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Assessment of diagnostic accuracy of ascetic fluid lactoferrin in diagnosis of spontaneous bacterial peritonitis

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ABSTRACT

Background: Liver cirrhosis is the end stage of liver damage brought on by a variety of chronic liver disorders. An acute infection of ascites is referred to as "spontaneous bacterial peritonitis" which is an abnormal accumulation of fluid in the abdomen without a definitive source of infection. **Aim of work:** is to assess the diagnostic accuracy of ascetic fluid lactoferrin in diagnosis of spontaneous bacterial peritonitis. **Subjects and methods:** Our diagnostic study was conducted upon all consecutive cirrhotic patients with ascites admitted to Endemic and Infectious department, Suez Canal University Hospital in the period from September 2022 till August 2023. This study included 80 cases. They were classified into two groups. Group I included patients with cirrhotic ascites without SBP while Group II included patients with cirrhotic ascites with SBP. All patients were subjected to full history taking, complete clinical examination and routine laboratory testing including ascetic fluid analysis. Ascitic fluid culture was also done to detect bacterial growth. In addition, we measured the ascetic fluid lactoferrin. **Results:** ascetic fluid lactoferrin level was higher in SBP group than non SBP groups, with positive correlation with polymorphonuclear leukocytes. Ascetic fluid lactoferrin at cut off value 98 ng/ml had 93% sensitivity, 75% specificity, 80% positive predictive value, 91% negative predictive value, 84% accuracy in diagnosis of SBP, likelihood ration 3.72. **Conclusion:** Patients with SBP had higher amounts of ascetic fluid lactoferrin than non-SBP patients. Ascetic fluid lactoferrin is considered potential and useful biomarker in spontaneous bacterial peritonitis diagnosis.

Introduction

Liver cirrhosis is the end stage of liver damage caused by a variety of chronic liver disorders. Although the triggers of cirrhosis differ in terms of location, chronic hepatitis C virus infection, alcohol drinking, and nonalcoholic fatty liver disease are the most prevalent causes in western nations, meanwhile HCV infection is the leading

cause of cirrhosis in Egypt. The onset of ascites is a critical point in the course of liver cirrhosis and decompensation. The severity of liver disease determined by The Child-Pugh score system which broke down patients into three categories: A - good hepatic function, B - moderately impaired hepatic function, and C - advanced hepatic dysfunction [1]. Throughout the initial year after diagnosis, 20% of cirrhotic patients who manifest with ascites at

diagnosis additionally fade away. An acute infection of ascites is referred to as "spontaneous bacterial peritonitis" (SBP), which is an abnormal accumulation of fluid in the abdomen without a definitive source of infection. SBP is virtually always present in patients with cirrhosis and ascites; the condition is suspected when a patient presents with fever, impaired mental status, or abdominal pain. The death rate has decreased in the forty years since SBP was first documented as a result of liver transplantation, quick diagnosis, and effective treatment [2]. For the first instance, the estimated hospital mortality ranges from 10% to 50%, and for the second or subsequent episodes, it ranges from 31% to 93%. According to recent researches, there is a greater than 20% chance of death within a month, a greater than 30% chance of death inside an inpatient setting, and a fifty percent to seventy-five percent chance of death within a year and two years following an SBP episode [3]. The clinical syndrome known as SBP is characterized by infected ascetic fluid, however there is no specific intra-abdominal source of peritonitis in those affected. PMN cell counts in ascetic fluid are used to diagnose SBP; counts of 250 cells/mm³ show SBP regardless of the presence of a positive blood or ascetic fluid culture. However, because of its operator dependent, it is prone to errors. If the cells become dead during the journey to the lab, false results may also happen [4]. Commercially available kits for the measurement of ascetic fluid lactoferrin can be used in a future development of a qualitative bedside assay. Furthermore, lactoferrin can be made into a useful marker for SBP by a bedside test because it is highly stable and resistant to degradation over an extended length of time at room temperature [5]. In this study the aim is to assess the diagnostic accuracy of ascetic fluid lactoferrin in diagnosis of spontaneous bacterial peritonitis

Materials and methods

Technical design: Our diagnostic study was conducted upon all consecutive cirrhotic patients with ascites admitted to Endemic and Infectious department, Suez Canal University Hospital in the period from September 2022 till August 2023. This study included 80 cases. They were classified into two groups. Group I (non-SBP) included patients with cirrhotic ascites without SBP while Group II (SBP) involved patients with cirrhotic ascites with SBP according to guidelines definition of ascites [6]. We included patients with decompensated chronic liver diseases (Child B and

C cirrhosis with ascites). Evidence of SBP included abdominal pain or tenderness, fever, malaise, hepatic encephalopathy. Bacterial peritonitis was diagnosed when ascetic fluid polymorph nuclear leukocyte equal or more than 250/mm³ without evidence of secondary source of peritoneal infection. On the other hand, we excluded patients with ascites due to any cause other than liver cirrhosis, having evidence of active infection other than ascetic fluid infection and with pre-hospitalization antibiotic administration within 2 weeks. We also excluded cases with any other cause of neutrocytic ascites such as pancreatitis, appendicitis, tuberculosis, peritoneal carcinomatosis, and hemorrhagic ascites or with history of abdominal surgery within 3 months of the study.

Methods

After approval of the protocol by ethical research committee of faculty of medicine in Suez Canal university under No (4901) and obtained informed consent from all participants after explaining the aim of study and expected benefits and drawbacks, the diagnosis of liver cirrhosis and ascites was based on clinical, biochemical and ultrasonographic findings. All patients were subjected to a structured interview-based questionnaire which consisted of two parts. First part included individual socio-demographic characteristics as (age, sex, occupation, residence, smoking, marital status, etc.), chronic illness. The second part included history of previous infection by hepatitis B, C viruses, bilharzias infection or alcohol use and physical characteristics including clinical features of liver cirrhosis (spider angioma, palmar erythema, ascites, asterixis, hepatomegaly, splenomegaly, and abdominal vein collaterals), GIT symptoms, clinical evidence of current infections and drug history regarding recent use of antimicrobials. We also performed for all participants' complete clinical examination and routine laboratory testing including complete blood count, liver and renal function tests, and ascetic fluid sample 20 ml was obtained under complete aseptic condition for ascetic fluid analysis. Ascetic fluid analysis including cell count and differentials, albumin and protein was performed for all patients. Ascetic fluid culture: 10 ml of ascetic fluid was collected under complete aseptic condition during the diagnostic abdominal paracentesis and put into a blood culture bottle. Ascetic fluid culture was done by inoculating the ascetic fluid into blood agar and

MacConkey agar. Preliminary results were obtained after 48 hours, followed by conventional biochemical identification tests. If ascetic fluid cultures were positive and the neutrophil count was >250 cells/mm³, patients were diagnosed as having culture-positive neutrocytic ascites or SBP. If ascetic fluid cultures were negative in the presence of neutrocytic ascites, patients were characterized as having culture negative neutrocytic ascites (CNNA). The ascetic lactoferrin samples were centrifuged for 20 min at $1000\times g$ at 2-8°C and collect the supernatant to carry out the assay. The minimal detection range was 0.32 ng/ml. Ascetic fluid lactoferrin was determined using Human Lactoferrin ELISA Kit (ELK Biotechnology CO., Cat# ELK1066, LTD Biolake, Donghu New & Wuhan city). This ELISA kit used the Sandwich-ELISA principle.

Statistical analysis

The statistical analysis carried to evaluate and compare between lactoferrin was assessed in cirrhotic ascetic patients with or without SBP to evaluate its role in the diagnosis of SBP; independent samples t-test or corresponding statistical analysis for nonparametric data was proposed. Data was collected, checked, revised, and organized in tables and figures using Microsoft Excel 2016. The collected data subjected to outliers' detections and normality for detection of parametric and nonparametric data using Shapiro-Wilk or Kolmogorov Smirnov normality test. Data was described statistically using both graphical and numerical description. Inferential statistics for comparing ascetic fluid lactoferrin in cirrhotic ascetic patients with or without SBP (A0, A1) by independent samples t-test or corresponding test for nonparametric data i.e., Chi-squared test and/or Wilcoxon or Man-Whitney for 2 groups at significance levels of 0.05. Data analyses were carried out using computer software Statistical Package for Social Science (SPSS) IBM- SPSS ver. 28.0 for Mac OS. The test results were considered significant when P value < 0.05 . Receiver operator characteristic (ROC) analysis, area under curve (AUC) and 95% confidence Interval (CI) was used to determine the optimum cutoff value of lactoferrin in diagnosis of SBP. Diagnostic performance was represented using the terms sensitivity, specificity, positive predictive value, negative predictive value, and Accuracy.

Results

The results of our study show no statistically significant difference in two groups regarding to age, residence and smoking status, but males significantly more common in SBP group $P = 0.041^*$ (**Table 1**). Also there was no statistically significant difference between two groups regarding chronic illness (**Table 2**). The most common etiology of liver diseases in this study in both groups is infection with hepatitis C virus followed with coinfection with hepatitis C virus and bilharziasis with no significant difference between two groups. (**Table 3**). The main clinical presentations of patients in our study were 57.5% had anorexia and malaise symptom in SBP and 42.5% and 35% in non SBP group respectively while 42.5% of SBP patients had abdominal distention followed by fever which represented 30% in SBP group. The rate of hepatic encephalopathy was higher in SBP group than non SBP group (**Table 4**). Ultrasound assessment revealed that 42.5% of patients had marked ascites in SBP and 37.5 % had moderate ascites in non SBP group. Also, there was no statistically significant difference between two groups regarding collection. Moreover, there is no significant difference in both groups regarding spleen size. About one quarter of patients has hepatic focal lesion in US image but no statistically significant difference between two groups (**Table 5**). Laboratory investigations shows that there was no statistically significant difference between the patients in both groups regarding biochemical characteristics except total bilirubin, and direct bilirubin which were slightly higher in SBP group with P value .036, and .038* respectively (**Table 6**). Assessment of ascetic fluid samples in both groups showed that there was statistically significant difference between the patients in both SBP and non SBP group regarding biochemical characteristics (TLC, LDH, Protein) except glucose, albumin, and SAAG. Also, the median score of lactoferrin concentration in ascetic fluid was 112.43 in SBP group, and 48.23 in non SBP group and there was statistically significant difference between two groups with P value .011*. (**Table 7**). Ascetic fluid culture was positive in 25 (62.5%) patient of SBP group, 15 (37.5%) *E.coli*, 5 (12.5%) *Staphylococci*, 3 (7.5%) *Klebsellia*, 2 (5%) *Pseudomonas*, meanwhile the remaining of patients were culture negative. Culture was negative in non SBP group. **Figure 1** Showed that mean of log₁₀ of TLC and

lactoferrin total score was 2.83, 2.08 in SBP group respectively, and 2.20 and 1.85 in non SBP group respectively. Analysis of (ROC)- (AUC) revealed AUC of 0.664 (95% CI: 0.539-.790) (**Figure 2a, Table 8a**). At optimal cutoff value ≥ 98 ng/ml, lactoferrin detected 38 out of 40 in SBP. 21 out of 40 in Non SBP group had lactoferrin levels <98 ng/ml. Ascetic fluid lactoferrin had 95% sensitivity, 53% specificity, 67% positive predictive value, 91% negative predictive value, 74% accuracy in diagnosis of SBP, likelihood ration 2.02 (**Table 8a**). Analysis of ROC-AUC after removing HCC cases in both groups revealed AUC of 0.796 (95% CI: 0.663-.929) (**Figure 2b, Table 8b**). At optimal cutoff value ≥ 98 ng/ml, lactoferrin detected 28 out of 30 in SBP and 21 out of 28 in non SBP group had lactoferrin levels <98 ng/ml. Ascetic fluid lactoferrin had 93% sensitivity, 75% specificity,

80% positive predictive value, 91% negative predictive value, 84% accuracy in diagnosis of SBP, likelihood ration 3.72 (**Table 8b**). **Table 9** showed that there was statistically negative correlation between ascetic fluid lactoferrin and HB, total bilirubin, direct bilirubin in non SBP groups with Rho -.436, -.354, .347 respectively, and P value .005, .025, and .028 respectively. Also, there was positive correlation between ascetic fluid lactoferrin and TLC of ascetic fluid with in both SBP and non SBP groups, no statistical significance difference ($P = 0.382, 0.054$) respectively. **Table 10** denoted that 22 out 57 of patients had HCC disease and positive SBP disease, 35 out of 57 hadn't HCC and positive SBP disease, 23 out of 23 hadn't HCC and hadn't disease with P value $<.001^*$. Also, there was no statistically significant difference between the two groups regarding history of other diseases .

Table 1. Sociodemographic characters of both SBP and non SBP groups.

	SBP group n=40		Non-SBP group n=40		P value
	N	%	N	%	
Age (years)					0.458
Mean ±SD	60.75 ± 8.02		62.28 ± 10.14		
Gender					0.041*
Male	28	70.0	18	45.0	
Female	12	30.0	22	55.0	
Marital status					0.003*
Married	37	92.5	25	62.5	
Widowed	3	7.5	15	37.5	
Residency					0.499
Urban	26	65	30	75	
Rural	14	35	10	25	
Smoking					0.481
Yes	38	95	34	85	
No	2	5	6	15	

*: Statistically significant at $p \leq 0.05$

Table 2. Comorbidity of both groups.

	SBP group n=40		Non-SBP group n=40		P value
	N	%	N	%	
Chronic illness					
HTN	16	40.0	19	47.5	0.652
DM	25	62.5	21	52.5	0.498
IHD	5	12.5	3	7.5	0.712
Impaired kidney diseases	6	15.0	3	7.5	0.481

Table 3. Etiology of liver disease.

	SBP group n=40		Non-SBP group n=40		P value
	N	%	N	%	
Etiology of liver disease					
HCV	25	62.5	24	60	1.000
HBV	2	5.0	2	5.0	1.000
HCV+Billharisiasis	12	30.0	14	35	1.000
HCV+HBV	1	2.5	0	0	1.000

Table 4. Clinical presentation of study groups.

	SBP group n=40		Non-SBP group n=40		P value
	N	%	N	%	
Complain					
Abdominal pain	11	27.5	6	15	0.001*
Abdominal distension	17	42.5	5	12.5	
GIT bleeding	7	17.5	7	17.5	
Vomiting	1	2.5	3	7.5	
Jaundice	3	7.5	2	5	
Encephalopathy	13	32.5	5	12.5	
Fever	12	30.0	5	12.5	0.099
Anorexia	23	57.5	17	42.5	0.263
Headache	7	17.5	10	25.0	0.586
Malaise	23	57.5	14	35.0	0.072

*: Statistically significant at $p \leq 0.05$ **Table 5.** Percentage distribution of SBP group and non-SBP group regarding history of ultrasound findings.

	SBP group n=40		Non-SBP group n=40		P value
	N	%	N	%	
Collection					0.766
Mild	3	7.5	6	15.0	
Moderate	16	40.0	15	37.5	
Marked	17	42.5	14	35.0	
Tense ascites	4	10.0	5	12.5	
Spleen size					0.832
Mean±SD	18.71±3.81		19.84±2.57		
Hepatic focal lesions	10	25.0	12	30.0	0.803

Table 6. Laboratory investigations of both SBP and non SBP groups.

Items	SBP group n=40		Non-SBP group n=40		P value
	Median	IQR	Median	IQR	
HB (g/dl)	9.05	3	8.80	2	0.740
TLC(x1000/mm ³)	8.45	21	8.45	7	0.758
PLT (x1000/mm ³)	94	43	93.50	75	0.729
PT	17.49	6	15.10	5	0.063
INR	1.30	0	1.20	0	0.075
ALT (U/L)	36.50	50	35	37	0.482
AST (U/L)	67.50	166	58.50	79	0.134
Total bilirubin (mg/dl)	2.60	4	1.55	3	0.036*
Direct bilirubin (mg/dl)	1.85	3	1.55	2	0.038*
NA (mmol/l)	130.50	9	130.50	12	0.707
K (mmol/l)	3.95	1	3.90	1	0.593
Creatinine (umol/L)	1.95	1	1.25	2	0.152
Albumin (g/dl)	2.40	0	2.50	0	0.352

*: Statistically significant at $p \leq 0.05$ **Table 7.** Ascetic fluid chemical analysis of study groups.

	SBP group n=40		Non-SBP group n=40		P value
	Median	IQR	Median	IQR	
TLC (cmm)	450	400	200	100	0.001*
LDH (U/L)	98	89	72	32	0.001*
Glucose (mg/dl)	128.5	109	138.5	71	0.881
Protein (mg/dl)	1545	1450	765	783	0.001*
Albumin (g/dl)	.80	0	.80	0	1.000
SAAG	1.50	0	1.60	0	0.950
Lactoferrin concentration in ascetic fluid (ng/ml)	112.43	139.25	48.23	1	0.011*

*: Statistically significant at $p \leq 0.05$ **Table 8a.** Receiver operating characteristic curve, sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and likelihood ratio for ascetic fluid lactoferrin in diagnosis and prognosis of spontaneous bacterial peritonitis.

	Area under the curve	Std. Error	P value	95% confidence interval		Cutoff value	Sensitivity (%)	Specificity (%)	PPV	NPV	Accuracy	Likelihood ratio
				Lower bound	Upper bound							
Lactoferrin	.664	.064	.011*	.539	.790	98	95	53	67	91	74	2.02

NPV, negative predictive value; PPV, positive predictive value. * Significant.

Table 8b. Receiver operating characteristic curve, sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and likelihood ratio for ascetic fluid lactoferrin in diagnosis and prognosis of spontaneous bacterial peritonitis.

	Area under the curve	Std. Error	P value	95% confidence interval		Cutoff value	Sensitivity (%)	Specificity (%)	PPV	NPV	Accuracy	Likelihood ratio
				Lower bound	Upper bound							
Lactoferrin	.796	.068	<.001*	.663	.929	98	93	75	80	91	84	3.72

Table 9. Correlation between ascetic fluid lactoferrin and different parameters among the studied groups.

Rho is spearman rank correlation test, and P value is significant <.05

	SBP group (n=40) (ascetic fluid lactoferrin)		Non-SBP group(n=40) (ascetic fluid lactoferrin)	
	Rho	P value	Rho	P value
laboratory investigations				
HB	-0.192	0.234	-.436-	0.005*
TLC	0.074	0.650	0.230	0.154
PLT	0.109	0.504	0.088	0.588
PT	0.090	0.579	0.031	0.852
INR	0.032	0.847	0.050	0.759
ALT	-0.202	0.212	-0.039	0.810
AST	-0.228	0.157	-0.099	0.541
TOTAL Bilirubin	0.061	0.709	-.354-*	0.025*
DIRECT Bilirubin	0.044	0.789	-.347-*	0.028*
NA	0.008	0.961	-0.100	0.540
K	0.043	0.792	0.172	0.288
Creatinine	-0.188	0.245	-0.056	0.732
Ascetic fluid analysis				
TLC	0.142	0.382	0.307	0.054
LDH	0.092	0.571	0.012	0.944
Glucose	-0.082	0.617	0.038	0.816
Protein	0.072	0.659	-0.035	0.831
Albumin	-0.213	0.187	-0.010	0.951
SAAG	-0.129	0.429	-0.175	0.280

Table 10. Relation between history of diseases, presence of disease based on cutoff point.

	Presence of disease				(P value)
	Yes		No		
	N	%	N	%	
HTN					
Yes	25	43.9	10	43.5	1.000
No	32	56.1	13	56.5	
DM					
Yes	31	54.4	15	65.2	0.458
No	26	45.6	8	34.8	
IHD					
Yes	6	10.5	2	8.7	1.000
No	51	89.5	21	91.3	
Impaired kidney disease					
Yes	6	10.5	3	13	1.000
No	15	89.5	20	87	
HCC					
Yes	22	38.6	0	0	0.001*
No	35	61.4	23	100	
HCV					
Yes	55	96.5	21	91.3	0.574
No	2	3.5	2	8.7	
HBV					
Yes	3	5.3	2	8.7	0.622
No	54	94.7	21	91.3	
Bilharziasis					
Yes	16	28.1	9	39.1	0.425
No	41	71.9	14	60.9	

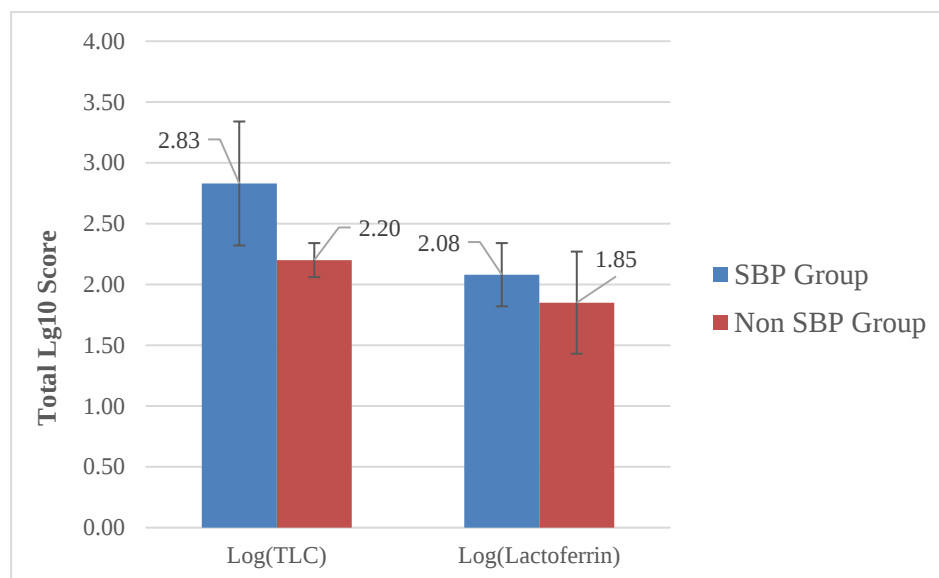
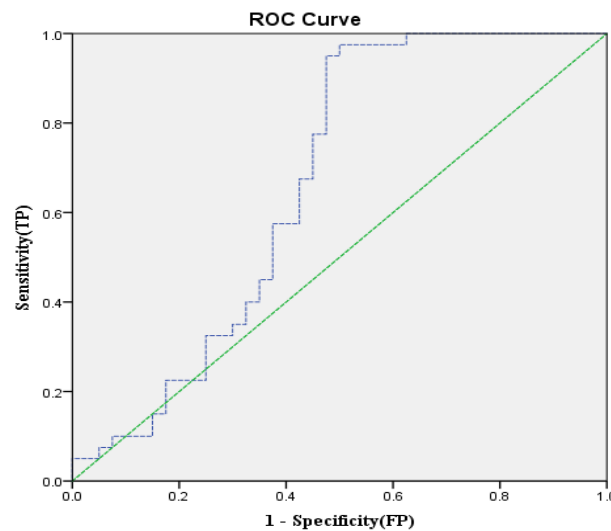
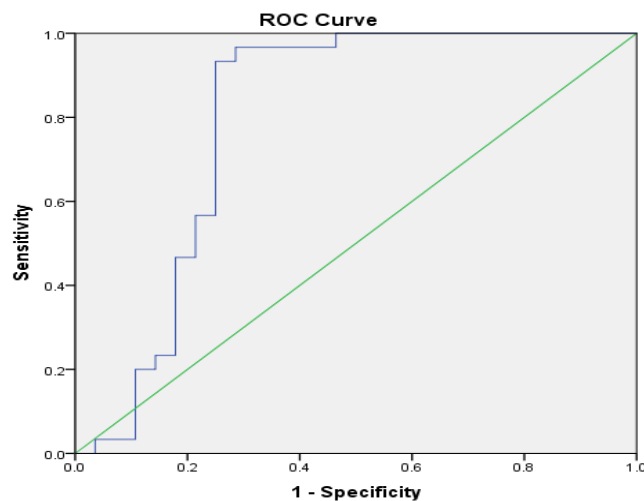
Figure1. Comparison of mean scores of both SBP group and non-SBP group regarding TLC and lactoferrin.

Figure 2a. ROC curve representing the clinical performance of lactoferrin as predictor of SBP.**Figure 2b.** ROC curve representing the clinical performance of lactoferrin as predictor of SBP after removal of HCC patients.

Discussion

The current study aimed at determining the diagnostic accuracy of ascetic fluid lactoferrin in diagnosis of spontaneous bacterial peritonitis among all consecutive cirrhotic patients with ascites admitted to Endemic and Infectious department, Suez Canal University Hospital to improve the care of patients with liver cirrhosis. This study was a diagnostic study that involved 80 patients with decompensated chronic liver diseases (Child B and C) cirrhosis with ascites. The outcomes of our study provide evidence of the clinical usefulness of ascetic fluid lactoferrin levels in patients with cirrhosis to differentiate those with and without SBP. The area under the ROC curve for the diagnosis of SBP in the

80 patients with ascites caused by cirrhosis after removing HCC patients was 0.796 (95% CI: 0.663-.929 $p < 0.001$). The sensitivity and specificity of the ascetic fluid lactoferrin assay was 93% and 75%, respectively, using a cut-off value ≥ 98 ng/ml. Analysis of ROC-AUC without removal HCC patients revealed AUC of 0.664 (95% CI: 0.539-.790). At optimal cutoff value ≥ 98 ng/ml, lactoferrin can detect 38 out of 40 in SBP. 21 out of 40 in non SBP group had lactoferrin levels < 98 ng/ml. Ascetic fluid lactoferrin had 95% sensitivity, 53% specificity. Analyzing 102 ascetic patients, Lee and his colleagues evaluated the usefulness of ascetic fluid lactoferrin level for the diagnosis of SBP. Of them, 24 patients had SBP, while 78 patients did not have SBP but had AF at a cut-off

level of 51.4 ng/mL, which had a 95.8% sensitivity and a 74.4% specificity. Regarding the evaluation of ascetic fluid lactoferrin's diagnostic accuracy in the diagnosis of spontaneous bacterial peritonitis, we concur with Lee's findings. Nevertheless, our ascetic fluid lactoferrin cut-off level was greater than the one found by Lee and his colleagues for the diagnosis of SBP [5]. Additionally, using 150 patients with cirrhosis and ascites divided into 100 patients with SBP and 50 patients without SBP, Abuefadl and his colleagues evaluated the diagnostic accuracy of AF lactoferrin and the optimal cutoff value for the diagnosis of SBP. They found that AF lactoferrin, at a cutoff level of 75.55 ng/ml, can distinguish patients with SBP from those without SBP with a sensitivity of 100% and a specificity of 98%. Regarding the ascetic fluid lactoferrin level's diagnostic accuracy as a biomarker for SBP in ascites patients, we concur with their findings. Nevertheless, our ascetic fluid lactoferrin cut-off level was greater than the one found by Parsi and his colleagues for the diagnosis of SBP [7]. In a study by Ali and his colleagues, the clinical usefulness of ascetic fluid lactoferrin as a biomarker for SBP was clarified. Using ROC analysis, it was discovered that a cut-off of 88 ng/ml for ascetic lactoferrin was necessary to identify patients as "with" or "without" SBP. Those with SBP had considerably greater mean ascetic fluid lactoferrin levels (180.8 ng/ml) than those without SBP (42.2 ng/ml, $P = 0.001$) [8]. Parsi and his colleagues assessed the utility of ascetic fluid lactoferrin level for the diagnosis of SBP in patients with cirrhosis in order to lessen the potential for false negative results and diagnostic mistake associated with a manual count of ascetic fluid PMN cells. We agree with Parsi's findings about the clinical relevance of ascetic fluid lactoferrin level as a biomarker for SBP in patients with ascites. However, the level of lactoferrin in our ascetic fluid that we used to diagnose SBP was lower than that of Parsi and his colleagues (a cutoff value surpassing 242 ng/ml was proved to have a 97% specificity and a 95% sensitivity) [9]. According to Essa and his colleagues, there was a highly significant rise in AF lactoferrin in the SBP group, with a cut-off level of 255 ng/ml. In the diagnosis of SBP, AF lactoferrin had a sensitivity of 100 and a specificity of 88.9%, respectively [10]. A positive bacterial culture is obtained in the minority of the patients with SBP and results are delayed for several days [11]. In the present study 40 SBP patients, 25 (62.5%) showed a

positive culture test. The most common microorganism identified in the present study was *E. coli* (37.5%) following by 5 (12.5%) *Staphylococci*, 3 (7.5%) *Klebsiella*, 2(5%) *Pseudomonas*, meanwhile the remaining of patients were culture negative. Culture was negative in non SBP group which was closer to a study done by Kalvandi and his colleagues, and Duah and Nkrumah [12,13]. In other studies, a ratio of 24% - 57% of ascetic fluid culture positivity has been noted. Common bacteria isolated from SBP patients have been *E. coli*, *Enterobacter*, *Enterococcus* and *Staphylococcus aureus*, *Klebsiella*, *Pseudomonas*, and *Streptococcus pneumoniae* [14]. The differences in the AF lactoferrin level cutoff value between our study and other studies may be explained by differences in the etiology of cirrhosis and the smaller sample sizes of SBP patients.

Conclusion and recommendations

Patients with SBP had higher levels of ascetic fluid lactoferrin than non SBP patients, so ascetic fluid lactoferrin can be used as a promising screening and diagnostic biomarker of SBP in cirrhotic patients. There was positive correlation between ascetic fluid lactoferrin and TLC of ascetic fluid in both SBP and non SBP groups with no statistical significance difference. The cut off points of ascetic fluid lactoferrin in diagnosis of SBP in different studies was variable, so to determine cut off value for diagnosis of SBP, we need to conduct more studies on a larger number of patients in multicenter.

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Conflicts of interest

The authors declare that they do not have any conflict of interest.

Data availability

All data generated or analyzed during this study are included in this published article.

Authors' contribution

All authors made significant contributions to the work presented, including study design, data collection, analysis, and interpretation. They also contributed to the article's writing, revising, or critical evaluation, gave final approval for the version to be published.

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