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Value of Different Diagnostic Markers in Spontaneous Bacterial Peritonitis in HCV Egyptian Cirrhotic Patients

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Abstract

Background: Spontaneous bacterial peritonitis (SBP) is a life-threatening infection occurring in 8% - 30% of ascitic cirrhotic patients; different laboratory diagnostics play a pivotal role for rapid and effective management of SBP patients. Polymorphonuclear leucocytic (PMNLs) count in Ascitic fluid (AF) is the mainstay for the diagnosis, whereas the diagnostic role of alternative biomarkers is rather controversial. In many studies, serum lipopolysaccharide binding protein (LBP) was elevated and Complement 3 (C3) level was significantly consumed in AF of SBP patients. Objectives: To evaluate the diagnostic value of serum LBP and AF C3 in HCV-cirrhotics with SBP in relation to other well-established serum and AF markers. Patients and Methods: One hundred and twenty patients with HCV-cirrhosis and ascites were enrolled and consented: 50 patients with non-SBP ascites in group A and 70 ascitic patients diagnosed with SBP according to clinical suspicion and PMLs count in AF ≥ 250 cells/mm^3 in group B in addition to 15 healthy individuals considered as a control group. Serum LBP, CBC, kidney and liver function tests, CRP, fasting and 2 h PP blood glucose and HCV antibodies were measured. AF samples were sent for C3 level, culture, PMNLs count, LDH, CRP, total proteins and albumin. Results: In patients with SBP, the level of serum LBP was not significantly high ($p > 0.05$) with best cut off value at 0.4500 and poor AUC (<0.6) with low sensitivity and specificity (53.3% & 57.7%, respectively). AF C3 was significantly reduced in AF ($p < 0.001$) with best cut off value at 144.2 and almost excellent AUC (0.889) with good sensitivity and specificity (82% & 84%, respectively). AF culture showed significant difference between both patients groups ($p < 0.05$) but with low sensitivity (33.3%). Serum and AF CRP and AF PMNLs count were of high significance in SBP diagnosis ($p < 0.001$). Conclusion: Serum LBP level showed low significance while AF C3 was significantly reduced in patients with SBP. AF culture showed significant difference between both groups but with low sensitivity while serum, AF levels of CRP and AF

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PMNLs count were highly significant, and the latter is still considered the gold standard for SBP diagnosis.

Keywords

Spontaneous Bacterial Peritonitis-Serum Lipopolysaccharide Binding Protein-Ascitic Fluid Complement 3-C-Reactive Protein-Ascitic Fluid Culture

1. Introduction

Spontaneous bacterial peritonitis (SBP) is a frequent, life-threatening bacterial infection occurring in patients with advanced liver cirrhosis and ascites [1]. Spontaneous bacterial peritonitis (SBP) is diagnosed by testing of ascitic fluid (AF) obtained by abdominal paracentesis. A polymorphonuclear leucocytic (PMNLs) count ≥250 cells/mm^3 has been considered the gold standard in SBP diagnosis as it is a highly sensitive diagnostic marker [2]. Growth of bacteria in the AF culture doesn't establish the diagnosis of SBP, because bacteria are detected only in about 40% of cases with SBP [3]. Identifying type of bacteria and detecting sensitivity to antibiotics among patients with SBP allow initiating early and effective antibiotic therapy [4]. SBP occurs when a bacterial infection spreads to the AF through the gut wall or lymphatics but less commonly via hematogenous spread in absence of a recognized intra-abdominal source of bacterial infection or malignancy [5]. SBP is probably related to impaired defensive mechanisms, such as depressed reticuloendothelial system and phagocytic activity, leucocyte dysfunction, reduced serum complement, and weak bactericidal properties of AF [5]. AF Complement 3 (C3) concentration and opsonic activities are the most important local protective mechanisms against SBP. The Complement 3 is reduced in patients with advanced cirrhosis [6]. Patients with reduced AF C3 concentration and opsonic activities were potentially at risk to develop SBP [7].

LBP (lipopolysaccharide binding protein) is a soluble acute-phase protein that binds bacterial lipopolysaccharide (LPS) to elicit immune responses by presenting the LPS to important cell surface pattern recognition receptors called CD14 (cluster of differentiation 14) and TLR4 (Toll-like receptor 4) [8]. Once in the circulation, endotoxins promote hepatic synthesis of LPS-binding protein (LBP). CD14 is a component of the LPS receptor, expressed on the membrane of myeloid containing cells that binds LPS-LBP complexes [9].

LBP peak occurs in plasma 2 to 3 days after transient bacteriemia or endotoxinemia, and levels are increased up to 3 days later [9] [10]. In several clinical studies, plasma level of LBP seems to reflect better the long-term exposure to bacteria with their endotoxins than endotoxin itself [11] [12]. LPS acts as the prototypical endotoxin because it binds the CD14/TLR4 receptor complex which promotes the secretion of pro-inflammatory cytokines in many cell types especially macrophages and B cells. Being of high importance to gram-negative bacteria, these molecules make candidate targets for new antimicrobial agents [13]. LPS function has been under experimental research for several years due to its role in activating many transcription factors [14]. *Said et al*. showed that LPS causes an IL-10-dependent inhibition of CD4 T-cell expansion and function by up-regulating PD-1 (programmed death-1) levels on monocytes, which leads to IL-10 production by monocytes after binding of PD-1 by PD-L (programmed death-1 ligand) [15]. Increased LBP is the only factor that was associated with severe bacterial infection in a multivariate analysis; monitoring of serum LBP could, therefore, help to plan for antibiotic prophylaxis in cirrhotic patients with ascites [16].

We aimed in this work to evaluate the value of serum LBP and AF Complement 3 levels in HCV-cirrhotic patients with ascites and SBP in relation to other previously used diagnostic methods such as: serum and AF CRP, PMNLs count and AF culture.

2. Patients and Methods

This was a prospective study carried on during 2013 till August 2014. A total of one hundred twenty Egyptian patients (66 males and 54 females) diagnosed with liver cirrhosis, ascites and with HCV antibodies positive were enrolled, The diagnosis of liver cirrhosis was based on imaging, clinical, and laboratory findings, They were prospectively recruited from Internal Medicine Out-patients clinics and Internal Medicine Department, Kasr EL-Aini Hospital, Cairo University, Their age ranged between 40 - 65 years, in addition to 15 healthy vol-

unteers considered as the control group who were age and sex matched with the patients. The patients were divided into 2 groups *Group A*: 50 patients with liver cirrhosis, ascites but without SBP. *Group B*: 70 patients with liver cirrhosis, ascites with clinical suspicion of SBP. Diagnosis of SBP was based on the presence of clinical signs of peritoneal infection (fever, altered mental status, and diffuse abdominal pain) or asymptomatic ascites with PMNLs count ≥250 cells/mm^3 (discovered accidentally on routine AF analysis in patients with resistant ascites or hepatorenal syndrome). An approval of the ethical committee was obtained before the start of this study and written consents were taken from all participants (or first degree relatives in patients with altered consciousness) after full explanation of all parts of the study.

Exclusion criteria: Evidence of secondary bacterial infection or secondary causes of abdominal sepsis (AF protein > 2.5 g/dl), patients with TB peritonitis, non-HCV causes of cirrhosis (Autoimmune hepatitis, HBsAg + ve Hemochromatosis, Biliary or Cryptogenic Cirrhosis), treatment with antibiotics in the last 6 weeks, presence of hepatocellular carcinoma, serum creatinine >1.5 mg/dL, DM, malnutrition (to exclude protein catabolic state), and refusal to participate. Bacterial infection was ruled out by clinical history, physical examination, total and differential leucocytic count, urine analysis and culture and chest radiograph. All patients were subjected to thorough history taking and clinical examination. All participants were subjected to laboratory investigations including: liver function tests [Transaminases (AST, and ALT), serum albumin, total proteins, total bilirubin, Prothrombin concentration and INR] done by colorimetric techniques using auto analyzer (SYNCHRON CX5 from Beckman), CBC, C-reactive protein, Fasting and 2 h postprandial blood glucose levels, HCV antibody (by ELISA), Urea, serum creatinine, sodium and potassium. Serum and ascitic C-reactive protein was measured using the latex agglutination kits (AVITEX CRP, Omega Diagnostics Ltd., Alva, Scotland, UK). Abdominal Ultrasonography was performed for all patients in El Ebrashy Gastroenterology and Hepatology Unit, Internal Medicine Hospital, Cairo university Using General Electric convex linear Ultrasonography (5 mega Hz, GE Medical System, *Milwaukee*).

Bedside AF samples were obtained from all patients on the day of admission under complete aseptic precautions and all samples were analyzed within one hour. Examination of the aspirated samples included: PMNLs counts done by automated system (SYSMEX cell counter), Assay of Complement 3, total proteins, albumin, LDH, C-reactive protein levels. Bacteriological examination of AF samples was done by direct inoculation of 10 ml of AF aseptically at 37˚C into aerobic and anaerobic BactAlert blood culture bottles which were then placed in a fully automated BacT/Alert culture system. Cultures were done on routine culture media including MacConkey agar, Mannitol agar plates and Blood agar plates, Culture negative cases were considered after 7 days. Serum lipopolysaccharide binding protein (LBP) and ascitic Complement 3 (C3) were done at Abou El Reesh Hospital immunology lab, Cairo University. Serum LBP was measured by immunometric assay substrate using an automated analyzing system and the kits supplied by (Immulite LBP; DPC, *Los Angeles*, *CA*, *USA*). The reference range was 0.78 - 50 ng/ml. C3 assay was done using kits supplied by (Assay Pro LLC, *St. Charles*, *Missouri*, *USA*) with reference range of 0.5 - 1.8 mg/ml.

3. Statistical Methodology

Analysis of data was done using SPSS (statistical program for social science version 17, produced by IBM SPSS Inc., *Chicago*, *USA*). Sensitivity, specificity, positive and negative predictive values were calculated. Spearman Correlation (*r*) co-efficient test was used to rank variables versus each other positively or inversely. ROC Curve (receiver operator characteristic curve) was used to find out the best cut off value, and validity of certain variable.

4. Results

Demographic and clinical characteristics were compatible and showed no statistically significant difference between group A and group B (**Table 1**). In group A, the number of patients in Child class B and C were 24% and 76% while in group B 11.4% and 88.6%, respectively. Abdominal pain and fever were the most frequent presentations in patients with SBP and were reported in 78.5% and 68.5% of patients, respectively (**Table 2**). Group B Patients showed a highly significant ascites inflammatory response than group A (**Table 3**) confirmed by more AF LDH (IU/L) (mean ± SD 185.06 ± 58.39 IU/L vs mean ± SD 84.37 ± 33.65 IU/L respectively, $p < 0.001$), higher PMNL count/mm^3 (mean ± SD 529.0 ± 250.18 vs mean ± SD 107.87 ± 60.39 respectively, $p < 0.001$) and more AF C-reactive protein (mg/dl) (mean ± SD 65.2 ± 24.40 vs 8.71 ± 7.99 respectively, $p < 0.001$).

Table 1. Demographic and clinical features of all patients.

Variable	Group A (n = 50)	Group B (n = 70)	*p*
Male gender	30 (60%)	36 (51.4%)	>0.05
Child B	12 (24%)	8 (11.4%)	>0.05
Child C	38 (76%)	62 (88.6%)	>0.05
Abdominal pain	7 (14%)	55 (78.5%)	**<0.05**
Altered consciousness	15 (30%)	24 (34.2%)	>0.05
GI bleeding	16 (32%)	8 (11.4%)	>0.05
Fever	4 (8%)	48 (68.5%)	**<0.05**

p value > 0.05 is considered non-significant while <0.05 is significant.

Table 2. Age and laboratory parameters in all participants.

Variable	Controls (n = 15)	Group A (n = 50)	Group B (n = 70)	*r*	*p*
Age (years)	42.66 ± 9.02	53.31 ± 6.66	54.73 ± 6.62	0.929	>0.05
WBC (mm^3)	6721 ± 1881	6660 ± 2330	7780 ± 4270	1.032	>0.05
Neutrophil count (mm^3)	5192 ± 1674	5080 ± 1851	6273 ± 3625	1.239	>0.05
Hemoglobin (gm/dl)	12.23 ± 1.23	9.73 ± 1.3	9.85 ± 1.17	0.887	>0.05
Platelets ×1000 (mm^3)	314.26 ± 2.6	90 ± 31.3	89 ± 37.1	1.123	>0.05
Serum albumin (g/dl)	4.14 ± 0.65	2.36 ± 0.51	2.11 ± 0.38	−2.529	**<0.05**
Total proteins (g/dl)	7.33 ± 0.66	6.01 ± 1.08	6.04 ± 0.83	0.127	>0.05
ALT (IU/l)	23.16 ± 9.27	67.50 ± 54.87	91.20 ± 41.13	3.313	**<0.05**
AST (IU/l)	25.30 ± 4.92	90.88 ± 34.92	79.63 ± 29.23	−2.465	>0.05
Total bilirubin (mg/dl)	1.01 ± 0.12	5.45 ± 4.50	4.23 ± 2.60	1.133	>0.05
INR	1.06 ± 0.05	1.84 ± 0.56	1.87 ± 0.78	0.198	>0.05
Urea (mg/dl)	31.01 ± 9.21	32.12 ± 7.48	33.67 ± 5.72	0.981	>0.05
Creatinine (mg/dl)	0.73 ± 0.25	0.87 ± 0.25	1.04 ± 0.16	3.895	**<0.05**
Sodium (mmol/l)	139.45 ± 3.78	130.36 ± 9.26	129.93 ± 10.53	0.178	>0.05
Potassium (mmol/l)	3.87 ± 1.4	3.76 ± 0.65	3.65 ± 0.79	0.586	>0.05
Fasting blood glucose	91.71 ± 5.98	88.14 ± 12.8	88.44 ± 10.96	−0.231	>0.05
2 h PP blood glucose	125.29 ± 19.28	117.2 ± 20.83	113.3 ± 17.16	−0.423	>0.05
Serum LDH (IU/l)	356.76 ± 141.42	362.98 ± 149.59	442.00 ± 116.59	−2.653	**<0.05**
Serum LBP (ng/ml)	0.41 ± 0.24	0.44 ± 0.34	0.56 ± 0.5	0.640	>0.05
Serum CRP (mg/dl)	7.76 ± 4.1	8.64 ± 4.3	22.2 ± 5.6	−2.372	**<0.05**

Data are presented by mean ± SD; CRP: C-reactive protein, INR: international normalized ratio; LDH: Lactate dehydrogenase; LBP: Lipopolysaccharide binding protein; *p* value > 0.05 is considered non-significant while <0.05 is significant.

Regarding AF Complement 3, the results were highly significant for SBP diagnosis (C3 in ng/ml) (mean ± SD 202.13 ± 75.71 vs 86.02 ± 48.91, respectively, $p < 0.001$). The results were also significant regarding AF albumin and total protein ($p < 0.001$). AF cultures were positive in 33.3% of patients in group B compared to 7.7% in group A (**Table 3**), However, in spite of low sensitivity it was statistically significant ($p < 0.05$). The results showed no significant difference regarding serum LBP between the studied groups ($p > 0.05$), as it was of low sensitivity and specificity (53.3% and 57.7%, respectively) in SBP diagnosis.

Regarding other laboratory parameters, there was a statistically significant difference as regard ALT, serum creatinine, albumin, LDH and serum CRP between group A and B ($p < 0.05$) (**Table 2**). We observed a statistically

Table 3. Ascitic fluid parameters.

Variable	Group A (n = 50)	Group B (n = 70)	*r*	*p* value
***Ascitic fluid analysis*:**				
Ascitic fluid LDH (IU/L)	84.37 ± 33.65	185.07 ± 58.39	−6.928	**<0.001**
Ascitic fluid T. proteins (g/dl)	0.52 ± 0.28	1.23 ± 0.23	−6.972	**<0.001**
Ascitic fluid Albumin (g/dl)	0.24 ± 0.22	0.50 ± 0.25	−4.506	**<0.001**
Ascitic fluid PMNLs (mm^3)	107.87 ± 60.39	529.00 ± 280.18	−7.511	**<0.001**
Ascitic fluid C3 (ng/ml)	202.13 ± 57.71	86.02 ± 48.91	−6.422	**<0.001**
Ascitic fluid CRP (mg/dl)	8.71 ± 7.99	65.2 ± 24.40	−6.621	**<0.001**
Ascitic fluid culture				
No growth (after 7 days of inoculation)	47 (92.3%)	46 (66.7%)		>0.05
Growth of gram-ve bacteria	3 (7.7%)	24 (33.3%)		**<0.05**

$p > 0.05$ is considered non-significant while <0.05 is significant, Data are presented by mean ± SD; LDH: Lactate dehydrogenase; CRP: C-reactive protein; C3: Complement 3; PMNLs: Polymorphonuclear leucocytic count.

significant positive correlation between serum LBP versus AF protein & albumin ($p < 0.05$) but correlations were not significant regarding other serum and ascites laboratory variants ($p > 0.05$) (**Table 4**).

In SBP group, There was a statistically significant positive correlation between AF culture versus AF PMNLs count, LDH and CRP ($p < 0.001$), and serum CRP ($p < 0.001$), while there was no significant correlation versus serum LBP, serum albumin, LDH and other serum and ascitic variables (**Table 4**).

Correlation between AF C3 and other serum and ascitic parameters in SBP group was not statistically significant (**Table 4**).

For diagnosis of SBP, Serum LBP showed best cut off value At 0.4500, AUC 0.543 (not good) with poor sensitivity and specificity (53.3% & 57.7%, respectively) with non significant $p > 0.05$ while AF C3 showed best cut off value at 144.2, AUC 0.899 (almost excellent), good sensitivity and specificity (82% & 84%, respectively) and highly significant *p value* < 0.001 (**Table 5**), (**Figure 1** and **Figure 2**).

5. Discussion

Spontaneous bacterial peritonitis (SBP) is the development of peritonitis despite the absence of an obvious primary source of infection [17]. Bacterial endotoxins promote the synthesis of lipopolysaccharide (LPS) binding protein (LBP), and forms a LPS-LBP complex which may increase in serum of patients with SBP [18]. Ascitic Fluid (AF) Complement 3 (C3) level is the most important factor to provide local protection against bacterial peritonitis and its level is markedly reduced in AF of patients with SBP [19]. In such cases, the serum level of LBP, AF C3, culture and PMNLs count were studied and correlated with other serum and AF parameters in cases with SBP. In SBP patients, the most frequently occurring symptoms are fever and abdominal pain [20], this was the position in our study (occurred in 68.5% and 75.5% of the patients, respectively) with $p < 0.05$ which was also in accordance with *Badawy AA et al*., [21] and *Oliviero R et al*., [22]. In our study , 88.6% of patients with SBP (group B) were in Child class C and the rest of the patients (11.4%) were in Child class B which denoted that SBP developed only in patients with Child classes B and C, this was in agreement with many studies concluded that SBP developed with more advanced liver disease [21]-[25].

For SBP diagnosis, AF PMNLs count (≥250 cell/mm^3) was chosen because it was considered a sensitive diagnostic marker [26] and growth of bacteria in the AF culture does not confirm the diagnosis of SBP, since bacteria are detected only in about 40% of SBP cases [27], which was agreed with our study (Sensitivity of AF culture and AF PMNLs count were 33.3% and 97.14% ,respectively significant *p* values) and with *Badawy AA et al*., and *Le et al.*, who found that PMNLs count was highly significant in AF of patients with SBP more than the non-SBP group ($p < 0.001$) and AF culture was positive in only about one-third of the cases despite being significant [21] [28].

Patients with SBP showed a highly significant AF inflammatory response than non-SBP group and this was confirmed by more AF LDH ($p < 0.001$), higher PMNL count/mm^3 ($p < 0.001$), AF albumin and total protein ($p < 0.001$) which was in agreement with *Badawy AA et al*., [21] and more AF CRP (mg/dl) (mean ± SD 65.2 ± 24.40 vs 8.71 ± 7.99 respectively, $p < 0.001$) which was in accordance with *Yildirim et al.*, and *Kamel et al.*,

Table 4. Correlation between serum LBP, AF culture and AF complement versus other variables in SBP group.

Variable	Ascitic fluid culture		Serum LBP		AF C3 level	
	r	*p*	*r*	*p*	*r*	*p*
Age	−1.095	>0.05	−0.007	>0.05	−0.137	>0.05
Urea (mg/dl)	−0.356	>0.05	0.117	>0.05	0.202	>0.05
Creatinine (mg/dl)	1.230	>0.05	0.036	>0.05	0.031	>0.05
ALT (IU/l)	−0.110	>0.05	0.113	>0.05	−0.033	>0.05
AST (IU/l)	−0.132	>0.05	−0.034	>0.05	0.012	>0.05
Serum albumin (g/dl)	1.158	>0.05	−0.049	>0.05	−0.026	>0.05
TP (g/dl)	0.445	>0.05	−0.094	>0.05	−0.051	>0.05
Serum LDH (IU/l)	−0.397	>0.05	−0.056	>0.05	0.126	>0.05
Total bilirubin (mg/dl)	−0.423	>0.05	−0.046	>0.05	0.114	>0.05
INR	−0.352	>0.05	0.10	>0.05	−0.130	>0.05
Serum CRP (mg/dl)	−2.230	**<0.05**	0.136	>0.05	−1.488	>0.05
AF PMLs (mm^3)	−2.097	**<0.05**	0.199	>0.05	−1.131	>0.05
AF protein (g/dl)	−1.476	>0.05	0.423	<0.05	−0.772	>0.05
AF albumin (g/dl)	−1.646	>0.05	0.137	<0.05	−1.544	>0.05
AF LDH (IU/l)	−2.46	**<0.05**	0.170	>0.05	−1.785	>0.05
AF CRP (mg/dl)	−2.213	**<0.05**	0.183	>0.05	−1.510	>0.05

$p > 0.05$ is considered non-significant while <0.05 is significant; C3: Complement 3; CRP: C-reactive protein; INR: International normalized ration; LDH: Lactate dehydrogenase; PMNLs: Polymorphonuclear leucocytic count; TP: Total proteins; AF: Ascitic fluid.

Table 5. Validity of serum LBP, AF C3, AF culture and ascetic PMNLs count in diagnosis of SBP among studied groups.

Variables	Serum LBP	AF fluid culture	AF PMNLs count (mm^3)	AF C3 level
Sensitivity	53.3%	33.33%	97.14%	82%
Specificity	57.7%	92.31%	98.00%	84%
PPV	42.3%	71.43%	40.96%	83.7%
NPV	46.7%	70.95%	50.00%	82.4%
p Value	>0.05	<0.05	<0.001	<0.001

PPV: Positive predictive value; NPV: Negative predictive value; LBP: Lipopolysacchraide binding protein; C3: Complement 3.

who found significant elevation of CRP levels in both AF and serum of SBP patients more than non-SBP group [29] [30] Similar results were obtained by the present study. In 2004, Runyon reported that AF protein concentration ≤1.0 g/dl, was associated with a significantly higher risk for spontaneous peritonitis which was not met in our study as most of the patients in SBP group had AF total protein ≥1.0 g/dl (Mean ± SD 1.23 ± 0.23 g/dl, $p < 0.001$) [31].

In this study, AF C3 level was significantly consumed in patients with SBP in comparison to non-SBP group ($p < 0.001$) which was agreed with *Mustafa et al.*, who found that AF C3 concentration was markedly consumed (7.3 ± 4.3 mg/dl) in patients with SBP in comparison to the non-SBP group (16.4 ± 11.3 mg/dl) ($p = 0.009$) [19]. *Bird et al.*, noticed that decreased plasma C3in SBP patients is primarily caused by increased activation of the classical pathway and not impaired hepatic synthesis. Activation and consumption of C3 is one factor causing the low AF C3 concentration observed in SBP patients and in agreed with our study [32]. *Kamal et al.*, reported that the reduced levels of AF C3 in SBP patients is mostly a predisposing factor rather than consumption by complement activation due to bacterial infection [33]. Many mechanism were suggested for the lower level of C3 in the AF: dilution, decreased hepatic synthesis of complement and greater consumption of C3 due to

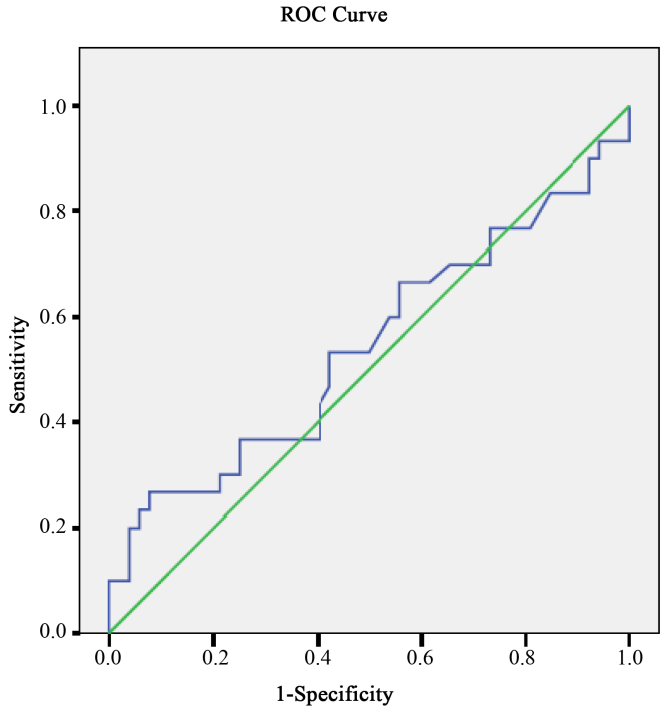

Figure 1. Roc curve shows sensitivity and specificity of serum LBP in diagnosis of SBP in cirrhotic, ascitic patients.

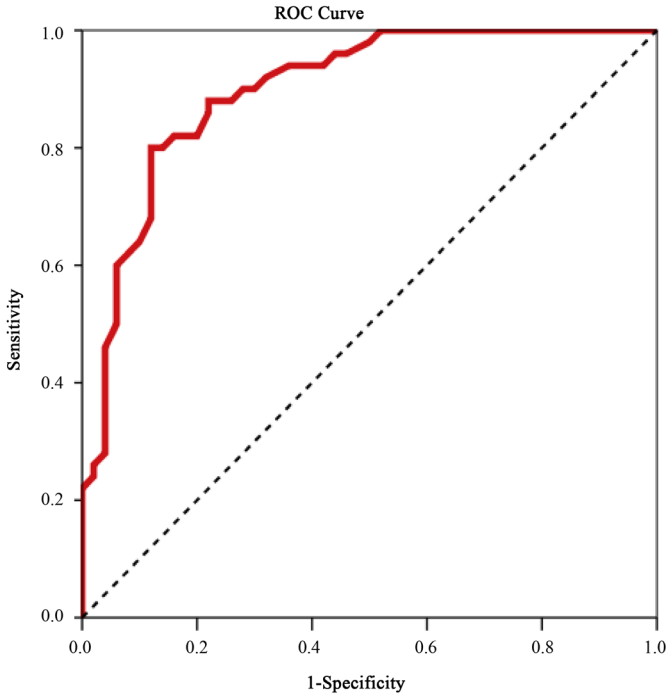

Figure 2. Roc curve shows sensitivity and specificity of ascitic fluid C3 in diagnosis of SBP in cirrhotic, ascitic patients.

activation of the alternative complement pathway [5]. The low percentage of positive AF cultures is mostly due to the relatively low concentration of organisms in the AF as compared with other organic fluids (e.g., urine),

relatively small volume of AF samples, inappropriate conditions for storage of the sample or delay in transferring the sample to the lab [22] [29]. The sensitivity of AF culture can be augmented by using bedside sampling and use of blood culture bottles rather than conventional method for culture as concluded by *Pawar GP, et al.* [34].

C-reactive protein (CRP) has been reported to be a dependable predictor for SBP and a good indicator of therapeutic effectiveness and outcome in cirrhotic patients [35] [36]. In our study, The concentrations of AF CRP and PMNLs count were significantly higher in patients with SBP than in those without SBP which was in accordance with *Le et al*., [28] and other Authors [21] [37] [38].

Serum lipopolysaccharide-binding protein (LBP) was not significantly higher in our SBP patients (0.56 ± 0.5 mg/dl) than non-SBP group (0.44 ± 0.34 mg/dl) ($p > 0.05$). These findings signify the low sensitivity of serum LBP in diagnosing SBP in this study (sensitivity 53.3% and specificity 57.7%). These findings were in agreement with *Maria Papp et al*., who evaluated the accuracy of some acute phase proteins in the identification of bacterial infections of AF, one of them was LBP [39]. These findings were not coinciding with *Tang NY and Chen WQ*, who studied the role of serum & AF LBP in 3 groups; cirrhotic group with SBP, cirrhotic group without SBP and cirrhotic group with no ascites. The serum levels of LBP were significantly higher in the cirrhotic group with SBP than in the cirrhotic group without SBP and the cirrhotic group with no ascites ($p < 0.001$) [40]. In 2004, *Albillos A et al.*, prospectively analysed the presence of severe bacterial infection in AF of 84 cirrhotic patients, they followed up for a median of 46 weeks. The total probability of such infection in patients with raised and normal LBP was 32.4% and 8.0% ($p = 0.004$), respectively [41]. So, monitoring of LBP could help to target ascitic cirrhotic patients for antibiotic prophylaxis which in turn, may give an additional value for monitoring of serum LBP level [41].

6. Conclusion

In conclusion, regarding SBP diagnosis, serum LBP was of low significance while AF fluid culture showed a significant difference between both patients groups but with low sensitivity. On the other hand, serum and AF levels of CRP and AF PMNLs count were highly significant. Because of the high diagnostic yield of AF Complement 3 level (which was significantly reduced), antibiotic therapy can be considered as a prophylactic measure against SBP in cirrhotic patients with low AF C3 level.

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Disclosure

The authors declare no conflicts of interest.

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