



A STUDY OF BIOCHEMICAL AND MICROBIOLOGICAL FINDINGS OF SPONTANEOUS BACTERIAL PERITONITIS (SBP) IN LIVER CIRRHOSIS.

General Medicine

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ABSTRACT

BACKGROUND: Liver cirrhosis patients were highly susceptible to bacterial infections due to defects in numerous host defense mechanisms. Spontaneous bacterial peritonitis (SBP) was commonest infection. Microbiological and biochemical findings of SBP will help to manage effectively.

MATERIAL AND METHODS: A cross-sectional observational study was conducted for duration of 2 years to assess clinical profile of patients on invasive Mechanical ventilation in medical Intensive Care Unit of tertiary care centre. A proforma was designed to collect the desired information from the patients. The preformed structured proforma consisted of recording of investigations was used as data collection tool. Statistical analysis performed using Statistical Package for Social Sciences (SPSS). The level of significance was fixed at 5% and $p \leq 0.05$ was considered statistically significant.

RESULTS: Mean age of the patients was 48.7 ± 10.6 years (29-77 years). M: F was 7.3:1. Majority of the patients' sample (88%) were culture negative and only 12% patients ascitic fluid sample were culture positive. No significant findings were seen for ascitic fluid biochemical parameters among SBP and non SBP cases ($p > 0.05$).

KEYWORDS

Biochemical, Microbiological, Liver Cirrhosis, Spontaneous bacterial peritonitis

INTRODUCTION:

Liver (Hepatic) Cirrhosis is the commonest hepatological disorder, found clinically. Liver cirrhosis was commonly indolent, asymptomatic and unsuspected until complications of liver disease present. The etiology of hepatic cirrhosis was commonly detected by the patient's history combined with serologic and histologic examination. Commonest causes of liver cirrhosis in western world are Alcoholic liver disease and hepatitis C infection, whereas Hepatitis B is commonly seen in Asia and sub-Saharan Africa.¹

Prevalence of cirrhosis was likely to be underestimated, as almost one-third of the patients were remaining asymptomatic. Findings from autopsy studies around the world had found prevalence of hepatic cirrhosis that were ranging from 4.5% to 9.5% of the general population.² Globally, more than fifty million people would be suffering from chronic liver disease. Currently, alcoholic hepatitis, non-alcoholic steatohepatitis (NASH) and viral hepatitis were the most common causative factors. During 2001, the projected worldwide mortality from cirrhosis was 771,000 people.³ Deaths from cirrhosis are going to rise and it would be 12th cause of death by 2020.⁴

Liver cirrhosis patients were highly susceptible to bacterial infections due to defects in numerous host defense mechanism.⁵ Spontaneous bacterial peritonitis (SBP) was commonest infection in cirrhotic patients followed by urinary tract infections (UTIs), pneumonia, and bacteremia.⁶ SBP was a commonest infection among patients with cirrhosis and ascites. Apparently, infection can be diagnosed up to 30% of cirrhosis patients with ascites. SBP is associated with significant mortality and morbidity.^{6,7}

Many past studies had reported that Gram-negative enteric bacteria were involved in the most of SBP episodes.⁸ Nonetheless, Gram positive bacteria and antibiotic resistant bacteria have been found responsible for SBP in last decade. Change in microbiology has led to long term, widespread use of quinolones and increased hospital admissions. These findings have raised doubts about currently recommended antibiotic strategy in SBP.^{9,10,11}

Majority of studies mainly focused on treating the underlying cause of liver cirrhosis and Portal hypertension.¹ Limited studies had performed in for evaluating SBP among liver cirrhosis patients. Present study was

conducted with the aim of evaluating clinical, biochemical and microbiological study of spontaneous bacterial peritonitis among liver cirrhosis patients, a descriptive cross-sectional had been planned in tertiary care center.

MATERIAL AND METHODS:

A cross-sectional observational study was conducted for duration of 2 years (October 2016-september 2018) to evaluate clinical, biochemical and microbiological study of spontaneous bacterial peritonitis among liver cirrhosis patients. The study was conducted in the department of medicine of Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune and is a numeration of patients of the department fulfilling the inclusion criteria. A total of 100 cases of liver cirrhosis during study duration admitted in medicine Department and fulfilling the inclusion criteria were enrolled in study.

Ethical clearance was obtained from Institutional Review Board and written informed consent for participation was obtained from the patients prior to conduction of study. The patients were informed regarding the purpose, procedures, risks and benefits of the study in their own vernacular language.

Inclusion criteria: Patients of liver cirrhosis aged above 12 years except pregnant women and other causes of peritonitis.

A proforma was designed to collect the desired information from the patients. The structured proforma consisted of recording of investigations such as Hemogram, ESR, BSL-Fasting, LFT, RFT, Serum Electrolytes, Lipid Profile, ECG, Ascitic fluid analysis: sugar, proteins, routine microscopy, ADA, culture sensitivity, HIV, HbsAg, Serum proteins, PT INR and radiological investigations like X-ray Ultrasonography of abdomen and pelvis, OGD scopy sos

The data collected was entered in Microsoft Excel and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS) and T test was applied to find any difference. The level of significance was fixed at 5% and $p \leq 0.05$ was considered statistically significant.

RESULTS:

Mean age of the patients in current study was 48.7 ± 10.6 years with

minimum age 29 years and maximum age 77 years. More than one-third (34%) of the patients were 41 – 50 years old and 2% > 70 years old. M: F was 7.3:1. In present study among ascitic fluid samples of liver cirrhosis, majority of the patients' sample (88%) were culture negative and only 12% patients ascitic fluid sample were culture positive. Among cirrhosis patients suffering from SBP (n=12), all had culture positive ascitic fluid, while among non-SBP patients (n=88), only 2.3% patients had culture positive ascitic fluid, this relationship of ascitic fluid culture findings and SBP was statistically significant ($p<0.05$).

DISCUSSION:

Liver cirrhosis patients were susceptible for bacterial infections because of defects in various host defense mechanism.^{12,13} SBP (Spontaneous bacterial peritonitis) was the commonest infection in patients who had liver cirrhosis.¹⁴ Spontaneous bacterial peritonitis was diagnosed by absolute neutrophil count more than 250 cells/mm³ in ascitic fluid samples. All patients suffering from cirrhosis and ascites were at higher risk of getting SBP and the prevalence of SBP in outpatients was 1.5% to 3.5% and around 10% to 30% in hospitalized patient. A delay in detecting spontaneous bacterial peritonitis leads to fatal outcome among hepatic cirrhosis patients.^{14,15}

Mean age of the patients in current study was 48.7 ± 10.6 years (range 29 – 77 years). Similar mean age was recorded by Harchand et al¹⁶ (49.7±10.3 years) and Bibi et al¹⁷ (46.5±13.8 years). however, higher mean age was recorded by Oladimeji et al¹⁸ (62±9 years), Heo et al¹⁹ (56±12 years) and Syed et al²⁰ (51.1±11.7 years) but lower mean age was recorded by Manohar and Shejpal²¹ (42.5 years).

In current study, majority of the patients (88%) were males with male female ratio of 7.3:1, similarly higher male female ratio was recorded by Harchand et al¹⁶ (6.5:1), Heo et al¹⁹ (3.4:1), Syed et al²⁰ (1.5:1) and Oladimeji et al¹⁸ (1.2:1). While contrasting results were recorded by Bibi et al¹⁷ (1:1.5) where female predominance was found.

In present study, 85% liver cirrhosis patients' ascitic fluid sample had <100 Polymorph nuclear neutrophil count per μ L (PMN/ μ L), 12% had > 250 PMN/ μ L and 3% patients who had 100 – 250 PMN/ μ L. These findings were indicating that 12% liver cirrhosis patients had positive SBP (Spontaneous bacterial peritonitis).

Comparison of ascetic fluid findings with various study			
Various Study	No. of patients	SBP positive	Culture positive
Present study	100	12%	14%
Harchand et al ¹⁶	113	51.3%	37.9%
Bibi et al ¹⁷	152	25%	19.1%
Oladimeji et al ¹⁸	31	67.7%	71%
Syed et al ²⁰	81	24.7%	9.9%

In current study, among cirrhosis patients suffering from SBP (n=12), all had culture positive ascitic fluid, while among non-SBP patients (n=88), only 2.3% patients had culture positive ascitic fluid, this relationship of ascitic fluid culture findings and SBP was statistically significant ($p<0.05$). Study by Bibi et al¹⁷ found 50% patients had positive ascetic fluid culture while among patients who did not had SBP, 7.9% had culture positive. In a study conducted in Ludhiana Harchand et al¹⁶ had found that among SBP patients who were culture positives.

In this study, among SBP patients, 100% patients had serum bilirubin level above normal level (1.2 mg/dl) though among non-SBP patients, 60.2% patients had serum bilirubin level above normal level and this relationship was statistically significant ($p<0.05$). Harchand et al¹⁶ had found non-significantly higher mean higher mean value of serum bilirubin in non-SBP patients (10.8±9.6 mg/dl) comparing to SBP patients (8.8 ± 8 mg/dl), however among both groups mean value of serum bilirubin was above normal value. Bibi et al¹⁷ had found that there was non-significantly lower level of serum bilirubin among SBP patients (2.6±2.7 mg/dl) comparing to patients who did not had spontaneous bacterial peritonitis (4.2±6.3 mg/dl).

Present study found that 75% each SBP and non-SBP patients had Ascitic sugar level above normal range. Similar observations was found by Safia Bibi et al¹⁷

In this study, patients who had SBP, 50% had Ascitic albumin below 1 gm/dL and among non-SBP patients (n=88), 40.9% patients had Ascitic albumin below 1 gm/dL this was statistically non-significant

($p>0.05$). A study by Harchand et al¹⁶ had noticed nearly similar levels of ascitic fluid protein and albumin levels in SBP patients and non-SBP patients. Similar findings were seen in various studies.^{17,18,20}

In current study, liver cirrhosis patients with SBP (n=12), 100% patients had SAAG (Serum–Ascites Albumin Gradient or gap) above 1.1 gm/dl but in non-SBP patients, 80.7% patients had SAAG above 1.1 gm/dl, however, this relation of SBP with SAAG was found to be statistically non-significant. findings of study matches with other study.^{16,17}

Table 1: Baseline Characteristics of study participants

Age group	No. of patients	Percent
29 - 40 years	24	24
41 - 50 years	34	34
51 - 60 years	29	29
61 - 70 years	11	11
> 70 years	2	2
Gender		
Male	88	88
Female	12	12

Table 2: Distribution of patients based on microbiological findings

Ascitic fluid Polymorph nuclear neutrophils	No. of patients	Percent
< 100 PMN/ μ L	85	85
100 - 250 PMN/ μ L	3	3
> 250 PMN/ μ L	12	12
Culture		
Positive	14	14
Negative	86	86

Table 3: Comparison of biochemical findings among SBP and non-SBP

Biochemical findings	SBP	Non-SBP	Total	P value
Serum Bilirubin				
< 1.2 mg/dl (normal range)	0	35 (39.8)	35 (35.0)	0.001
1.3 - 5 mg/dl	9 (75.0)	52 (59.1)	61 (61.0)	
> 5 mg/dl	3 (25.0)	1 (1.1)	4 (4.0)	
Ascetic Sugar level				
10 – 110 gm/dL (normal range)	3 (25.0)	22 (25.0)	25 (25.0)	1.000
> 110 gm/dL	9 (75.0)	66 (75.0)	75 (75.0)	
Ascetic Albumin level				
< 1 gm/dL	6 (50.0)	36 (40.9)	42 (42.0)	0.522
1 – 2 gm/dL	6 (50.0)	44 (50.0)	50 (50.0)	
2 – 3 gm/dL	0	8 (9.1)	8 (8.0)	
Ascetic Globulin level				
< 1 gm/dL	6 (50.0)	42 (47.7)	48 (48.0)	0.914
1 - 2 gm/dL	3 (25.0)	27 (30.7)	30 (30.0)	
>2 gm/dL	3 (25.0)	19 (21.6)	22 (22.0)	
SAAG (Serum–Ascites Albumin Gradient or gap)				
≤ 1.1 gm/dl (normal range)	0	17 (19.3)	17 (17.0)	0.211
> 1.1 gm/dl	12 (100.0)	71 (80.7)	83 (83.0)	

*SBP- Spontaneous bacterial peritonitis

REFERENCES:

- Schuppan D, Afdhal NH. Liver Cirrhosis. Lancet [Internet]. 2008 Mar 8;371(9615):838–51. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2271178/>
- Lim Y-S, Kim WR. The global impact of hepatic fibrosis and end-stage liver disease. Clin Liver Dis. 2008;12(4):733–46.
- Mathers CD, Lopez AD, Murray CJL. The burden of disease and mortality by condition: data, methods and results for 2001. Glob Burd Dis risk factors. 2006;45:88.
- Sarin SK, Maiwall R. Global burden of liver disease: a true burden on health sciences and economics. World Gastroenterol Organ. 2012;17(2).
- Sueh J, Runyon BA. Spontaneous bacterial peritonitis. Clin Infect Dis. 1998;669–74.
- Fernández J, Navasa M, Gómez J, Colmenero J, Vila J, Arroyo V, et al. Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and non-fluoroquinolone prophylaxis. Hepatology. 2002;35(1):140–8.
- Tandon P, Garcia-Tsao G. Renal dysfunction is the most important independent predictor of mortality in cirrhotic patients with spontaneous bacterial peritonitis. Clin Gastroenterol Hepatol. 2011;9(3):260–5.
- Liver EAFTSOT. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010;53(3):397–417.
- Cholongitas E, Papatheodoridis G V, Lahanas A, Xanthaki A, Kontou, Kastellanou C, Archimandritis AJ. Increasing frequency of Gram-positive bacteria in spontaneous bacterial peritonitis. Liver Int. 2005;25(1):57–61.
- Tandon P, DeLisle A, Topal JE, Garcia-Tsao G. High prevalence of antibiotic-resistant bacterial infections among patients with cirrhosis at a US liver center. Clin Gastroenterol Hepatol. 2012;10(11):1291–8.
- Alexopoulou A, Papadopoulos N, Eliopoulos DG, Alexaki A, Tsiriga A, Toutouza M, et

- al. Increasing frequency of gram positive cocci and gram negative multidrug resistant bacteria in spontaneous bacterial peritonitis. *Liver Int.* 2013;33(7):975–81.
12. Such J, Runyon BA. Spontaneous bacterial peritonitis. *Clin Infect Dis.* 1998;669–74.
13. Runyon BA. Early events in spontaneous bacterial peritonitis. *Gut.* 2004;53(6):782–4.
14. Fernández J, Navasa M, Gómez J, Colmenero J, Vila J, Arroyo V, et al. Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and norfloxacin prophylaxis. *Hepatology.* 2002;35(1):140–8.
15. Rimola A, Soto R, Bory F, Arroyo V, Píera C, Rodes J. Reticuloendothelial system phagocytic activity in cirrhosis and its relation to bacterial infections and prognosis. *Hepatology.* 1984;4(1):53–8.
16. Harchand P, Gupta V, Ahluwalia G, Chhina R. Clinical and Bacteriological Profile of Spontaneous Bacterial Peritonitis in Cirrhotic Patients. *J Gastrointest Infect.* 2017;7(1):15–20.
17. Bibi S, Ahmed W, Arif A, Khan F, Alam SE. Clinical, Laboratory and Bacterial Profile of Spontaneous Bacterial Peritonitis in Chronic Liver Disease Patients. *J Coll Physicians Surg Pakistan.* 2015;25(2):95–9.
18. Oladimeji AA, Temi AP, Adekunle AE, Taiwo RH, Ayokunle DS. Prevalence of spontaneous bacterial peritonitis in liver cirrhosis with ascites. *Pan Afr Med J [Internet].* 2013 Aug 9;15:128. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3830462/>
19. Heo J, Seo YS, Yim HJ, Hahn T, Park SH, Ahn SH, et al. Clinical features and prognosis of spontaneous bacterial peritonitis in Korean patients with liver cirrhosis: a multicenter retrospective study. *Gut Liver.* 2009;3(3):197.
20. Syed VA, Ansari JA, Karki P, Regmi M, Khanal B. Spontaneous bacterial peritonitis (SBP) in cirrhotic ascites: a prospective study in a tertiary care hospital, Nepal. *Kathmandu Univ Med J (KUMJ).* 2007;5(1):48–59.
21. Manohar TP, Shejpal A. Spontaneous bacterial peritonitis in patients of cirrhosis of liver with ascites. *Int J Infect Dis.* 2016;45:142.