients with ascites, which is consistent with the rates reported in the world literature.

In studies conducted in recent years, SBP was reported to be present in 27-56% of cases, CNNA in 41-65%, and MNB in 8-21% (21-23). Of the patients in our sample, 31 (38.8%) had SBP, 41 (51.2%) had CNNA, and eight (10%) had MNB, indicating a similar range to the literature. A possible reason for the higher incidence of CNNA than the other subgroups similar to the literature is that patients were evaluated in the emergency department before being referred to the gastroenterology service and bedside culture analysis was not undertaken in all cases.

Although fever (50-75%), abdominal pain (27-72%), chills (16-29%), and nausea-vomiting (8-21%) have been reported in the literature as the admission symptoms of patients with SAI, there may also be completely asymptomatic cases (13%) (24-27). In our study, the three most common reasons for the presentation of patients with SAI to the hospital were altered mental status in 26 (32.5%), abdominal pain in 22 (27.5%), and abdominal bloating in nine (11.3%). In contrast to the literature, approximately half of our patients had problems related to consciousness and abdominal bloating, which may be due to both patients and physicians considering these symptoms as a sign of a serious condition, and thus presentation or referral to a tertiary center.

In the literature, the in-hospital mortality rate has been reported to be 21% to 40% in patients with SAI (20, 21, 28-30). We calculated in-hospital mortality rate as 31.3%, and the one-year mortality rate as 35%. The most likely reasons for the majority of mortality occurring at hospital (89.3%) are considered to be half the patients having decompensated cirrhosis while the relatively low one-year mortality in outpatient setting may be due to well-performed secondary prophylaxis after discharge from hospital.

In this study, the most common etiology of cirrhosis was determined as chronic HBV infection in 21 (26.3%) patients, followed by alcohol in 14 (17.5%) and NASH in 14 (17.5%). Cirrhosis related to other etiologies constituted 31 (39.2%) of the cases. Similarly, in two other studies conducted in Turkey, HBV was found to be the most frequent cirrhosis etiology in patients with SAI (22, 31). We detected no etiological differences between the SBP, CNNA and MNB groups.

When SBP, CNNA and MNB groups were compared in terms of in-hospital and one-year mortality rates, the difference between the three groups was not statistically significant ($p = 0.260$ and $p = 0.548$, respectively). However, in-hospital mortality rate was found higher in SBP (42%) group than to the other 2 groups (in CNNA group 24.4% and in MNB group 25%). Suggests that we need to be more careful in follow up those patients.

Studies evaluating patients with SBP have shown an association between in-hospital mortality and serum leukocyte, neutrophil, N/L ratio, CRP, CTP class, MELD-Na score, urea, creatinine and CRP/albumin ratio, mean arterial pressure, advanced age, and ascites PML number being higher than 1,000/mm3 (22,32-39). In our study, according to the univariate analysis, the significant predictors of in-hospital mortality were the history of SAI, presence of HE and hypotension at presentation, blood lymphocyte count, blood Na level, CTP class, MELD-Na score, serum albumin, serum creatinine, serum CRP, INR, NLR, and NMR. The multivariate analysis revealed the MELD-Na score, N/M ratio, history of SAI, and presence of HE at presentation were the predictors of in-hospital mortality.

In this study, the N/M ratio was associated with in-hospital mortality in both univariate analysis and multiple logistic regression analyses, which has not been previously reported in the literature. In the ROC curve analysis of the N/M ratio, when the cut-off value was accepted as 9.1, this

ratio was able to predict in-hospital mortality at 72% sensitivity and 61.8% specificity. The N/M ratio is an inexpensive, effective and fast marker that can be simply calculated by a hemogram analysis. In clinical practice, the N/M ratio can provide physicians with an indication of possible mortality and allow them to closely monitor selected patients. In patients with a high N/M ratio, greater care should be taken in the close follow-up and effective antibiotic selection. On the other hand, the N/L ratio is used as an indicator of inflammation in many inflammatory and neoplastic diseases. This ratio has been shown to be superior to a white blood cell count in predicting the negative outcomes of pancreatitis, appendicitis, acute coronary syndrome, major vascular surgery, rheumatoid arthritis and other diseases requiring intensive care (40-45).

In conclusion, SAI is a serious clinical condition with a variety of clinical presentations, and with a high mortality rate. In our study, significant predictors of in-hospital mortality were MELD-Na score, N/M ratio, history of SAI, and presence of HE at presentation. Although the others are well-known mortality predictors, our study revealed first time in the literature that N/M ratio, as a cheap and fast marker could be used to predict in hospital mortality in patients with SAI. That first result warrants more studies involving more patients.

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