The Egyptian Journal of Hospital Medicine (January 2022) Vol. 86, Page 228-237

Clinical, Biochemical and Inflammatory Predictors of Mortality in Patients with Spontaneous Bacterial Peritonitis

Talaat Zakareya Ibrahim*[1], Wael Mohamed Abd El-Razek[1], Mohamed Akl Rady[1], Heba Mohamed Abdallah[2], Ahmed Ali El-Awady[3], Mohamed Ali Abbasy[1]

Departments of [1]Hepatology and Gastroenterology, [2] Clinical Pathology, National Liver Institute, Menoufia University, Egypt

Department of [3]Internal Medicine and Hepatology, El Mahalla Liver Teaching Hospital, Gharbia, Egypt

***Corresponding author:** Talaat Zakareya Ibrahim, **Mobile:** (+20)1111815877, **E-mail:** talaatzakareya@gmail.com

ABSTRACT

Background: Spontaneous bacterial peritonitis (SBP) is a serious complication of liver cirrhosis. It contributes to high morbidity and mortality in this population. In-hospital mortality of SBP ranges between 20% and 40%, suggesting that further refinements are essential in managing SBP. Early recognition of high-risk patients would enable us to reduce the short-term mortality.

Objective: The current study aimed to evaluate the value of clinical, biochemical and inflammatory markers in the prediction of 1-month and 3-month cumulative mortality in patients with SBP.

Patients and methods: Two hundred patients with a confirmed diagnosis of SBP were enrolled. They were admitted and received the proper treatment at the National Liver Institute Hospital-Menoufia University, Egypt. Patients were prospectively followed up for mortality over a period of three months. Predictors of mortality were assessed and analyzed.

Results: Mortality rates were 20% and 41% at 1 month and 3 month respectively. Our findings showed that low blood pressure, abdominal pain, fever, higher Child-Pugh score, MELD score, serum bilirubin, INR, serum creatinine, C-reactive protein to albumin (CRP/Albumin) ratio, neutrophil–lymphocyte ratio (NLR), massive splenomegaly and large ascites have been demonstrated as risk factors associated with short-term mortality.

Conclusion: SBP carries a high risk of mortality among cirrhotic patients. Clinical parameters (low blood pressure, abdominal pain, fever, massive splenomegaly and large ascites), prognostic scores (Child-Pugh and MELD) and inflammatory markers (CRP, CRP/albumin ratio, and NLR) seem to be accurate and reliable tools that could independently predict short-term mortality in patients with SBP.

Keywords: Spontaneous bacterial peritonitis, SBP mortality predictors, C-reactive protein, CRP-albumin ratio, Neutrophil–lymphocyte ratio.

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis is considered a serious complication that contributes to the high morbidity and mortality rate seen in this population. In the early 1970s, Harold Conn used the term "spontaneous bacterial peritonitis" for the first time to describe a condition characterized by bacterial infection of the ascitic fluid in the absence of any obvious intra-abdominal or surgical source [(1)]. The reported yearly incidence of SBP in cirrhotic patients varies between 7 and 30% [(2)].

In general, there are five variants of ascitic fluid infection; the most common type is SBP. The principal mechanism of SBP is bacterial translocation; where bacteria travel from the gut lumen to the mesenteric lymph nodes and thereafter to the blood stream and other extra-intestinal sites [(3)].

The most common causative microorganisms isolated from the ascitic fluid in patients with SBP are Escherichia coli (70%), Klebsiella (10%), Proteus species (4%), Enterococcus faecalis (4%) and Pseudomonas species (2%) [(4)].

The most common clinical manifestations of SBP are fever, abdominal pain and tenderness; however, it may be asymptomatic. The definitive diagnosis of SBP is established when polymorph nuclear leukocytes (PMNL) in ascitic fluid is 250 cell/mm^3 or more with a positive ascitic fluid culture for a single organism [(5-7)].

A culture negative neutrocytic ascites is a common variant of ascitic fluid infection. It is essentially diagnosed when ascitic PMNL count ≥250 cells/ mm^3 in the absence of culture positivity [(8,9)].

A lot of complications can occur due to SBP e.g.: sepsis, septic shock, hepatic encephalopathy, renal failure, or even death. In-hospital mortality of SBP ranges between 20% – 40%, suggesting that further refinements are essential in managing SBP. Early recognition of high-risk patients would enable us to reduce the short-term mortality [(5,6)].

Patients' clinical status, laboratory data, as well as inflammatory markers might be used to stratify those patients as regards the risk of mortality [(10)].

The current study aimed to evaluate the value of clinical, biochemical and inflammatory markers in the

Received: 21/10/2021
Accepted: 29/12/2021

prediction of 1-month and 3-month cumulative mortality in patients with SBP.

PATIENTS AND METHODS

This prospective study included a total of two hundred patients with a confirmed diagnosis of SBP, admitted and received treatment at the National Liver Institute Hospital-Menoufia University, Egypt.

The diagnosis of liver cirrhosis was essentially built up on clinical, laboratory, and radiological data. Diagnosis of SBP was considered when PMNL count in ascitic fluid was equal or exceeded 250 cells/mm^3 with or without a positive ascitic fluid culture.

Exclusion criteria: Patients with one or more of the following, at the time of recruitment, were excluded: hepatocellular carcinoma (HCC) or other extra hepatic malignancies, active infections other than SBP, variceal bleeding, significant cardiopulmonary disease, antibiotic usage in the last 2 weeks before inclusion, immunosuppressive medications and suspected secondary bacterial peritonitis.

All patients were subjected to full history taking, complete physical examination and standard laboratory tests including complete blood count (CBC), serum albumin, serum bilirubin, prothrombin time (PT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea, serum creatinine, blood electrolytes (Na and K), hepatitis C virus (HCV) antibodies and hepatitis B virus (HBV) surface antigen. All patients were tested for inflammatory markers, as well, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

The following ratios and scores were calculated for all patients: neutrophil to lymphocyte ratio (NLR), CRP to albumin ratio, Child-Pugh (CP) and model for end stage liver disease (MELD) scores. For each patient, the blood sample taken for laboratory tests was divided into 5 mL on a plain vacutainer tube to separate serum for viral hepatitis markers, liver and kidney panels using the Cobas 6000 analyzer (c501 module, GmbH, Germany), and CRP using the Cobas 6000 analyzer (c501 module, Tokyo, Japan). A further 3 mL of blood was delivered to an EDTA vacutainer tube for CBC including white blood cell (WBCs), absolute neutrophil and lymphocyte counts using the Automated Hematology Analyzer Sysmex XT 1800i (Sysmex Corporation, Kobe, Japan). The remaining sample was put on a 3.8% citrate solution in a dilution of 1:9 for analysis of the coagulation profile including PT and international normalized ratio (INR) by the Sysmex CS-1600 automated hemostasis testing. All patients underwent radiologic assessment by abdominal ultrasonography. Splenomegaly was graded into moderate or massive when craniocaudal dimension was 11-20 cm or > 20 cm respectively [(11)]. Ascites were classified as grade I or mild (only detectable by ultrasonography), grade II or moderate (moderate symmetrical abdominal distension), and grade III or large (massive abdominal distension) [(12)]. All the previous workup was done at the time of diagnosis of SBP. Patients were prospectively followed up for survival outcome over a period of three months. Mortality rates within 1 month and 3 months were calculated and predictors of mortality were assessed and analyzed.

Ethical consideration:

This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans and has been approved by Institutional Review Board of National Liver Institute, Menoufia University, Egypt. An informed written consent was signed by each eligible patient before inclusion.

Statistical analysis

Data were coded, processed and statistically analyzed using the SPSS version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Frequencies and percentages were used to express qualitative variables. Chi square test ($\chi 2$) and Fisher exact were used to test the difference between qualitative variables as indicated. Mean and the standard deviation (SD) were used to present quantitative data. Comparison between parametric variables in 2 independent groups was done using the independent samples t-test, while non-parametric data variables were compared using the Mann Whitney U test. Receiver operating characteristic (ROC) curve analysis was established for assessing how far tested variables could predict mortality. Dependent and independent predictors of binary outcome were tested using univariate and multivariate logistic regression analysis. Statistical significance for all analyses was considered when the P value was less than 0.05.

RESULTS

Out of 238 recruited patients, 200 were eligible and included, while 38 patients did not fulfil the inclusion criteria.

The mean age was 61.43 ± 12.72 years. Males were predominant (60%). Child-Pugh class-C represented 57% of patients. The mortality rates were 20% and 41% at one and three months respectively. As regards ascitic fluid culture, no organism could be isolated in 98% of cases. Only 2% of ascitic fluid samples were culture positive. The most commonly isolated organism was E. coli. The rest of the patients' characteristics are shown in Table 1. The flow chart of the study and causes of mortality are demonstrated in Figure 1.

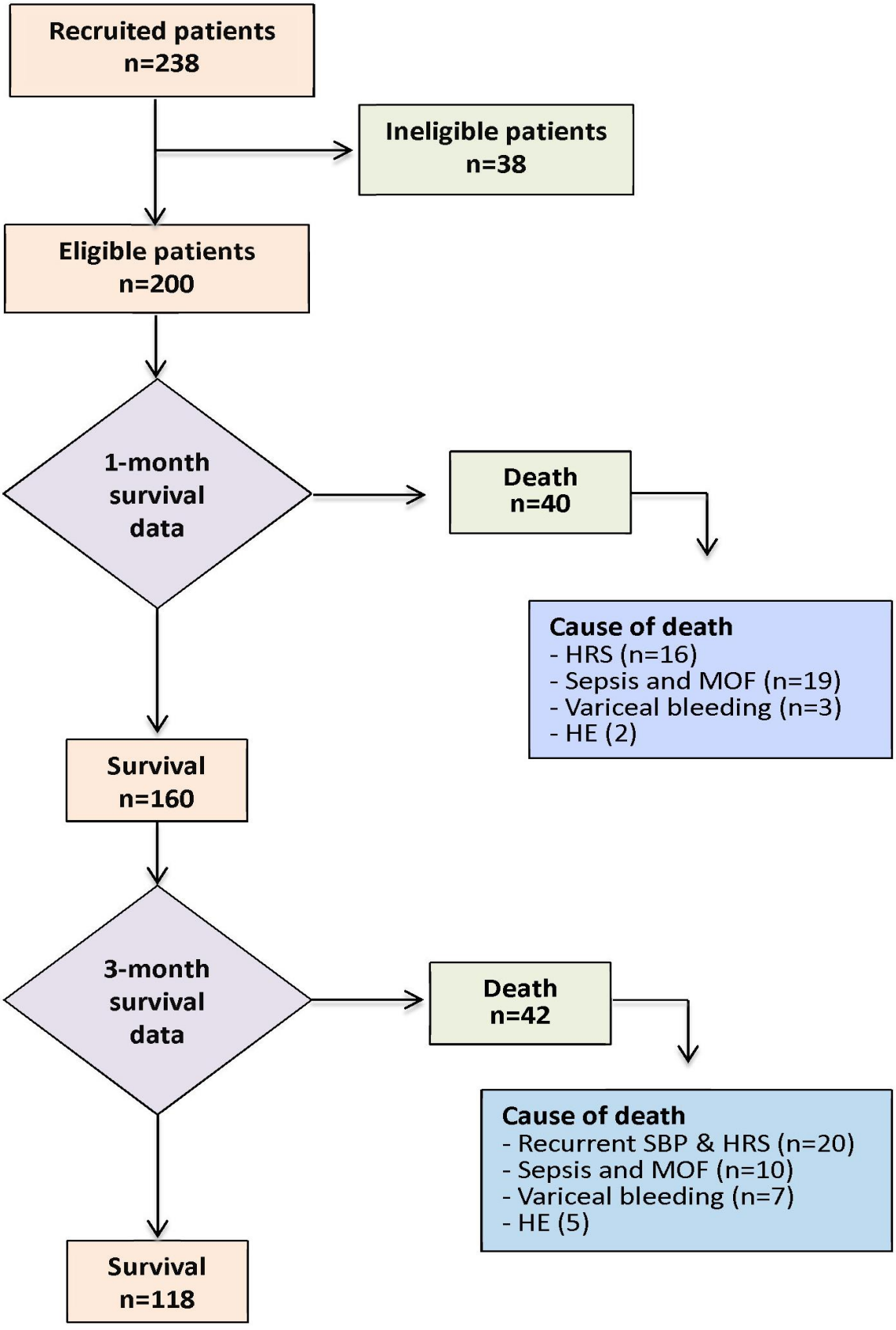

Figure (1): Flowchart of the study showing causes of mortality

SBP, spontaneous bacterial peritonitis; HRS, hepatorenal syndrome; MOF, multi-organ failure; HE, hepatic encephalopathy

Table (1): Demographic, clinical, laboratory, radiological and survival data of the studied patients

Patients' characteristics		n= 200
Age	Years	61.43 ± 12.72
Sex	Male	120 (60%)
	Female	80 (40%)
Child-Pugh class	Class-B	86 (43%)
	Class-C	114 (57%)
Ascitic fluid Culture	E.Coli	38 (19%)
	Streptococci	26 (13%)
	Klebsiella	20 (10%)
	Staph. aureus	14 (7%)
	Staph. epidermidis	4 (2%)
	No growth	98 (49%)
Degree of splenomegaly	Moderate splenomegaly	137 (68.5%)
	Massive splenomegaly	63 (31.5%)
Grade of ascites	Mild ascites (grade1)	6 (3%)
	Moderate ascites (grade2)	135 (67.5%)
	Large ascites (grade3)	95 (47.5%)
Mortality rate	Mortality within 1 month	40 (20%)
	Mortality within 3 months	82 (41%)

Comparison of different studied variables in survivors and non-survivors revealed that mortality was significantly associated with male gender, lower serum albumin and higher levels of serum bilirubin, creatinine, INR, NLR and CRP to albumin ratio (Table 2).

Table (2): Demographic and laboratory data in survivors and non-survivors

Variables	Survived (n: 118)	Died (n: 82)	P-value
Age [years]	61.22 ± 12.36	62.21 ± 12.04	0.640
Sex [n (%)**]**			
Males	64 (54.2)	56 (68.3)	0.046*
Females	54 (45.8)	26 (31.7)	
Bilirubin (mg/dl)	2 ± 0.97	3.15 ± 4.8	0.027*
Albumin (g/dl)	2.31 ± 0.79	1.89 ± 0.75	0.023*
ALT (IU/l)	41 ± 25	43 ± 23	0.868
AST (IU/l)	39 ± 28	42 ±3 1	0.225
Hemoglobin (g/dl)	10.11 ± 2.08	10.24 ± 1.94	0.717
WBCs (x10^3/ml)	7.55 ± 5.1	8.65 ± 6.2	0.183
Platelets (x10^3/ml)	112.6 ± 48.7	108.5 ± 43.2	0.156
INR	1.41 ± 0.46	1.70 ± 0.53	0.015*
Creatinine (mg/dl)	1.09 ± 0.56	1.65 ± 0.81	0.005*
Urea (mg/dl)	87.5 ± 18.5	90 ± 25.1	0.150
Na (mEq/l)	128.59 ± 3.61	125.40 ± 5.54	0.165
K (mmol/l)	4.41 ± 1.09	4.28 ± 1.13	0.476
ESR (mm/h)	19 ± 8	21 ± 9	0.147
CRP	33 ± 12	36 ± 14	0.240
CRP/Albumin ratio	13.16 ± 3.32	18.31 ± 5.35	0.011*
NLR	2.02 ± 1.1	5.07 ± 2.89	< 0.001*

ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cells; INR, International normalized ratio; Na, sodium; K, potassium; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NLR, neutrophil-lymphocyte ratio; *, statistically significant p-value.

As regards the clinical presentation of the patients, mortality was significantly associated with abdominal pain and/or fever (with or without diarrhea) (Table 3). Mortality was significantly higher in patients with Child-Pugh class-C, higher MELD score, massive splenomegaly and large ascites (Table 3).

Table (3): Clinical data and mortality risk scores in survivors and non-survivors

Variables	Survived (n: 118)	Died (n: 82)	P-value
Symptoms/signs			
– Pain	67 (56.8%)	72 (87.8%)	< 0.001*
– Fever	70 (59.3%)	71 (86.6%)	< 0.001*
– Diarrhea	35 (29.7%)	32 (39%)	0.075
– Pain + fever	56 (47.5%)	71 (86.6%)	< 0.001*
– Pain + diarrhea	12 (10.2%)	11 (13.4%)	0.358
– Fever + diarrhea	18 (15.3%)	24 (29.3%)	0.041*
Child-Pugh score	9.64 ± 1.48	12.40 ± 1.73	0.005*
Child-Pugh class			
– Child-Pugh (B)	71 (60.2%)	15 (18.3%)	0.001*
– Child-Pugh (C)	47 (39.8%)	67 (81.7%)	
MELD score	16±4.48	21±6.15	< 0.001*
DM	29 (24.6%)	21 (25.6%)	0.736
Hypertension	6 (5.1%)	5 (6.1%)	0.784
WBCs in ascitic fluid	1175 (783-1775)	1200 (850-2100)	0.719
PMNs in ascitic fluid	900 (573-1200)	925 (637.5-1400)	0.245
Degree of splenomegaly			
– Moderate splenomegaly	103 (87.3%)	34 (41.5%)	< 0.001*
– Massive splenomegaly	15 (12.7%)	48 (58.5%)	
Degree of ascites			
– Mild ascites	6 (5.1%)	0 (0%)	0.003*
– Moderate ascites	100 (84.7%)	35 (42.7%)	
– Large ascites	12 (10.2%)	47 (57.3%)	

MELD, model for end stage liver disease; DM, diabetes mellitus; WBC, white blood cells; PMNs, polymorphonuclear leukocytes; *, statistically significant p-value.

The independent predictors of 1-month mortality, as indicated by multivariate logistic regression analysis, were fever, abdominal pain, low blood pressure, large ascites, massive splenomegaly, higher serum bilirubin, creatinine, INR, Child-Pugh score, MELD score and NLR (Table 4).

Table (4): Univariate and multivariate analysis for prediction of 1-month mortality (n=40)

Variables	Univariate analysis	Multivariate analysis		
	P value	B	95% CI	P value
Age	0.249			
Male gender	0.251			
Pain	<0.001*	1.620	1.125-2.310	0.029*
Fever	<0.001*	1.498	1.058- 2.182	0.041*
Diarrhea	0.248			
Low blood pressure	<0.001*	1.943	1.624-2.687	0.021*
Positive cultures	0.162			
Child-Pugh score	0.003*	1.526	1.115-2.030	0.033*
MELD score	0.005*	1.442	1.048-1.805	0.045*
Total bilirubin	0.012*	1.718	1.240-2.339	0.03*
Albumin	0.224			
INR	0.025*	1.002	0.732- 1.548	0.230
ALT	0.486			
AST	0.842			
Urea	0.611			
Creatinine	0.015*	1.143	0.879-1.617	0.048*
Na	0.478			
K	0.264			
Hemoglobin	0.148			
WBCs	0.208			
Platelets	0.491			
CRP	0.064			
ESR	0.096			
CRP/Albumin ratio	0.016*	1.356	0.841-1.738	0.059
NLR	0.004*	1.694	1.172-1.806	0.031*
DM	0.618			
HTN	0.574			
WBCs in ascitic fluid	0.082			
PMNs in ascitic fluid	0.458			
Massive splenomegaly	0.001*	2.86	2.51-3.28	0.021*
Large ascites	0.012*	1.42	1.18-2.24	0.001*

MELD, model for end stage liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Na, sodium; K, potassium; INR, International normalized ratio; WBC, white blood cells; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-lymphocyte ratio; PMNs, polymorphonuclear leukocytes; DM, diabetes mellitus; *, statistically significant p-value.

The multivariate analysis of the 3-month cumulative mortality revealed that low blood pressure, fever, abdominal pain, large ascites, massive splenomegaly, higher serum bilirubin, serum creatinine, Child-Pugh score, MELD score, NLR, and CRP/albumin ratio were the independent predictors of mortality (Table 5).

Table (5): Univariate and multivariate analysis for prediction of 3-month mortality (n=82)

Variables	Univariate analysis	Multivariate analysis		
	P value	B	95% CI	P value
Age	0.215			
Male gender	0.391			
Low blood pressure	0.001*	1.889	1.340-3.085	0.001*
Positive cultures	0.490			
Child-Pugh score	0.012*	1.436	1.061-2.453	0.044*
MELD score	< 0.001*	1.824	1.273- 2.982	0.023*
Pain	< 0.001*	1.406	1.008-2.108	0.048*
Fever	< 0.001*	1.672	1.230-2.351	0.025*
Diarrhea	0.280			
Total bilirubin	0.03*	1.446	1.115- 1.948	0.012*
Albumin	0.001*	0.736	0.328- 0.928	0.165
INR	0.011*	1.517	1.241 - 2.28	0.054
ALT	0.278			
AST	0.999			
Urea	0.999			
Creatinine	0.031*	0.528	0.398 – 1.05	0.040*
Na	0.152			
K	0.408			
Hemoglobin	0.782			
WBCs	0.144			
Platelets	0.260			
CRP	0.643			
ESR	0.124			
CRP/Albumin ratio	0.001*	2.150	1.512- 2.664	0.010*
NLR	0.001*	1.840	1.263- 2.395	0.015*
WBCs in ascitic fluid	0.296			
PMNs in ascitic fluid	0.544			
DM	0.429			
Hypertension	0.584			
Massive splenomegaly	0.001*	2.31	1.84-2.71	0.012*
Large ascites	0.03*	1.68	1.13-2.97	0.03*

MELD, model for end stage liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Na, sodium; K, potassium; INR, International normalized ratio; WBC, white blood cells; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-lymphocyte ratio; PMNs, polymorphonuclear leukocytes; DM, diabetes mellitus; *, statistically significant p-value.

Data derived from ROC curve analysis including AUC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and best cutoff point for the prediction of 1 and 3-month mortality are presented in (Table 6). MELD score has the highest AUR for both 1-month and 3-month mortality (0.991 and 0.749 respectively, P<0.001*).

Table (6): Performance of different variables in the prediction of 1 and 3-month mortality

	ROC curve data	MELD	CP	NLR	CRP/Albumin ratio
1-month mortality	AUC	0.991	0.808	0.739	0.719
	P Value	<0.001*	<0.001*	<0.001*	0.044*
	Cutoff point	22	9	2.33	24.17
	Sensitivity	97.5%	92.5%	72.5%	62.5%
	Specificity	93.1%	53.1%	68.2%	75.6%
	PPV	95.6%	84.6%	74.8%	68.2%
	NPV	98.2%	76.2%	66.4%	77.6%
3-month mortality	AUC	0.749	0.647	0.765	0.582
	P Value	<0.001*	0.003*	<0.001*	0.101
	Cutoff point	19	10	2.07	6.71
	Sensitivity	100%	54.8%	78.6%	73.8%
	Specificity	74.1%	70.9%	60.2%	41.8%
	PPV	82.2%	68.4%	75.2%	62.6%
	NPV	100%	72.5%	64.2%	54.4%

ROC, receiver operating characteristic curve; AUC, area under ROC curve; PPV, positive predictive; NPP, negative predictive value; MELD, model for end stage liver disease; CP, Child-Pugh score; NLR, neutrophil-lymphocyte ratio; CRP, C-reactive protein.

DISCUSSION

In the current study, although the mean age in the deceased group was higher than survivors, it didn't reach a statistically significant difference. Within the same context, **Niu *et al.*** [13] reported that the age was significantly higher in the deceased patients than those who survived. Regarding the ascitic fluid culture, the most common isolated organisms were E. coli, klebsiella, staph. aureus and staph. epidermidis. This was consistent with the findings of **Hafez *et al.*** [14] **and Oladimeji *et al.*** [15]**.**

We reported that ascitic fluid WBC and PMN counts were slightly higher in the deceased group; however it did not attain a statistically significant value. On the contrary, **Oliveira *et al.*** [16] reported a statistically significant higher ascitic fluid neutrophil count in the non-survivor group compared to the survivor group. Also, **Sanglodkar *et al.*** [10] reported that a white cell count above a cutoff value of 10,000 cells/ml was more commonly reported in non-survivors than in survivors. This disagreement could be referred to the variability in the sample size, inclusion criteria, and the time of diagnosis and treatment of SBP.

In the current study, mortality rate was 20% within 1 month and 41% within 3 months. This came in agreement with **Iliaz *et al.*** [17]**,** who showed similar 30 and 90-day mortality rates (26.1% and 50.7% respectively). **Kim *et al.*** [18] found that in-hospital mortality was 18% in patients with SBP. In another study, 30-day mortality was found to be 37.7% [19]. This variance in mortality rates among different studies may be due, in part, to local practices and guidelines. Also, the heterogeneity of patients' characteristics, variability in the onset of diagnosis and the time at which antibiotics were started, as well as resistance to antibiotics, could influence the mortality.

In the current study, the mean Child-Pugh score in the survived patients was significantly lower than in the non-survived patients. Furthermore, Child-Pugh class-C represented a significantly higher proportion of the non-survivors compared to survivors. Similar results were obtained by **Popoiag *et al.*** [20] who reported a statistically significant higher distribution of Child-Pugh class-C than class-B in non-survivors compared to survivors. On the other hand, no statistically significant differences were observed in the Child-Pugh score between both groups in the study of **Bal *et al.*** [21].

In the current study, the mean serum bilirubin, serum creatinine, INR and MELD score values were significantly higher in the non-survivors than in the survived patients. Similar results were reported by **Sanglodkar *et al.*** [10]**, Bal *et al.*** [21] **and Musskopf *et al.*** [22]**.**

The predictors of short-term mortality in patients with SBP were quite variable among different studies. In the study by **Wong *et al.*** [23]**,** a MELD score of more than 20 was found to be an independent predictor of both 30 and 90-day mortality (p = 0.007 and 0.038, respectively), whereas in the study by **Bal *et al.*** [21]**,** acute kidney injury, septic shock, and MELD-Na were found to be independent predictors of 50-day mortality (p = 0.001, 0.029, and 0.001, respectively). **Illiaz *et al.*** [10] reported high serum WBC count, high NLR, high CRP/albumin, and high MELD score as independent predictors of 30 day mortality. Ascitic fluid culture positivity and serum creatinine > 1.1 mg/dl were the independent predictors of mortality in the study by **Kamani *et al.*** [24] (p = 0.002 and 0.02 respectively). **Suliman *et al.*** [25] reported that renal impairment at diagnosis of SBP was the only independent predictor of in-hospital mortality. Likewise, **Follo *et al.*** [26] disclosed that impaired kidney function was the strongest predictor of in-hospital mortality in SBP. **Tsung *et al.***

[27] reported that mortality was associated with a higher Child–Pugh score, MELD score, serum bilirubin, serum creatinine, prothrombin time, and the presence of hepatocellular carcinoma. **Melcarne *et al.*** [28] reported that extremes of WBC count (leukopenia or leukocytosis), hepatic encephalopathy and elevated blood urea nitrogen (BUN) were independent risk factors for 30-day mortality. **Poca *et al.*** [29] reported that low mean arterial pressure, high serum leukocyte count, and serum urea were strongly related to mortality. Besides, **Oliveira *et al.*** [16] reported that hepatorenal syndrome and higher CRP were independent risk factors for 30-day mortality. **Terg *et al.*** [30] identified bilirubin > 4 mg/dl or creatinine > 1 mg/dl as independent risk factors for short-term mortality in patients with SBP. In the study conducted by **Melcarne *et al.*** [28]**,** the authors reported that BUN, age, temperature > 37.5 °C, serum creatinine and bilirubin were independent predictors for 90-day mortality. **Devani *et al.*** [31] reported that patients with acute kidney injury had a six-fold increase in mortality over those without acute kidney injury.

In our cohort, low blood pressure, abdominal pain, fever, massive splenomegaly and large ascites were the clinical independent predictors of 1-month and 3-month mortality. As regards laboratory data, inflammatory markers and prognostic scores, total bilirubin, creatinine, NLR, Child-Pugh score and MELD score independently predicted 1-month and 3-month mortality. CRP/albumin ratio came as an additive inflammatory predictor of 3-month mortality; however it failed to predict 1-month mortality in the multivariate logistic regression analysis. The best cutoff point of MELD score to predict 1-month mortality was 22. In the study by **Iliaz *et al.*** [10]**,** the MELD cutoff value for predicting 30-day mortality was 20.5. In a similar study, **Tsung and colleagues** identified 20 as the best predictive MELD cutoff point [27]. In addition, **Wong *et al.*** [23] reported that a MELD score > 20 was predictive of 30-day (OR 13.9, 95%CI 2.1–93.7, P=0.007). In our study, a MELD of 19 was the best cutoff point for predicting 3-month mortality. In parallel, **Wong *et al.*** [23] reported that a MELD score > 20 was predictive of 90-day mortality (OR 3.3, 95%CI 1.1–10.2, P = 0.038). We also disclosed that a Child-Pugh score beyond 9 could accurately predict short-term mortality in our population. Similar results were obtained by **Popoiag *et al.*** [20]**,** who reported that Child-Pugh score was significantly higher in the non-survivors. However, no cutoff value was specified to predict mortality.

Additionally, we reported 2.33 as the best cutoff value for NLR to predict 1-month mortality, whereas the best cutoff point to predict 3-month mortality was 2.07. **Iliaz *et al.*** [10] defined a NLR of 9.2 as the ideal cutoff value to predict mortality. This cutoff point is relatively higher than that we found. This could be referred to the relatively small sample size (70 patients) in the study of **Iliaz *et al.*** [10]**.**

We also reported that the best cutoff point of CRP/Albumin ratio to predict 1-month mortality was 24.17. This came in consistency with what was reported by **Iliaz *et al.*** [10] who determined a CRP/Albumin ratio cutoff value of 28.04 as the best point to predict mortality in patients with SBP.

In our study, massive splenomegaly and large ascites were identified as significant risk factors associated with 1-month and 3-month mortality. We did not find any data in the literature about this concern. However, both clinical findings could reflect the severity of underlying liver disease, particularly portal hypertension, which might explain the higher mortality rates reported in these patients.

We acknowledge that this cohort had some limitations, including the relative small sample size and being a single center study, yet its value is strengthened by its prospective nature.

CONCLUSION

Spontaneous bacterial peritonitis is a serious complication in patients with liver cirrhosis and is associated with a considerable risk of mortality. Hepatorenal syndrome and sepsis are the most common complications associated with worse prognosis and poor survival. Clinical, laboratory and inflammatory parameters could be reliably used to stratify the risk of mortality in these patients. Our results need to be verified in a larger multicenter study.

Financial support and sponsorship: Nil.
Conflict of interest: Nil.

REFERENCES

1. **Conn H, Fessel J (1971):** Spontaneous bacterial peritonitis in cirrhosis: variations on a theme. Medicine, 50:161-97.
2. **Sherlock S, Dooley J (2002):** Spontaneous Bacterial Peritonitis. In: Sherlock and Dooley's diseases of the liver and biliary system, 11th Ed. Oxford: Blackwell. Pp. 132-4.
3. **Guarner C, Soriano G (2005):** Bacterial translocation and its consequences in patients with cirrhosis. Eur J Gastroenterol Hepatol., 17:27-31.
4. **Arroyo V (2000):** Spontaneous Bacterial Peritonitis, Eds. O'Grady and Lake's comprehensive clinical hepatology, 1st Ed. Barcelona: Mosby. Pp. 10-14.
5. **Rimola A, Garcia-Tsao G, Navasa M *et al.* (2000):** Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. J Hepatol., 32:142-53.
6. **Dever J, Sheikh M (2015):** Review article: spontaneous bacterial peritonitis--bacteriology, diagnosis, treatment, risk factors and prevention. Aliment Pharmacol Ther., 41:1116-31.
7. **Fernández J, Bauer T, Navasa M *et al.* (2000):** Diagnosis, Treatment and Prevention of spontaneous bacterial peritonitis. Baillieres Best Pract Res Clin Gastroenterol., 14(6):975-990.
8. **Such J, Runyon B (1998):** Spontaneous bacterial peritonitis. Clin Infect Dis., 27: 669–676.

9. **Sheera T, Runyonb B (2005):** Spontaneous Bacterial Peritonitis. Dig Dis., 23:39–46.
10. **Sanglodkar U, Jain M, Venkataraman J (2020):** Predictors of immediate and short-term mortality in spontaneous bacterial peritonitis. Indian J Gastroenterol., 39(4):331-337.
11. **Poulin E, Mamazza J, Schlachta C (1998):** Splenic artery embolization before laparoscopic splenectomy. An update. Surg Endosc., 12(6):870-5.
12. **Moore K, Wong F, Gines P *et al.* (2003):** The Management of Ascites in Cirrhosis: Report on the Consensus Conference of the International Ascites Club. Hepatology, 38(1):258-66.
13. **Niu B, Kim B, Limketkai B *et al.* (2018):** Mortality from spontaneous bacterial peritonitis among hospitalized patients in the USA. Dig Dis Sci., 63(5):1327–33.
14. **Hafez M, Abdallah H, Abdellatif K (2020):** Prevalence of Spontaneous Bacterial Peritonitis in Cirrhotic Patients with Ascites and Its Pattern in Aswan University Hospital. The Egyptian Journal of Hospital Medicine, 81(2): 1444-48.
15. **Oladimeji A, Temi A, Adekunle A *et al.* (2013):** Prevalence of spontaneous bacterial peritonitis in liver cirrhosis with ascites. Pan Afr Med J., 15: 128-133.
16. **Oliveira A, Branco J, Barosa R *et al.* (2016):** Clinical and microbiological characteristics associated with mortality in spontaneous bacterial peritonitis: a multicenter cohort study. Eur J Gastroenterol Hepatol., 28:1216–22.
17. **Iliaz R, Ozpolat T, Baran B *et al.* (2018):** Predicting mortality in patients with spontaneous bacterial peritonitis using routine inflammatory and biochemical markers.European journal of gastroenterology & Hepatology, 30(7): 786-91.
18. **Kim J, Tsukamoto M, Mathur A *et al.* (2014):** Delayed paracentesis is associated with increased in-hospital mortality in patients with spontaneous bacterial peritonitis. The American Journal of Gastroenterology, 109(9), 1436–42.
19. **Alexopoulou A, Vasilieva L, Agiasotelli D *et al.* (2016):** Extensively drug-resistant bacteria are an independent predictive factor of mortality in 130 patients with spontaneous bacterial peritonitis or spontaneous bacteremia. World J Gastroenterol., 22(15):4049–56.
20. **Popoiag R, Panaitescu E, Suceveanu A *et al.* (2021):** Spontaneous bacterial peritonitis mortality trends of cirrhotic patients in the last decade in Constanta County. Experimental and Therapeutic Medicine, 22(1):732-38.
21. **Bal C, Daman R, Bhatia V (2016):** Predictors of fifty days in-hospital mortality in decompensated cirrhosis patients with spontaneous bacterial peritonitis. World J Hepatol., 8:566–72.
22. **Musskopf M, Fonseca F, Gass J *et al.* (2012):** Prognostic factors associated with in-hospital mortality in patients with spontaneous bacterial peritonitis. Annals of Hepatology, 11(6): 915-920.
23. **Wong Y, Kalki R, Lin K *et al.* (2020):** Short-and long-term predictors of spontaneous bacterial peritonitis in Singapore. Singapore Medical Journal, 61(8):419-25.
24. **Kamani L, Mumtaz K, Ahmed U *et al.* (2008):** Outcomes in culture positive and culture negative ascitic fluid infection in patients with viralcirrhosis: cohort study. BMC Gastroenterol., 8:59-64.
25. **Suliman M, Khalil F, Alkindi S *et al.* (2012):** Tumor necrosis factor-α and interleukin-6 in cirrhotic patients with spontaneous bacterial peritonitis. World J Gastrointest Pathophysiol., 3(5):92-8.
26. **Follo A, Llovet J, Navasa M *et al.* (1994):** Renal impairment after spontaneous bacterial peritonitis in cirrhosis: incidence, clinical course, predictive factors and prognosis. Hepatology, 20: 1495-501.
27. **Tsung P, Ryu S, Cha I *et al.* (2013):** Predictive factors that influence the survival rates in liver cirrhosis patients with spontaneous bacterial peritonitis. Clinical and Molecular Hepatology, 19(2):131-9.
28. **Melcarne L, Sopeña J, Martínez-Cerezo F *et al.* (2018):** Prognostic factors of liver cirrhosis mortality after a first episode of spontaneous bacterial peritonitis. A multicenter study. Rev Esp Enferm Dig., 110(2):94-101.
29. **Poca M, Alvarado-Tapias E, Concepción M *et al.* (2016):** Predictive model of mortality in patients with spontaneous bacterial peritonitis. Alimentary Pharmacology & Therapeutics, 44(6): 629-37.
30. **Terg R, Gadano A, Cartier M *et al.* (2009):** Serum creatinine and bilirubin predict renal failure and mortality in patients with spontaneous bacterial peritonitis: a retrospective study. Liver International, 29(3): 415-19.
31. **Devani K, Charilaou P, Jaiswal P *et al.* (2019):** Trends in hospitalization, acute kidney injury, and mortality in patients with spontaneous bacterial peritonitis. Journal of clinical Gastroenterology, 53(2): 68-74.