

## SPONTANEOUS BACTERIAL PERITONITIS IN ASYMPTOMATIC CIRRHOTIC PATIENTS WITH ASCITES IN A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY

Asif Aziz, Sarwat Ashraf, Mir Tahir Hussain Talpur, Nasrullah Aamer\*, Sagheer Ahmed Solangi, Khalil Ullah Shabir, Moiz Ahmed, Kiran Abbas

Jinnah Postgraduate Medical Center, Karachi Pakistan, \*People's University of Medical and Health Sciences, Nawabshah Pakistan

### ABSTRACT

**Objective:** To determine the frequency of spontaneous bacterial peritonitis in asymptomatic cirrhotic patients with ascites.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** Medical outpatient department, Medical unit III, Ward-7, JPMC, Karachi, from Feb 2018 to Aug 2018.

**Methodology:** All patients between the age of 18 to 60 years and presenting with confirmed ascites due to liver cirrhosis were included. Those with ascites due to other causes were excluded from the study. After obtaining consent, diagnostic ascitic paracentesis was done and sent to the laboratory for evaluation.

**Results:** A total of 130 patients were enrolled in the study. The mean age of ascites patients was  $46.94 \pm 7.67$  years. There were 73 (56.2%) male while 57 (43.8%) were female. Spontaneous bacterial peritonitis was detected among 38 (29.2%) patients. Among these, 15 patients (11.5%) had positive culture of spontaneous bacterial peritonitis and detected organisms like *E.coli* (5.4%), *Klebsiella* (3.1%), *Pneumococcus* (2.3%) & *Streptococcus viridians* (0.8%). Frequency of spontaneous bacterial peritonitis increased with increasing age. Male gender was more affected of spontaneous bacterial peritonitis. Lower the weight increasing duration of ascites were associated with higher incidence of spontaneous bacterial peritonitis ( $p$ -value = 0.001 and 0.311 respectively).

**Conclusion:** Spontaneous bacterial peritonitis was detected among one-third of the patients suffering from cirrhosis, making it a grave complication that requires prompt treatment.

**Keywords:** Ascites, Cirrhosis, Spontaneous bacterial peritonitis.

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### INTRODUCTION

Cirrhosis is a chronic disease of the liver which affects at least 1% of the population of the world<sup>1</sup>. A large cause of hospital admission; the cirrhosis in Pakistan is one of the few major killers diseases<sup>2,3</sup>. Complications of cirrhosis are mainly responsible for this mortality burden.

Ascites is the most common of the 3 major complications of cirrhosis; and was present in 59% of patients in Pakistan. Presence of ascites is a severe complication of the disease that significantly affects the prognosis and increases the risk of developing other complications such as refractory ascites, spontaneous bacterial peritonitis (SBP), hepato-renal syndrome (HRS) and

hyponatremia. Development of ascites in cirrhosis indicates a poor prognosis with a mortality of approximately 40% at 1 year and 50% at 2 years<sup>4,5</sup>.

Cirrhotic patients with ascites have an increased susceptibility to develop infections. It is because of the fact that defense mechanisms are inadequate in these patients. The most frequent and the most severe one is spontaneous bacterial peritonitis (SBP). Spontaneous bacterial peritonitis (SBP) accounts for about 24% of in hospital mortality in Pakistan, especially in Sindh<sup>4</sup>.

First time introduced in 1964 by Conn, the term SBP defines presence of an infection of previously sterile ascitic fluid, without any apparent intra-abdominal source of infection. The infecting organisms are usually those found among the normal intestinal flora<sup>5</sup>.

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**Correspondence:** Dr Moiz Ahmed, Jinnah Postgraduate Medical Center, Karachi Pakistan

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SBP is one of the most frequent and life-threatening complications of patients with cirrhosis. Mortality rates have stayed constant in spite of the development of new antibiotic treatments and early diagnosis of SBP infection<sup>6</sup>. SBP occurs in patients with advanced cirrhosis however; its presentation initially remains clinically unrecognized in about 40% cases until its worsening when it appears with symptoms like fever and abdominal pain<sup>7,8</sup>. Due to complications like acute variceal bleeding, development of hepatorenal syndrome, or progressive liver failure; the in-hospital mortality rate may peak to 30% despite strong infection control measures. This arises the need of early diagnosis which supported by adequate treatment and prevention of new episodes can spare a patient's life<sup>9,10</sup>.

Pakistan is also an endemic country to of HBV and HCV infections therefore; prevalence of cirrhosis and its complications like SBP are increasing. In the midst of such a grave situation, very limited research data and contradictory evidence is available on the magnitude of burden of SBP among local population of cirrhotic patients. Therefore; the current study was conducted to fulfill this gap- taking patients from a very busy and centrally located tertiary care hospital. The main objective of this study was to determine the frequency of spontaneous bacterial peritonitis in asymptomatic cirrhotic patients with ascites. The results of this study will help to suggest policies to screen such patients in order to early detect and promptly treat them.

## METHODOLOGY

A cross-sectional study was conducted at Medical OPD, G.I OPD, Medical unit III, Ward-7, Jinnah Postgraduate Medical Centre (JPMC) Karachi, from February 2018 to August 2018 after obtaining ethics approval from Institutional Review Board Committee of JPMC (No.F.2-81/2019-GENL/32023/JPMC). A non-probability consecutive sampling technique was applied. Sample size of 130 was calculated using select statistics with a chronic liver disease and prevalence of cirrhosis in Pakistan to be 46%<sup>2</sup>. Cirrhotic

patients of either gender, age limits 18-60 years and presenting with confirmed ascites due to liver cirrhosis were included. SBP was said when a patient on ascitic fluid report had total leucocyte count  $>500/\text{mm}^3$  with Neutrophils count  $>250/\text{mm}^3$  and positive ascitic fluid culture for bacteria.

Already diagnosed cases of SBP, Ascites due to other causes, i.e. Abdominal TB, Heart failure, etc. were excluded. The written and verbal consent for study was duly taken prior to study start. After applying full protocol of aseptic techniques, diagnostic ascitic paracentesis was done and 20 ml of ascetic fluid was aspirated with disposable syringe. 10 ml of fluid was drawn into the commercially available aerobic blood culture bottle. The culture bottle was immediately transported to the standardized laboratory for incubation and bacterial culture. Rest of the 10 ml ascetic fluid was sent for ascetic fluid D/R including PH, chemistry panel including, glucose, LDH, protein, total and differential leucocyte count. Reporting was done by a qualified microbiologist. Pre-approved Proforma was used to collect and document data. Data was entered & analyzed into SPSS version 19. Descriptive analysis was followed by application of chi-square test taking the  $p$ -value  $\leq 0.05$  as significant.

## RESULTS

A total of 130 diagnosed cases of ascites due to liver cirrhosis at Jinnah Postgraduate Medical Centre were enrolled in this study. The mean age of ascites patients was  $46.94 \pm 7.67$  years (26-60). Other descriptive data on weight, duration to ascites, pH value, specific gravity, protein value, glucose level, leucocytes, neutrophils, lymphocytes and LDH value of ascitic fluid were also given in table # 1. Most of the patients (43.1%) were of age group of 46-55 years. Male gender predominated i-e; 73 (56.2%) while females were 57 (43.8%).

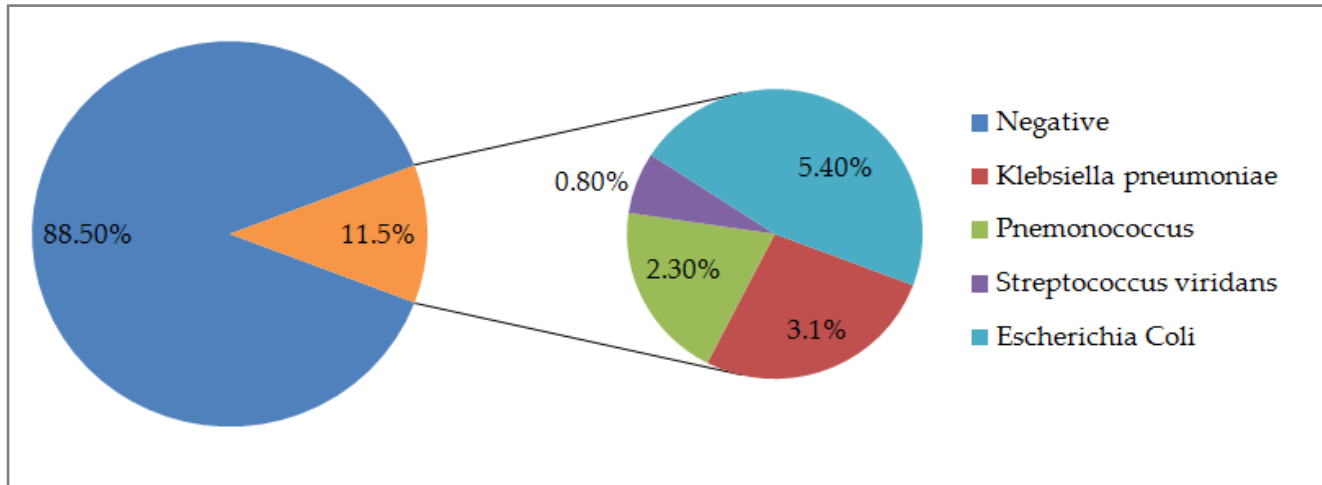
Spontaneous bacterial peritonitis in patients presenting with ascites was found in 38 patients (29.2%). Among these patients with SBP positive, 15 patients (11.5%) had positive culture of SBP

and detected organisms were *Escherichia coli* (5.4%), *Klebsiellapneumoniae* (3.1%), *Pneumococcus* (2.3%) while *Streptococcus viridians* were (0.8%). Remaining 115 patients (88.5%) had a negative SBP culture (figure).

value=0.001, table-II) while increasing duration of ascites was associated with higher incidence of SPB (*p*-value = 0.311, table-II).

**DISCUSSION**

With the increasing burden of viral hepatic



**Figure: Culture sensitivity and detected microorganisms in spontaneous bacterial peritonitis.**

For this study we applied univariate analysis according to which the frequency of SBP increased with statistical significance that increasing age from 15.8% in 25-35 years group to 41.1% in

chronic infections, the Pakistani nation is bearing an increasing load of chronic liver disease- cirrhosis and its complications. Spontaneous bacterial peritonitis- an acute bacterial infection of ascitic

**Table-I: Demographic and clinical profile of participants (n=130).**

Characteristic	Mean ± SD	Minimum	Maximum
Age of Patient (Years)	46.94 ± 7.67	26	60
Weight (Kgs)	61.64 ± 10.63	90	90
Duration of ascites (Days)	60.62 ± 10.59	41	79
pH value of ascitic fluid	7.69 ± 0.45	7.10	8.50
Specific gravity value of ascitic fluid	1.014 ± 0.00763	1.013	1.035
Glucose value of ascitic fluid (mg/dL)	131.42 ± 65.23	50	385
Protein value of ascitic Fluid (g/dL)	2.35 ± 1.72	0.28	5.40
Total Leucocyte count value of ascitic fluid(/mm <sup>3</sup> )	703.35 ± 1062.02	60	6000
Neutrophils count value of ascitic fluid (/mm <sup>3</sup> )	283.28 ± 305.83	65	1200
Lymphocytes value of ascitic fluid (/μL)	65.70 ± 65.70	20	90
LDH value of ascitic fluid (unit/L)	94.89 ± 17.38	50	130

36-45 years group- then it decreased to 7.9% in patients of >55 years age (*p*-value=0.015, table-II). Male gender was found to be significantly more affected by SBP i.e; 73.7% compared to females 26.3% (*p*-value=0.010; table-II). Further it was also noted that lower the weight of patients, lower was the frequency of SBP in ascites patients (*p*-

fluid, whose source of the infecting agent is usually not identifiable, is an emerging medical problem. SBP affects cirrhotic patients having a decompensated disease status. Decreased hepatic synthetic function: low total protein level, prolonged prothrombin time (PT) and low complement levels are associated findings. There is 10 times

more risk of SBP in patient having <1g/dL protein levels in ascitic fluid those with a protein level greater than 1g/dL<sup>10,11</sup>. It makes these patients prone to sever consequences however; if detected early, they can be saved from much morbidity.

**Table-II: Association of spontaneous bacterial peritonitis with different variables including; age, gender, weight, and duration of disease.**

Groups	Non-Systolic Blood Pressure n (%)	Systolic Blood Pressure n (%)	p-value
<b>Age</b>			
25-35	2 (2.2%)	6 (15.8%)	0.015
36-45	33 (35.9%)	16 (41.1%)	
46-55	43 (46.7%)	13 (34.2%)	
>55 years	14 (15.2%)	3 (7.9%)	
<b>Gender</b>			
Female	47 (51.1%)	10 (26.3%)	0.010
Male	45 (48.9%)	28 (73.7%)	
<b>Weight</b>			
40-50	15 (16.3%)	5 (13.2%)	0.001
51-60	39 (43.4%)	7 (18.4%)	
61-70	35 (38.0%)	17 (44.7%)	
>70	3 (3.3%)	9 (23.7%)	
<b>Duration of Ascites</b>			
24-40	20 (21.7%)	11 (28.9%)	0.311
41-50	31 (33.7%)	9 (23.7%)	
51-60	17 (18.5%)	4 (10.5%)	
>60	24 (26.1%)	14 (36.8%)	

The current study was conducted to measure the burden of SBP in ascites as it remains mainly asymptomatic in most of these patients. It was found that only 11.5% were suffering with SBP with positive culture reports. The contemporary studies by Saadi *et al*, Verma *et al* and others have noticed however; that range of SBP was from 42% to 67.7%<sup>12-16</sup>. Further in these studies rates of culture positive SBP were also higher (26.7% to 66.7%)<sup>14-17</sup>, while in the current study it was only 11.5%. This is noticeable difference and may be due to the inability of the cultures to detect all infecting bacteria<sup>18</sup>. This disparity needs to be addressed in further larger studies with comprehensive study designs and methods. Eckmann *et al*, in a study, found that the *Escherichia coli* was

the commonest bacteria isolated, followed by *Pseudomonas aeruginosa* and *Acinetobacter species*<sup>19</sup>. In another study, *Escherichia coli* was on top followed by *Pseudomonas aeruginosa*, *Acinetobacter species*, *Enterobacter species*, *Proteus mirabilis*, *Klebsiellapneumoniae*, *Enterococcus species*, *Streptococcus species*<sup>20</sup>. In our study of distribution of microorganisms of 15 SBP cases were the similar as *Escherichia coli* was on top with 46.7%, followed by *Klebsiella Pneumonia* 26.6%, *pneumococcus* 20.0% and *streptococcus viridians* 6.7%. This shows resemblance with results of other studies confirming the susceptibility of ascites fluid with infection by gram negative intestinal/ abdominal bacilli<sup>12-14,16</sup>.

The current study evaluated the association of age, gender and weight of patients with occurrence of SBP among cirrhotic patients presenting with ascites. The mean age of patients was 46.94 ± 7.67 years which was relatively less than studies by Saadi, Peck and Banker wherein the mean age was from 55 to 64 years<sup>12,21,22</sup>. This might be due to fact that our population gets infected with HBV/HCV in early ages and develop cirrhosis at early age. However; it was worth noting that late 4th and 5th decade of life more affected of SBP compared to more elder and younger patients (*p*-value = 0.015). Other studies by Cekin and Perumalswami, have not found this pattern and elder age patients were found to be main victims of SBP<sup>15,16</sup>. Simultaneously; we noted that males cirrhotics with ascites were more affected with SBP (with 3:1) compared to females counterparts. (*p*-value=0.010). Saadi, Verma, Cekin documented no significant gender difference of SBP<sup>12,14,15</sup>. It is reasonable to suggest here that in western countries due to different reason of cirrhosis the demographic statistics are varying than our population.

Finally, the current study also detected that lower weight and shorter duration of ascites was associated with lower frequency of SBP in ascites patients (*p*-value=0.001 & 0.311 respectively). In a 2015 study by Sundaram *et al*, it was revealed that obese patients with end stage liver disease had a higher prevalence of bacteremia, urinary tract infections, and soft tissue infections as compared

to non-obese patients<sup>23</sup>. The current study was short duration, smaller sample sized and single centered study with smaller scope. Despite these limitations, it has highlighted a very crucial area of cirrhotic patient care which requires prompt attention to carry out a quick diagnostic paracentesis in order to reduce morbidities and avoid mortalities.

Quick diagnostic paracentesis within 24 hours of admission for culture, estimation of cell count and biochemical parameters should be done a routine practice. It must be followed by prompt management in these patients so as to reduce mortality and achieve a better survival rate. Clinicians should be aware of increased resistance of bacteria to cefotaxime. Ciprofloxacin could be a promising alternative antimicrobial in management of SBP.

## CONCLUSION

In the preset study, spontaneous bacterial peritonitis was detected among one-third of the patients suffering from cirrhosis, making it a grave complication that requires prompt treatment in order to reduce mortality and achieve a better survival rate among patients.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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