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Evaluation of Ascitic Calprotectin Level in Diagnosis of Spontaneous Bacterial Peritonitis in HCV Egyptian Patients with Liver Cirrhosis and Its Outcome

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ABSTRACT

Background: A dangerous side effect of cirrhosis, particularly in people with hepatitis C, is spontaneous bacterial peritonitis (SBP). A diagnosis made early is essential for better results. As a potential diagnostic marker for SBP, ascetic calprotectin has demonstrated promise.

Objective: This study aimed to assess ascetic calprotectin levels in the diagnosis of SBP and its consequences in liver cirrhosis patients with HCV in Egypt.

Methods: This was a case-control hospital-based study on 120 cirrhotic Egyptian patients with ascites with different demographic data presented to the Hepatology Department of Shebin El-Kom Teaching Hospital and the Internal Medicine Department of Menoufia University Hospitals during the period from March 2023 till June 2024.

Results: Logistic regression analysis indicated ascetic calprotectin, ascetic TLC, urea, GFR, albumin and respiratory rate were the most significant independent factors associated with the mortality among the studied patients ($p<0.05$). While, other variables did not show significant relation with mortality rate ($p>0.05$).

Conclusion: Logistic regression analysis indicated ascetic calprotectin, ascetic TLC, urea, GFR, albumin and respiratory rate were the most significant independent factors associated with the mortality among the studied patients ($p<0.05$). While other variables did not significant relation with mortality rate ($p>0.05$).

Keywords: Ascetic calprotectin, Bacterial peritonitis, HCV, Liver cirrhosis, Outcome, Spontaneous.

INTRODUCTION

A serious and frequent side effect of liver cirrhosis, especially in patients with ascites, is spontaneous bacterial peritonitis (SBP). It is typified by ascetic fluid infection that lacks a clear intra-abdominal source that can be surgically treated. Hospitalized cirrhotic patients with ascites have a 10% to 30% incidence of SBP and a death rate of about 30% [(1)].

Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease and cirrhosis worldwide, with Egypt experiencing one of the highest prevalence rates. The progression from HCV infection to cirrhosis significantly raises the possibility of complications including SBP. Early and accurate diagnosis of SBP is crucial, as prompt antibiotic therapy can markedly reduce morbidity and mortality [(2)].

Traditionally, the diagnosis of SBP relies on the detection of an elevated polymorph nuclear leukocyte (PMNL) count (≥250 cells/mm^3) in ascetic fluid obtained via paracentesis. However, this method has limitations, including potential delays in obtaining results and the invasive nature of the procedure. Consequently, there is a need for more rapid, reliable, and less invasive diagnostic markers [(3)].

Calprotectin, a calcium and zinc-binding protein predominantly found in neutrophils, has emerged as a potential biomarker for SBP. Its presence in body fluids correlates with neutrophil activity, making it a useful indicator of inflammation and infection. Studies have demonstrated that elevated levels of calprotectin in ascetic fluid are associated with SBP, suggesting its potential as a diagnostic marker [(2)].

Calprotectin, a protein released by activated neutrophils, serves as a marker of inflammation. Elevated levels in ascetic fluid have been associated with SBP. According to **Heikl *et al.* [(4)] and Dibas *et al.* [(5)],** ascitic calprotectin is a highly accurate SBP marker in HCV-related cirrhosis.

Abd Ellatif Afifi *et al.* [(6)] found ascitic calprotectin and serum procalcitonin to be reliable SBP markers, with calprotectin showing 95.4% sensitivity and 85.2% specificity at 445 ng/mL and strongly correlates with inflammatory markers and offers a rapid, reliable tool for early SBP diagnosis. Implementing calprotectin measurement in clinical practice could facilitate timely diagnosis and treatment of SBP, thereby improving patient outcomes. To evaluate the clinical utility of ascetic calprotectin in a variety of patient populations and to develop uniform cutoff levels, more research is necessary [(7)].

In conclusion, ascetic fluid calprotectin level measurement presents a viable method for the prompt and precise detection of SBP in Egyptian patients with liver cirrhosis associated with HCV. By using this biomarker in clinical practice, prompt and effective therapeutic interventions may improve patient outcomes [(8)]. Examining ascetic calprotectin levels in the diagnosis of SBP and its consequences in HCV Egyptian patients with liver cirrhosis was the study's goal.

PATIENTS AND METHODS

Population and Study Design: 120 cirrhotic Egyptian patients with ascites who presented to the internal medicine department of Menoufia University Hospitals and the hepatology department of Shebin El-kom Teaching Hospital between March 2023 and June 2024

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were the subjects of this case-control hospital-based study.

Criteria of diagnosis of spontaneous bacterial peritonitis: Symptoms: fevers, chills, nausea, vomiting, abdominal pain and tenderness, general malaise, shortness of breath, and ascites PMN cell count of ≥ 250 PMNs/mm^3.

Sample size estimation: According to **Josifovikj *et al.*** **(9)**, the average calprotectin level in the SBP group was 1.5 ± 0.40 µg/mL, while it was lower (0.4 ± 0.30) in the non-SBP group, the minimal sample size calculated is 120 participants divided into 2 equal groups at 80% power and 95% CI. Total sample size: 120 participants. A total of 120 cirrhotic patients with ascites were enrolled and divided into two equal groups: with and without spontaneous bacterial peritonitis.

Inclusion criteria: Adults (>18 years) with HCV-related liver cirrhosis and ascites, divided into SBP and non-SBP groups.

Exclusion criteria: patients with ascites from non-portal hypertension causes (e.g., heart failure, pancreatic or chylous ascites, hemoperitoneum, peritoneal TB & HCC), or recent abdominal surgery (within 1 month).

All cases were subjected to the following: Clinical assessment: Detailed medical history (special attention was given to age and gender, history of vascular or cellular decompensation, history of paracentesis, history of spontaneous bacterial peritonitis, co-morbid diseases, history of previous malignancy, drug history, HCV duration, complications of cirrhosis and recent antibiotic use), physical examination (signs of peritonitis, jaundice, hepatosplenomegaly, and ascites severity), lower limb oedema, jaundice and temporal waste. Besides, central nervous system examination, cardiovascular system examination, hernia and divarication of recti, abdominal tenderness, dullness, shifting dullness, and transmitted thrill. General examination included vital signs, conscious level, and pallor.

Anthropometric measurements: Weight and height were measured using standard tools, and BMI (kg/m^2) was calculated to assess obesity.

Laboratory investigations included complete blood count (hemoglobin, platelets & white blood cells with differential) at baseline and post-therapy using the Sysmex XT 1800i (Japan). Liver function tests (ALT, AST, serum albumin, total and direct bilirubin, INR, and prothrombin time) along with renal function tests (blood urea, serum creatinine, and estimated GFR) were conducted using the Cobas 6000 analyzer (c501 module, Roche Diagnostics, Germany). Anti-HCV antibodies were detected via electrochemiluminescence immunoassay (ECLIA) on the Roche Elecsys e 411 analyzer. Ascitic fluid analysis (baseline and post-treatment) included total and differential WBC count, RBC count, albumin, and calprotectin, assessed by the Sysmex XT 1800i. Liver cirrhosis severity and prognosis were evaluated using the Child-Pugh score (five clinical parameters) and MELD score, calculated using serum bilirubin, INR, and creatinine: MELD = 3.78 × ln[bilirubin] + 11.2 × ln [INR] + 9.57 × ln[creatinine] + 6.43. Abdominal ultrasonography was performed to assess liver morphology, portal vein, focal hepatic lesions, ascites, spleen, and collateral circulation.

Patient outcome: Hepatorenal syndrome, hepatic encephalopathy, hemorrhagic ascites, hepatopulmonary syndrome, and death were among the problems that were tracked in the study, along with therapeutic response. Cefotaxime (2 g every 8 hours) was the first empirical antibiotic used to treat SBP without waiting for culture results. To assess responsiveness, a follow-up paracentesis was performed 48 hours later. Antibiotics were changed according to culture sensitivity or swapped out for a broad-spectrum substitute if treatment failed, which was typically the result of bacterial resistance. The course of treatment was maintained for at least five days until the ascitic fluid neutrophil count fell below 250/mm^3. Albumin was given at 1.5 mg/kg on day one and 1 mg/kg on day three to avoid hepatorenal syndrome.

Ethical Approval: Prior to the commencement of the study, each participant completed a written consent that was authorized by Menoufia Faculty of Medicine's Local Ethical Research Committee. Additionally, the Institutional Review Board approval was obtained. The study was conducted in accordance with ethical standards, including the Declaration of Helsinki and its amendments [under code no. 768/2022].

Statistical analysis of the data

Statistical analysis was performed using SPSS version 26. Quantitative data were analyzed with the unpaired Student's t-test and presented as mean ± SD. Qualitative data were compared using the Chi-square test and shown as frequencies and percentages. Univariate logistic regression assessed variable relationships. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

From an initial pool of 130 patients with HCV-induced cirrhosis and ascites, 10 individuals were excluded (3 declined to participate and 7 did not fulfill the inclusion criteria). The final sample consisted of 120 patients, equally categorized into two groups: 60 diagnosed with SBP and 60 without SBP **(Figure 1)**.

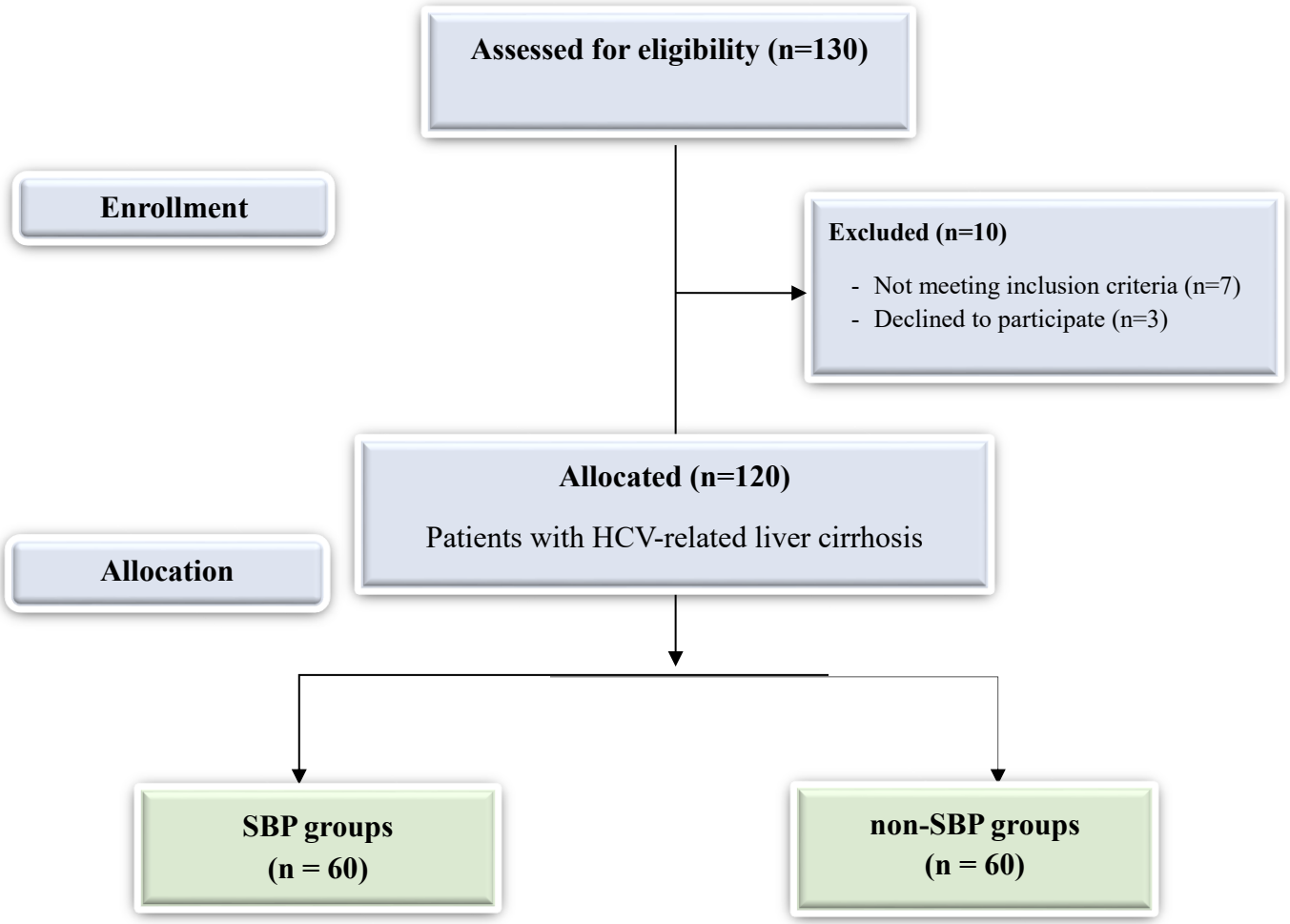

Figure (1): Flowchart of patients with HCV-related liver cirrhosis under study.

A comparative analysis revealed no statistically significant differences between the SBP and non-SBP groups in terms of demographic and basic clinical parameters such as age, gender, BMI, heart rate, or blood pressure. In contrast, the SBP group showed notably elevated respiratory rates (19.30 ± 2.65) and body temperatures (38.10 ± 0.50 °C) compared to the non-SBP group (14.60 ± 2.19 and 36.92 ± 0.30 °C respectively), with both differences reaching statistical significance ($P < 0.05$) **(Table 1)**.

Table (1): Demographic data and general examination of vital signs of the studied groups.

Variables	non-SBP (n=60)		SBP (n=60)		t	P value
Age/year	71.00±12.52		68.30±12.57		0.833	0.408
Sex	**N**	**%**	**N**	**%**	**X^2=** 0.000	1.000
Male	30	50.0	30	50.0		
Female	30	50.0	30	50.0		
BMI (kg/m²)	22.80±2.61		22.30±3.37		**U**= 400.500	0.461
Pulse	72.60±8.35		73.67±7.60		0.517	0.607
Respiratory rate	14.60±2.19		19.30±2.65		7.480	**<0.001***
Systolic blood pressure	114.00±16.53		113.00±15.79		0.240	0.811
Diastolic blood pressure	69.00±7.12		71.00±11.55		0.807	0.423
Temperature	36.92±0.30		38.10±0.50		11.002	**<0.001***

Regarding laboratory parameters, serum alanine aminotransferase (ALT) levels were significantly higher among SBP patients (59.10 ± 40.97) compared to those without SBP (34.30 ± 24.34). Conversely, serum albumin was significantly reduced in the SBP group (2.14 ± 0.29) compared to the non-SBP group (2.62 ± 0.53). No meaningful group differences were observed for aspartate aminotransferase (AST), total bilirubin, or direct bilirubin. **Kidney function indicators** showed significant disparities concerning urea and creatinine levels were elevated in SBP patients, while estimated glomerular filtration rate (GFR) was significantly lower (37.70 ± 21.21 vs. 78.10 ± 32.20 in non-SBP), all with $P < 0.05$. Hemoglobin levels were also significantly lower in the SBP group, while no differences were observed in

platelet counts, WBC and INR. Ascitic fluid analysis revealed significantly elevated total leukocyte count (TLC) and calprotectin levels in the SBP group (P < 0.05) **(Table 2)**.

Table (2): Liver function, renal function tests, laboratory investigations including complete blood count, INR and laboratory investigations including ascitic fluid calprotectin and TLC ascitic among the studied group.

Variables	non-SBP (n=60)	SBP (n=60)	t	P value
ALT (u/l)	34.30± 7.65	59.10±12.25	2.850	**0.006***
AST (u/l)	42.50±9.62	49.40± 11.35	0.933	0.355
Albumin level (gm/dl)	2.62±0.53	2.14±0.29	4.344	**<0.001***
Bilirubin total (mg/dl)	1.68± 0.32	1.89±0.27	0.878	0.383
Bilirubin direct (mg/dl)	0.73±0.16	0.77±0.16	0.404	0.688
Urea level (mg/dl)	51.40± 11.80	107.70± 22.75	3.921	**<0.001***
Creatinine level(mg/dl)	1.05±0.16	2.57±0.45	4.221	**<0.001***
GFR (ml/min/1.73m^2)	78.10± 17.52	37.70±7.42	**U=** 126.00	**<0.001***
PLT (*10^9/L)	102.00±21.93	98.00±22.36	400.50	0.463
WBCS (*10^9/L)	6.33±1.12	6.51±1.20	445.50	0.947
Hb (g/L)	9.76±1.60	8.39±1.04	3.92	**<0.001***
INR	1.51±0.26	1.68±0.31	337.50	0.092
TLC ascitic (cells/mm^3)	154.00± 35.61	1176.00±288.26	180.65	**<0.001***
Ascitic calprotectin (ng/ml)	1.17±0.18	9.62±2.11	532.87	**<0.001***

ALT: alanine transaminase. AST: aspartate transaminase.

There was no significant difference in the MELD scores between groups (P = 0.109). However, Child-Pugh grade C was more prevalent among SBP patients, whereas grade B predominated in the non-SBP group (P = 0.002). Ultrasound assessment revealed significantly higher liver and spleen scores in the non-SBP group (P < 0.05). Clinical presentations such as tense ascites, peripheral edema, hepatic encephalopathy, gastrointestinal bleeding, acute kidney injury, and abdominal pain were not significantly different across groups. Notably, prehepatic coma was significantly more frequent in non-SBP cases (30% vs. 0%, P < 0.05). Comorbid conditions including ESRD, COPD, HTN, CKD, and focal or cardiac ultrasound findings showed no significant differences. However, diabetes mellitus was notably more common among SBP patients (70% vs. 60%, P < 0.05) **(Table 3)**.

Table (3): Diagnostic scoring, radiological investigations, abdominal examinations, comorbidities of general clinical examination among the studied group

Variables	non-SBP (n=60)		SBP (n=60)		t	P value
Meld score Mean ± SD.	18.80±3.57		15.40±2.77		**U=** 342.00	0.109
Child score B C	48 (80%) 12 (20%)		24 (40%) 36 (60%)		10.00	0.002*
Liver US Mean ± SD.	12.37±1.81		10.91±1.06		**U=** 246.00	**0.002***
Spleen US (Mean ± SD.)	15.13±1.90		16.70±1.25		**U=** 252.00	**0.003***
	N	**%**	**N**	**%**		
Tense ascites	54	90.0	60	100.0	3.158	0.076
LL edema	42	70.0	42	70.0	0.000	1.000
Hepatic encephalopathy	6	10.0	0	0.0	3.158	P^{FE}=0.076
Prehepatic coma	18	30.0	0	0.0	10.588	P^{FE}= **0.001***
Bleeding per rectum	0	0.0	0	0.0	---	---
Melena	6	10.0	6	10.0	0.000	1.000
AKI	6	10.0	0	0.0	3.158	P^{FE}=0.076
Abdominal pain	0	0.0	6	10.0	3.158	P^{FE}=0.076
ESRD	6	10.0	0	0.0	3.158a	P^{FE}=0.076
COPD	6	10.0	0	0.0	3.158a	P^{FE}=0.076
HTN	24	40.0	9	30.0	0.659	0.417
DM	18	30.0	42	70.0	9.600	**0.002***
CKD	12	20.0	6	10.0	1.176	P^{FE}=0.278
Cardiac	0	0.0	6	10.0	3.158	P^{FE}=0.076

ROC analysis showed that ascitic calprotectin had strong predictive value for SBP in HCV cirrhotic patients (AUC = 0.73, P = 0.0061), with 93.72% sensitivity and 81.52% specificity at a cut-off ≥ 3.89. In comparison, ascitic TLC had slightly lower performance (AUC = 0.691) with 90.05% sensitivity and 86.11% specificity at a cut-off ≥ 747 (Table 4 & figure 2).

Table (4). The cut-off value ascitic calprotectin and TLC for diagnosis of spontaneous bacterial peritonitis in HCV Egyptian patients with liver cirrhosis.

	AUC	Cutoff Value ≥	P value	Sensitivity %	Specificity %	Asymptotic 95% CI	
						Lower Bound	Upper Bound
Ascitic calprotectin	0.730	3.89	.0061*	93.72	81.52	.372	.864
Ascitic TLC	0.691	747	0.045*	90.05	86.11	.467	.915

Confidence Interval (CI),

Kaplan–Meier analysis showed significantly longer hospital stays in SBP patients (mean = 6.47 days) compared to non-SBP patients (mean = 1.90 days, P = 0.001) (Table 5 & figures 3 & 4).

Table (5): Estimate means and medians for the hazard rate based on hospital stay using Kaplan–Meier survival analysis among the studied patients.

Means and Medians for Survival Time								
Groups	Mean				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Non-SBP	1.900	0.147	1.613	2.187	2.000	0.220	1.568	2.432
SBP	6.467	0.274	5.929	7.004	6.000	0.388	5.240	6.760
Overall	4.183	0.335	3.527	4.840	3.000	0.645	1.735	4.265
			Chi-Square		P value			
Log Rank (Mantel-Cox)			63.38		0.001*			
Breslow (Generalized Wilcoxon)			54.94		0.001*			
Tarone-Ware			59.28		0.001*			

Confidence intervals (CI), *Significant.

Logistic regression identified ascitic calprotectin, ascitic TLC, urea, GFR, albumin, and respiratory rate as significant independent predictors of mortality (P<0.05), while other variables showed no significant association (P>0.05) (Table 6).

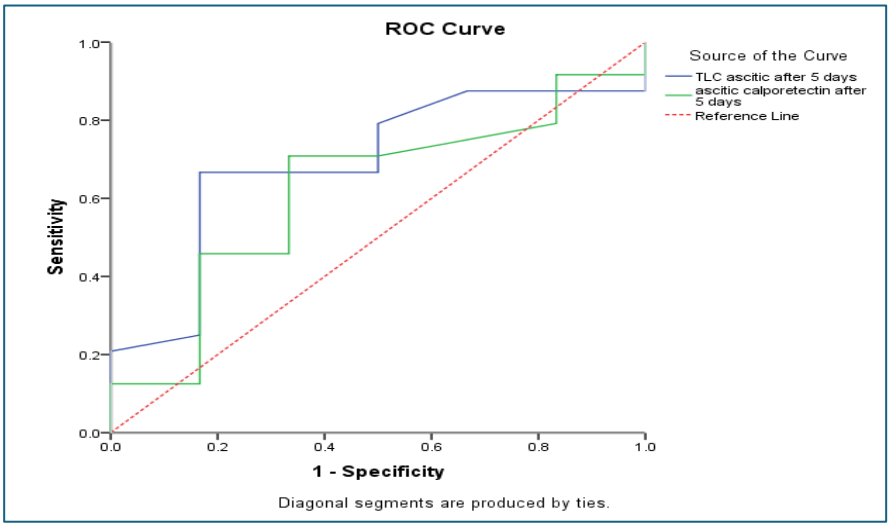

Figure (2): ROC analysis of ascitic calprotectin level.

Table (6): Logistic regression analysis for the predictor factors associated with mortality of patients under study.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
Ascitic calprotectin	.099	.006	.896	15.374	.001*	.086	.112
TLC ascitic	.001	.000	.646	14.839	.001*	.000	.001
Urea	-.001	.000	-.135	-4.152	.001*	-.002	-.001
DM	-.140	.038	-.140	-3.729	.055	-.215	-.065
GFR	.004	.001	.301	5.297	.001*	.003	.006
Albumin	-.188	.041	-.182	-4.543	.001*	-.271	-.105
Creatine	.058	.017	.181	3.496	.061	.025	.091
Temperature	-.132	.042	-.190	-3.141	.053	-.217	-.048
Respiratory rate	.039	.006	.263	6.108	.005*	.026	.052
Hb	.058	.012	.175	4.975	.067	.035	.082

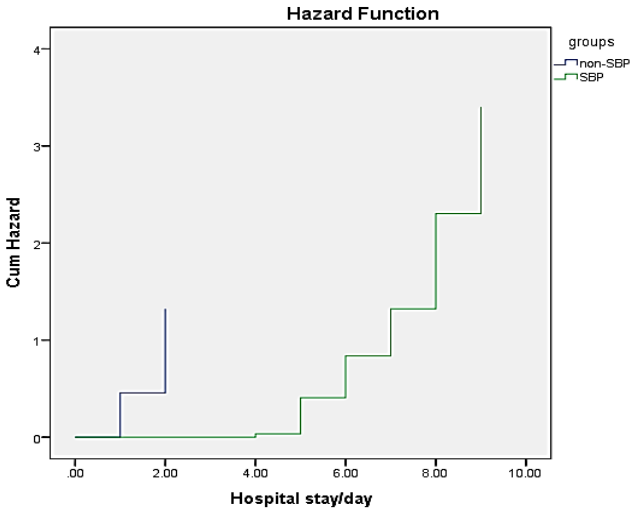

Figure (3): Estimate means and medians for the survival function based on hospital stay using Kaplan–Meier survival analysis among the studied patients.

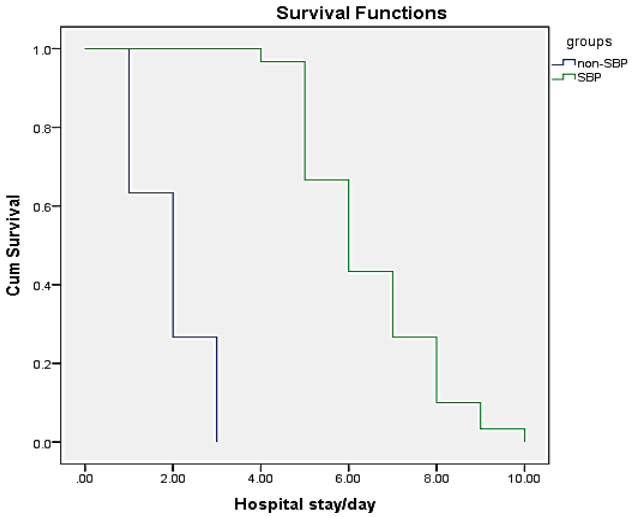

Figure (4): Estimate means and medians for the hazard function based on hospital stay using Kaplan–Meier survival analysis among the studied patients.

DISCUSSION

Ascetic fluid calprotectin may play a significant role in the diagnosis of SBP and be a quick bedside test for the prompt treatment of SBP by detecting a neutrophil count of 250 cells/mm^3 or above [6]. Calprotectin may be a useful diagnostic tool for assessing the onset and progression of hepatic encephalopathy and SBP because cirrhosis patients' gastrointestinal tracts show numerous alterations to the mucosal barrier, such as neutrophil infiltrates [10]. This case-control hospital-based study aimed to assess ascitic calprotectin levels for diagnosing SBP and predicting outcomes in Egyptian HCV patients with liver cirrhosis. A total of 120 cirrhotic patients with ascites were enrolled from March 2023 to June 2024 at Shebin El-Kom Teaching Hospital and Menoufia University Hospitals. They were divided into two equal groups: 60 patients without SBP and 60 with SBP.

Our study showed that ascetic TLC and ascetic calprotectin were significantly higher in patients with SBP compared to those without SBP.

In the same line, **El-Kassas *et al.*** [10] showed that ascetic calprotectin had mean values of 376.06 and 613.28 ng/ml in the non-SBP group and SBP group, indicating a significant increase in association with SBP. Using a cut-off point of 433.7 ng/ml, ascetic calprotectin had sensitivity and specificity of 73.3% and 85.1%, respectively, for detecting patients with SBP. The calprotectin function is unknown; however, it has been demonstrated to have antibacterial properties. Calprotectin stops the spread of E. coli, S. aureus, Staphylococcus epidermidis, Klebsiella spp., and Candida spp., but only at concentrations lower than those found in the blood of people who have bacteremia, which may be present in some circumstances. Killing occurs at dosages that are two to four times higher than the lowest inhibitory limits.

A study by **El-Kassas *et al.*** [10] showed that ascetic fluid calprotectin was significantly linked to TLC and PMNs, while it had a significant negative correlation with ascetic albumin and serum-ascites albumin gradient (SAAG). It is unclear how calprotectin

is connected to the amount of glucose in ascetic fluid. There was a link between the amount of calprotectin in the ascetic fluid and C-reactive protein (CRP), the number of PMN cells in the ascetic fluid and the amount of LDH in the ascetic fluid. It was discovered that there was no link between calprotectin in ascetic fluid and blood leukocytes, ascetic protein, and albumin.

Additionally, **El-Kassas *et al.*** [10] suggested that ascetic fluid calprotectin has the potential and can be used to find people with cirrhosis and ascites who have SBP. While, a 433.7 ng/ml cut-off yielded reasonable sensitivity and specificity limitations remain. Further research is needed to refine its use, but calprotectin may become a valuable addition to existing methods like neutrophil count for a more comprehensive SBP diagnosis.

In another study, **Mohamed *et al.*** [11] found that calprotectin can significantly diagnose SBP with AUC of 0.937, at cut off point value of 5.045. In the same line, **Abdel-Razik *et al.*** [12] showed that the median values of ascetic calprotectin were 762.6 and 270.7 ng/ml in the SBP and non-SBP groups, Also, **Elbanna *et al.*** [13] discovered that people with SBP had much higher amounts of ascetic calprotectin than people who did not have SBP. Additionally, **Nabiel *et al.*** [14] reported that the same ascetic marker had mean values in the SBP and non-SBP groups. Furthermore**, Ali and Mohamed** [15] reported that ascetic calprotectin showed a significant rise with the development of SBP. It had mean values of 569.15 and 237.64 ng/ml in the SBP and non-SBP groups respectively. All previous studies confirmed our findings regarding ascetic calprotectin in association with SBP. However, **Abdel-Rahman *et al.*** [16] discovered that the median ascetic calprotectin was higher in patients with SBP. Compared to 2.5% of patients without SBP, 95% of SBP patients had positive results from the ascetic leucocyte esterase test.

Abd Ellatif *et al.* [6] discovered that group I had a considerably greater level of ascetic fluid calprotectin than group II. With an area under the curve. Ascetic fluid calprotectin proved significant for diagnosing SBP at a cutoff level of 18 ng/ml. Ascetic fluid calprotectin, on the other hand, had a negative correlation with ascetic fluid albumin and a positive correlation with ascetic fluid PMNLs in group I. In this investigation, patients with indications of SBP had a considerably higher median ascetic fluid calprotectin level than the control group.

In our study, Ascetic calprotectin levels were found to have predictive solid ability with an area under the ROC curve of 0.73. Using a cut-off of ≥ 3.89, there was 93.72% sensitivity and 81.52% specificity for predicting SBP in Egyptian HCV patients with liver cirrhosis. As compared to ascetic TLC, which had sensitivity of 90.05% and 86.11% specificity at cut-off level ≥ 747 with area under curve of 0.691. Similarly, **Ibrahim *et al.*** [17] also evaluated the accuracy of ascetic fluid calprotectin as a diagnostic marker for SBP and reported even stronger performance. According to their ROC curve analysis, the cutoff value of ascetic calprotectin was 783 ng/ml, with a sensitivity of 90% and specificity of 100%, and an AUC of 0.980. They also evaluated the calprotectin-to-total protein ratio, which showed high diagnostic performance but was not superior to calprotectin alone. These findings support our conclusion regarding the strong predictive value of calprotectin, although their reported AUC was higher.

In agreement with our results, **Ibrahim *et al.*** [17] assessed ascetic calprotectin and reported that a cutoff of > 2 ng/mL yielded a sensitivity of 90%, specificity of 92.5%, and an AUC of 0.963. Moreover, they identified calprotectin as an independent predictor of SBP in multivariate analysis. These findings corroborate our results, highlighting the diagnostic value of calprotectin in cirrhotic Egyptian patients. Consistently, **Selim *et al.*** [18] demonstrated that ascetic calprotectin, at a cutoff of 620 ng/ml, showed a sensitivity of 90.91% and a specificity with high NPV and PPV. Their data reinforced the findings, supporting the utility of calprotectin in SBP diagnosis, although their cutoff value and AUC were somewhat higher.

Likewise, **Fernandes *et al.*** [19] found that calprotectin had high diagnostic performance at a cutoff of 1.57 µg/ml, with sensitivity and specificity of 87.8% and they also showed improved diagnostic performance when combining calprotectin with SAAG values. These results align with our findings regarding calprotectin's diagnostic accuracy, though their AUC and specificity were higher.

Furthermore, **Abdel-Razik *et al.*** [20] reported that ascetic calprotectin, at a cutoff of 445 ng/mL, had a sensitivity of 95.4%, specifically of 85.2%, and an AUC of 0.921, with a high NPV and PPV. These outcomes are consistent with ours, affirming the role of calprotectin as a valuable biomarker for SBP, even though the diagnostic metrics slightly differ.

LIMITATIONS

In our study, the calprotectin in the ascetic fluid was assessed utilizing the ELISA tests and tests that can be done at the point of care. This study looked at several factors and diagnostic methods that can be used instead of counting cells by hand. The current study had some limitations. The first was its nature as a study that only looked at one center and had a small sample size. The second was that the prognostic value of calprotectin as a marker of SBP, as well as its value in monitoring treatment response, should be further evaluated.

CONCLUSION

Ascetic calprotectin levels were found to have predictive solid ability using a cut-off of ≥ 3.89, with 93.72% sensitivity and 81.52% specificity for predicting SBP in Egyptian HCV patients with liver cirrhosis. As compared to Ascetic TLC, which had sensitivity 90.05% and 86.11% specificity, logistic

regression analysis indicated ascetic calprotectin, ascetic TLC, urea, GFR, albumin and respiratory rate were the most significant independent factors associated with the mortality among the studied patients ($p < 0.05$). While other variables did not have significant relation with mortality rate ($p > 0.05$). Ascetic calprotectin levels show promise as a diagnostic tool for SBP in HCV-infected Egyptian patients with liver cirrhosis and elevated calprotectin in ascetic fluid can aid in early detection of SBP, potentially leading to timely treatment and better outcomes. This biomarker might also help differentiate between infectious and non-infectious ascetic causes and could be helpful for monitoring disease progression.

Consent for publication: Not applicable.
Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request .
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