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Liver Function Status in Bacterascites versus Spontaneous Bacterial Peritonitis in Patients with Liver Cirrhosis

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ABSTRACT

Background: Spontaneous bacterial peritonitis (SBP) is a severe complication of decompensated cirrhosis, and the in hospital mortality for SBP ranges from 21.3% to 37%.

Objective: The aim of the present study was to assess the clinical characteristics, microbiological findings, and clinical course in patients diagnosed with bacterascites in comparison with patients with spontaneous bacterial peritonitis, regarding liver status.

Patients and methods: This study was conducted on 50 Patients with ascites who were admitted at Internal Medicine Department, Benha University Hospital.

Results: There was no significant difference between the two studied groups. There was no significant difference between the two studied groups regarding hemoglobin, total leukocyte count (TLC) and platelets. There was no significant difference between the two studied groups regarding liver parameters. There was a significant difference between the two studied groups regarding polymorphonuclear neutrophil (PMN) count. There was a significant difference between the two studied groups regarding positive cultures and prevalence of isolated organisms from the ascitic fluid. There was a significant difference between the two studied groups regarding antimicrobial agents use.

Conclusion: Bacterascites is a complication of cirrhosis comparable to SBP with respect to clinical background and prognosis. There is a significant difference between the two studied groups regarding positive cultures and prevalence of isolated organisms from the ascitic fluid. There is a significant difference between the two studied groups regarding antimicrobial agents use.

Keywords: Bacterascites, Spontaneous Bacterial Peritonitis, Liver Cirrhosis.

INTRODUCTION

Ascites is the accumulation of lymphatic fluid within the peritoneal cavity**.** It is one of the major complications of decompensated liver disease, along with variceal hemorrhage and hepatic encephalopathy. Additionally, ascites is the most common cause of hospitalization in cirrhotic patients [(1)]**.** The development of ascites is a marker of prognosis in liver cirrhosis, as it indicates a reduction in 1- and 5-years survival rates by 15% and 23.5%, respectively [(2)]**.**

Spontaneous bacterial peritonitis (SBP) is a severe complication of decompensated cirrhosis. The inhospital mortality for SBP ranges from 21.3% to 37%. Bacterial translocation is the major cause of SBP. Therefore, no intra-abdominal source of infection can be found. Ascites culture is the gold standard for SBP diagnosis, and a high ascites polymorphonuclear leukocyte (PMN) count is accepted as an early indicator of SBP. An ascites PMN count $\geq 250/mm^3$ is considered to indicate empirical antibiotic therapy based on the current guidelines [(3)].

Bacterascites is defined by an ascitic fluid polymorphonuclear neutrophil (PMN) count below 250/μL and a positive ascitic fluid culture results in the absence of an evident intra- abdominal, surgically treatable source of infection. It is a different clinical entity than spontaneous bacterial peritonitis (SBP), which is characterized by a neutrophil reaction in ascites regardless of the bacterial culture result. Bacterascites is prevalent in 8%- 11% of all patients with cirrhosis and ascites, and the clinical significance seems to vary according to how the infection was acquired [(4)].

Several hypotheses have been proposed to explain the potential underlying pathophysiological mechanisms. The most common theory implicates that the bacterial colonization of ascites is caused by bacterial translocation from the intestinal lumen or by secondary translocation from a concomitant infection from extra-intestinal sites (e.g. urogenital or respiratory tract) [(5)]**.**

The absence of an inflammatory response could be interpreted as an early phase of SBP in which the neutrophil response has not commenced yet, or a spontaneously resolving infection, determined by good host defences or less virulent pathogens. Furthermore, bacterascites caused by commensal skin bacteria has been attributed to exogenous contamination of the ascitic fluid sample and bacterascites with multiple pathogens may be caused by traumatic paracentesis. The indication for antibiotic treatment of bacterascites is generally regarded to be dependent on the supposed pathophysiological mechanism and the clinical situation [(6)].

The AASLD practice guideline regarding the management of ascites states that patients with ascites and convincing signs or symptoms of infection should receive empiric antibiotic treatment [(7)]. This

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recommendation is based on one study with 36 cases of bacterascites receiving a follow- up paracentesis, in which 62% of the cases spontaneously resolved and 38% progressed to SBP [8].

The EASL clinical practice guideline endorses this recommendation and further states asymptomatic patients should undergo a second paracentesis when culture results come back positive. Patients in whom the repeated ascitic PMN count is greater as or equal to 250/μL should be treated for SBP, and the remaining patients (i.e. PMN count below 250/μL) should be followed up [9]. This guideline is based on a consensus document of the International Ascites Club in 2000. [10].

Although bacterascites is not an uncommon condition, relatively few studies on prognostic factors and outcome of this ascitic fluid infection have been reported [6].

The aim of the study was to assess the clinical characteristics, microbiological findings, and clinical course in patients diagnosed with bacterascites in comparison with patients with spontaneous bacterial peritonitis, regarding liver status.

PATIENTS AND METHODS

This study was conducted at Internal Medicine Department, Benha University Hospital. This study was conducted on 50 patients with ascites who were admitted at Internal Medicine Department, Benha University Hospital.

Inclusion criteria: Patients admitted with ascites from both sexes included.

Exclusion criteria: Patients refused to be implicated in the study.

Patients were subjected to full history taking, complete clinical examination, and investigations as:

Routine Laboratory Tests: CBC (Hemoglobin (Hb), white blood cells (WBCs), and platelets count). Fasting blood sugar (mg/dl), and HBA1c for diabetic patients.

Markers of Liver injury: Alanine amino transferase (ALT) (U/L), and aspartate amino transferase (AST) (U/L).

Liver function tests: Serum bilirubin (total, direct) (mg/dl), serum albumin (g/dl), and prothrombin time (second) and INR (International normalized ratio).

Markers: HCV-Ab (Hepatitis C virus antibody) and HBs Ag (Hepatitis B virus surface antigen) by third generation enzyme linked immunosorbent assay (ELISA).

- **Quantitative PCR for HCV RNA.**
- **Renal function tests:** serum creatinine (mg/dl), blood urea.
- **Serum alpha feto protein (AFP) (ng/dl).**
- **Paracentesis and examination of ascetic fluid:**
  1. White blood cell (WBC) and PMN count in ascites.
  2. Glucose, protein, LDH and serum ascites albumin gradient.
  3. **Radiological investigations:**

Pelvi-Abdominal Ultrasonography: Liver: size, texture, border, reflectivity, homogeneity, periportal thickening, hepatic veins and pattern. Portal vein: diameter, patency, direction of flow, respiratory variation and velocity by color Doppler assessment. Spleen: size, splenic vein diameter, collaterals. Presence of ascites and internal echoes. Lymph nodes and extrahepatic spread, and portal hypertension and superior mesenteric vein patency.

SBP is diagnosed when: Ascitic fluid polymorphonuclear leucocytes (PMN) count ≥ 250 cells/μL. Ascitic fluid culture was positive, and there was no evident intra-abdominal surgically treatable source for infection [11].

The diagnosis of BA was made when: The ascitic fluid PMN count < 250 cells/μL, ascitic fluid culture was positive, there was no evident intra-abdominal surgically treatable source for infection [10], and severity of cirrhosis was assessed at the time of the SBP or BA diagnosis using the Model for End-Stage Liver Disease (MELD) score [12] and Child-pugh classification [13].

Ethical consent:

An approval of the study was obtained from Benha University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation. 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.

Statistical Analysis

All data were collected, tabulated and statistically analyzed using SPSS 24.0 for windows (SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) and Fisher exact test were used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD for parametric and median and range for non-parametric data. Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively. All statistical comparisons were two tailed with significance Level of P-value ≤ 0.05 indicates significant, p < 0.001 indicates highly significant difference while, P > 0.05 indicates Non-significant difference.

RESULTS

Regarding demographic data, there was no significant difference between the two studied groups (Table 1).

Table (1): Demographic data distribution between the two studied groups

		SBP (N=30)	Bacterascites (N=20)	t / χ^2	P
Age (years) Mean ± SD		55.32 ± 8.46	54.28 ± 7.54	.444	.659
Sex	Male	18 (60%)	13 (65%)	.127	.721
	Female	12 (40%)	7 (35%)		
BMI (kg/m^2) Mean ± SD		26.37 ± 3.69	25.58 ± 3.74	.738	.464
Residence	Urban	21 (70%)	12 (60%)	.535	.465
	Rural	9 (30%)	8 (40%)		

There was no significant difference between the two studied groups regarding severity scores (Table 2).

Table (2): Severity assessment among the two groups

		SBP (N=30)		Bacterascites (N=20)		X^2/t	P
		N	%	N	%		
Ascites	Mild	9	30	8	40	.691	.708
	Moderate	17	56.7	9	45		
	Severe	4	13.3	3	15		
Child-Pugh Class	B	16	63.3	13	65	.005	.945
	C	9	36.7	7	35		
Child-Pugh score Mean ± SD		12.35 ± 1.29		12.09 ± 1.22		.713	.479
MELD Mean ± SD		20.64 ± 4.98		20.14 ± 4.55		.359	.721

There was no significant difference between the two studied groups regarding hemoglobin, TLC and platelets (Table 3).

Table (3): CBC parameters between the two studied groups before treatment

	SBP (N=30) Mean ± SD	Bacterascites (N=20) Mean ± SD	t	P
Hb (g/dL)	11.22 ± 1.67	11.81 ± 1.22	1.36	.182
TLC (x 10^3/L)	18.23 ± 4.04	17.98 ± 4.39	.154	.878
PLT (x 10^3/L)	175.85 ± 9.15	164.35 ± 9.19	.747	.459

There was no significant difference between the two studied groups regarding liver function parameters (Table 4).

Table (4): Liver function parameters between the two studied groups

Variable	SBP (N=30) Mean ± SD	Bacterascites (N=20) Mean ± SD	t	p
FBS (mg/dl)	117.9 ± 8.21	114.45 ± 6.24	.319	.751
ALT (U/L)	75.27 ± 9.89	82.34 ± 7.95	.841	.405
AST (U/L)	89.9 ± 4.66	93.52 ± 7.95	.348	.729
Albumin (g/dL)	2.57 ± 0.705	2.43 ± 0.826	.642	.524
PT (%)	48.13 ± 3.67	46.54 ± 5.13	.386	.701
Total bilirubin (mg/dl)	5.35 ± 1.28	5.17 ± 1.09	.172	.864
TC (mg/dl)	179.45 ± 20.14	184.3 ± 18.63	.859	.395
TG (mg/dl)	145.94 ± 13.82	140.1 ± 14.22	1.45	.154
LDL (mg/dl)	95.22 ± 17.87	92.36 ± 15.65	.582	.563
AFP (ng/mL)	576.29 ± 49.75	655.24±42.38	.661	.512

There was a significant difference between the two studied groups regarding PMN count (Table 5).

Table (5): Ascitic fluid findings between the two studied groups before treatment

	SBP (N=30) Mean± SD	**Bacterascites (N=20)** Mean± SD	**t**	**P**
PMN count (cells/μL)	386.51 ± 9.32	52.2 ± 6.47	**14**	**.000**
Glucose (g/dL)	102.34 ± 7.51	111.81 ± 1.22	.597	.533
Total proteins (g/dL)	1.48 ± 0.745	1.23 ± 0.619	1.24	.221
Albumin (g/dL)	0.955 ± 0.091	0.834 ± 0.047	.730	.469
pH	7.4 ± 0.052	7.47 ± 0.08	.723	.473
pH <7.3	14 (46.7%)	8 (40%)	.217	.642

There was a significant difference between the two studied groups regarding positive cultures and prevalence of isolated organisms from the ascitic fluid (Table 6).

Table (6): Organisms isolated from the ascitic fluid distribution among the two groups.

	SBP (N=30)		**Bacterascites (N=20)**		**X^2**	**P**
	N	**%**	**N**	**%**		
Negative culture	18	60	0	--	**21.6**	**.003**
Escherichia coli	5	16.7	6	30		
Klebsiella pneumoniae	3	10	3	15		
Streptococcus	1	3.3	4	20		
S. aureus	1	3.3	4	20		
Listeria	1	3.3	1	5		
Pseudomonas	1	3.3	1	5		
Enterococcus	0	--	1	5		

DISCUSSION

The present study showed that there was no significant difference between the two studied groups regarding hemoglobin, TLC and platelets. Besides, there was no significant difference between the two studied groups regarding liver parameters. Also, there was no significant difference between the two studied groups regarding creatinine and urea. Our results are supported by study of **Bibi *et al.*** [14] as they reported that none of the laboratory findings differed significantly between SBP and non-SBP patients. According to **Paul *et al.*** [15], the mean hemoglobin in patients of SBP was 9.9 ± 1.9 g/dl and mean total leukocyte count was 12322 ± 6659/mm^3. Ten cases of SBP had a total leukocyte count more than 13000/mm^3. Thrombocytopenia was present in 22 out of 25 cases of SBP. Liver function tests were abnormal in all patients of SBP. Serum Bilirubin of > 4 mg/dl was present in 12 patients. INR was significantly higher in patients with SBP compared to those without SBP. Fifteen cases of SBP had serum sodium levels of < 135 meq/l. Seventeen patients (68 %) of SBP had serum creatinine of > 1.3 mg/dl.

A classic case of SBP is diagnosed on the basis of a positive ascitic fluid culture and a neutrophil count greater than 240/cmm. Two variants of SBP i.e. culture negative neutrocytic ascites (CNNA) and Bacterascites (BA) have been described based on the ascitic fluid analysis (cell count and C/S) results. CNNA has a negative culture with a higher neutrophil count (i.e. > 240/cmm) while in bacterascites, ascitic fluid culture is positive but neutrophil count is < 240/cmm. Besides the symptoms or ascitic fluid cell count, different biochemical tests like serum proteins, albumin, serum ascites albumin gradient (SAAG), ascitic fluid proteins/albumin and ascitic fluid glucose levels are also shown to predict or suggest the presence of SBP in cirrhotic [14].

As regards ascitic fluid findings, the current study showed that there was a significant difference between the two studied groups regarding PMN count. Concerning results of ascitic fluid culture of SBP patients, **Hafez *et al.*** [16] found that 37 patients (59.7 %) among 62 SBP had CNNA with PMNL > 250/mm^3, while 25 (40.3%) patients had culture-positive ascitic fluid. **Purohit *et al.*** [17] studied 217 clinically suspected cases of SBP. They concluded that 71 (43.80%) had ascitic fluid polymorph nuclear cells (PMN) count ≥250/mm^3, 31 (43.6%) cases were culture-positive and 40 (56.4%) cases were culture-negative neutrocytic ascites. **Castellote *et al.*** [18] revealed that in one case, the reagent strip (RS) was 2, showing a conventional leukocyte count of 750 cells/ml and a differential of 500 PMN/ml. Moreover, the ascitic culture was negative and was finally diagnosed as culture-negative

neutrocytic ascites or culture-negative SBP. In the last case the RS was 3, the total leukocyte count showed 420 cells/ml, while the differential count showed 21 PMN/ml. Thus, they considered this case a false positive of the reagent strip.

In the study in our hands, there was a significant difference between the two studied groups regarding positive cultures and prevalence of isolated organisms from the ascitic fluid. The commonest organism was E coli. **Hafez *et al.* [16]** found that positive cultures were gram-negative in 15 patients (60%) predominantly E Coli (66.6%) and Klebsiella (33.3) and gram-positive in 10 patients (40%) predominantly Staphylococcus aureus (60%) and streptococcus SPP (40%). This agrees with **Oladimeji *et al.* [19]** who found that in those with SBP, 93% had gram-negative bacilli being responsible in 66.7% of the cases with E coli (70%) was the predominant organism followed by Klebsiella species. Gram-positive organisms accounted for 33.3% with Streptococcal species (60%) was the predominant organism followed by Staphylococcus aureus (40%). **Hafez *et al.* [16]** reported that for all of 25 culture-positive patients, the causative microorganism was found to be E coli in 10 patients (40%) followed by Staphylococcus aureus in 6 patients (24%) and then Klebsiella SPP in 5 patients (20%) and lastly Streptococcus SPP. According to **Bibi *et al.* [14],** out of a total 38 patients diagnosed with SBP, ascitic fluid culture was positive in 19 (50%) patients. Distribution of pathogens among these patients was E. coli as the predominant pathogen that was isolated in 12 (63.2%) cases.

The present study showed that there was a significant difference between the two studied groups regarding antimicrobial agents use. Our results are supported by study of **Li *et al.* [20],** as they reported that 229 patients with bacterascites (90.2%) received antibiotic treatment. The median of time interval between paracentesis and start of antibiotics was 1 day (range 0-3). A total of 104 (45.4%) patients received empirical antibiotics treatments at the same day of paracentesis because the suspected SBP was the predominant indication. Among the 229 patients, classical beta-lactams plus beta-lactamase inhibitor (22.7%) comprised the most frequently prescribed treatment, followed by third-generation cephalosporins (16.6%) and carbapenems (14.8%). The most frequent antibiotic classes prescribed for culture-positive SBP patients were carbapenems (25.6%) and classical beta-lactams plus beta-lactamase inhibitor (23.2%). The clinical efficacy rate of antibiotic treatment for patients with bacterascites was higher than that for culture-positive SBP patients (91.3% vs 77.4%; P < .001). In the study of **Paul *et al.* [15],** following paracentesis, all patients started empiric antibiotic therapy in form of Inj. Cefotaxime two-gram IV every 12 hours and latter antibiotics were changed according to AF culture and sensitivity. Three patients had E coli on AF culture, one had Klebsiella and one had Staphylococcus aureus on AF culture. Antibiotics of these patients were changed latter on, according to AF culture and sensitivity report. Out of 25 cases, 14 (56%) cases responded within 48 hours of treatment, in terms of subsidence of abdominal pain and fever. Three patients had no response to treatment and kept on deteriorating despite treatment and died during hospitalization.

CONCLUSION

Bacterascites is a complication of cirrhosis comparable to SBP with respect to clinical background and prognosis. There was a significant difference between the two studied groups regarding positive cultures and prevalence of isolated organisms from the ascitic fluid. There was a significant difference between the two studied groups regarding antimicrobial agents use.

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