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To Study Prevalence, Clinical and Microbiological Profile of Spontaneous Bacterial Peritonitis in Cirrhosis of Liver with Ascites and Its Association with Severity of Cirrhosis

[1]Dr. Pardeep Kumar, MBBS, Junior Resident, Department of Medicine, SGRD Institute of Medical Sciences and Research, Amritsar, Punjab, India

[2]Dr. Jasmine Kaur, MD Medicine, Associate Professor, Department of Medicine, SGRD Institute of Medical Sciences and Research, Amritsar, Punjab, India

[3]Dr. Tejinder Sikri, MD Medicine, Professor, Department of Medicine, SGRD Institute of Medical Sciences and Research, Amritsar, Punjab, India

[4]Dr. Gurinder Mohan, MD Medicine, Professor, Head of Department, Department of Medicine, SGRD Institute of Medical Sciences and Research, Amritsar, Punjab, India

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Corresponding Author: Dr. Jasmine Kaur, MD Medicine, Associate Professor, Department of Medicine, SGRD Institute of Medical Sciences and Research, Amritsar, Punjab, India

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Abstract

Background and goals

SBP is a common consequence in people with chronic liver disease and ascites. This might happen gradually and insidiously, or it can go unnoticed until symptoms occur. The mortality rate after a single episode is between 20 - 40%, and early diagnosis is required for adequate treatment and prevention of new episodes. The goal of this study was to look at the prevalence, clinical, and microbiological profiles of SBP and its variants in patients with liver cirrhosis and ascites.

Materials and methods

This observational study was conducted on 104 cirrhotic patients with ascites admitted to a tertiary care hospital. Patients' basic demographics, symptoms, and clinical indicators were documented. Diagnostic

paracentesis was done aseptically and immediately sent for ascitic fluid cytology, biochemistry, and culture. Bacterial examination and antibiotic sensitivity tests were carried out by standard microbiological techniques.

Results

This study was done on 104 cirrhotic patients with ascites. Alcohol was the most common etiological factor followed by Hepatitis C infection. The most common clinical features were abdominal distension followed by icterus, pedal edema, and abdominal pain. The majority of the patients were in Child Pugh's Grade C. Out of 104 patients, 28 (26.9%) had SBP with 20 (71.4%) of them presenting with CNNA and 8 (28.6%) were culture positive as 5 (17.8%) had classical SBP, and 3 (10.8%) had MNB. Gram-negative isolates were predominant (75%). Escherichiacoli were the commonest isolate.

Interpretation and Conclusion

SBP was found in 26.9% of cirrhotic patients, with Gram-negative isolates being the most common**.** Diagnostic paracentesis is performed at the time of hospitalization so that infection can be detected early and treated promptly as they have a poor prognosis and high mortality if not treated early

Keywords

Bacterascites, Cirrhosis, Ascites, Culture-negative Neutrocytic ascites, Spontaneous bacterial peritonitis.

Introduction

Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation of the liver. The most common causes include alcohol intake, viral hepatitis, non-alcoholic steatohepatitis (NASH), and autoimmune diseases. Clinically, patients may be asymptomatic (compensated) or clinically ill with jaundice, ascites, hepatic encephalopathy, or bleeding varices (decompensated).[1]

Ascites is free fluid within the peritoneal cavity. It develops as a result of disorders that directly affect the peritoneum (infection, cancer), as well as diseases that are not related to the peritoneum (liver disease, heart failure, hypoproteinemia). Cirrhosis is the commonest cause of ascites in the Western world (~75%), followed by peritoneal malignancy (12%), cardiac failure (5%), and peritoneal tuberculosis (2%). In patients with cirrhosis, the development of ascites marks the transition from compensated to decompensated cirrhosis and is, by far, the most frequent first decompensating event. Its pathophysiology is mostly explained by portal(sinusoidal) hypertension and sodium retention dueto vasodilation and consequent activation of sodium retaining systems. Spontaneous bacterial peritonitis is the most prevalent infection in cirrhosis. It is called spontaneous because it occurs in the absence of a contiguous source of infection and the absence of an intra-abdominal inflammatory focus.[2]

Bacterial translocation, systemic, and local immune dysfunction, particularly a decreased opsonization activity in ascitic fluid, are the main elements in the pathogenesis of spontaneous bacterial peritonitis. Accordingly, gut microflora including E. coli, Klebsiella spp., Enterobacter spp., Enterococci, and Streptococci are common causative organisms.[3]

Ascitic fluid infection can be classified into 5 categories based on ascitic culture results, polymorph nuclear (PMN) count, and presence or absence of a surgical source of infection. Of the 3 subtypes of spontaneous ascitic fluid infection, the prototype is spontaneous bacterial peritonitis.

Table 1: Classification of ascitic fluid infection[4]

Type of infection	PMN cell count/ mm3	Bacterial culture result
Spontaneous Bacterial Peritonitis(SBP)	>250	Positive (Usually 1 organism)
Culture Negative Neutrocytic Ascites (CNNA)	>250	Negative
Bacterial Neutrocytic Bacterascites(MNB)	<250	Positive (1 Organism)
Secondary Bacterial Peritonitis	250	Positive (Poly microbial)
Poly microbial Bacterascites	<250	Positive (Ploy microbial)

Aims and Objectives

1. To estimate the prevalence of spontaneous bacterial peritonitis and its variants in patients of cirrhosis of the liver with ascites.
2. To study the clinical and microbiological profile of spontaneous bacterial peritonitis and its variants.
3. To study spontaneous bacterial peritonitis with the severity of cirrhosis according to Child-Pugh Score.

Material and Methods

This prospective observational study approved by the Institutional Ethical Review Committee was conducted on 104 cirrhotic patients with ascites admitted to Sri Guru Ramdas Medical College and Hospital Amritsar, Punjab, India, from June 2019 to May 2021. For this purpose, all newly diagnosed and already diagnosed patients with cirrhosis of the liver with ascites coming to hospital OPD and IPD were enrolled after taking written and informed consent.

Methods

Ascitic fluid for analysis was aspirated as soon as the patient was admitted, and diagnosed to be suffering from cirrhosis of the liver, before giving any antibiotics. Diagnostic paracentesis was performed on all patients within 24 hours of their hospitalization. With aseptic measures, 20 cc of ascitic fluid was tapped in each patient.

1. 10 ml of ascitic fluid was immediately inoculated into blood culture bottles at the bedside for microbiological analysis.
2. 10 ml of ascitic fluid was utilized for biochemical and cytological examination.

The ascitic fluid of all patients was analyzed for the type of cells and cell count. The presence of pathogenic organisms was determined by the culture of ascitic fluid.

Inclusion Criteria

1) Patients with a confirmed diagnosis of cirrhosis of the liver with ascites
2) Patient age >18 years

Diagnostic Criteria

Cirrhosis of the liver was diagnosed by the following diagnostic tools: -

1) History: - Patients presenting with chief complaints of abdominal distention, yellow discoloration of eyes, swelling of the feet along withthe history of alcohol intake, viral hepatitis (HBV, HCV), or a

known case of chronic liver disease with hematemesis, ascites,or altered sensorium,suggests cirrhosis

2) Physical findings: -On general physical examination patients with stigmata of liver disease like palmar erythema, terry's nails, clubbing of the fingernails, Dputryen contracture, asterixis, gynecomastia, spider telangiectasia's, dilated abdominal veins, temporal hallowing, parotid enlargement, testicular atrophy, loss of axillary or pubic hair and systemic findings of an enlarged left hepatic lobe with splenomegaly or shrunken liver suggests cirrhosis.
3) Biochemical features: - Elevated or Normal liver enzymes, hypoalbuminemia, reversal of albumin to globulin ratio, prolonged prothrombin time, hyponatremia, thrombocytopenia support the history and physical findings of cirrhosis of the liver
4) Imaging studies: USG, CT/CECT helps to make a diagnosis of cirrhosis. Ultrasound abdomen showing coarse echotexture with nodule formation & portal hypertension with spleenomegaly, ascites.

Spontaneous bacterial peritonitis was diagnosed by the following criteria: -

1. An ascitic fluid neutrophil count greater than 250 cells/ mm^3

   Or
2. A positive ascitic fluid culture,

   And
3. An absence of a primary source of infection in the abdomen.

Exclusion Criteria

1) Those who were suspected to have secondary peritonitis such as perforated colon, ruptured appendix.
2) Those who had ascites due to renal, cardiac, tubercular, or malignant cause
3) Patient who had undergone abdominal surgery within 3 months before admission.

Statistical analysis of the data was performed using unpaired Student's t-test for independent variables and chi-square ($\chi 2$) test for categorical variables. A p-value < 0.05 was considered statistically significant.

Observation and Results

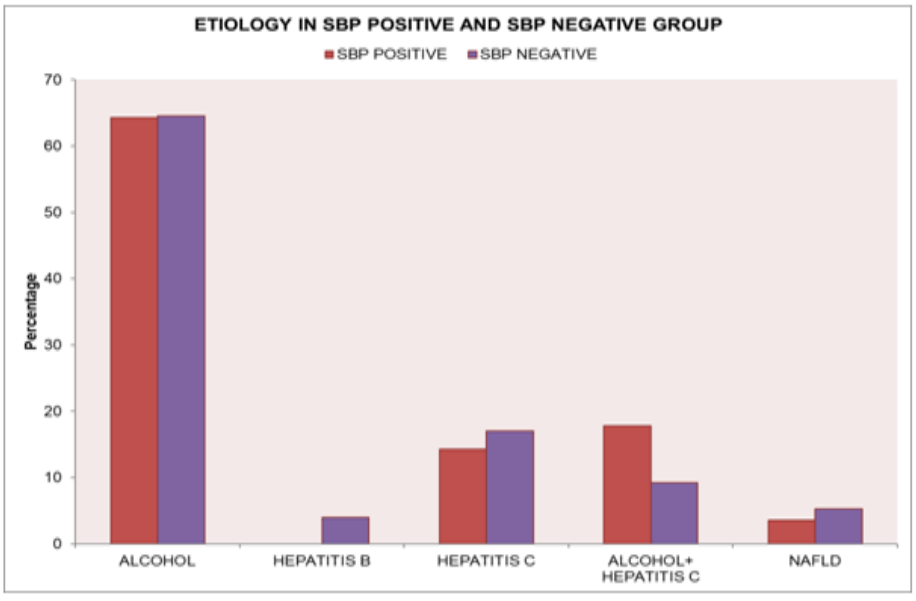
A total of 104 cirrhotic patients with ascites included 86 (82.7%) males and 18 (17.3%) females. The majority of the patients were in the age group of 41 to 50 years followed by patients between 51 and 60 years. The mean age was 51.5 ±12.29 years. In the study group, the most common etiology of cirrhosis was alcohol intake (64.4%) followed by hepatitis C infection (16.3%; Table 2). The most common clinical features in patients with SBP and those without SBP are depicted in Table 3. A maximum number of patients with SBP presented with abdominal distention followed by icterus and pedal edema and the result was statistically non-significant ($p > 0.005$). The majority of patients (68) belonged to Child–Pugh's Grade C (29.4% SBP; 70.6% w/o SBP) followed by (35) Child Pugh's Grade B (22.9% SBP; 77.1% w/o SBP). Of 104 cirrhotic patients with ascites, 28 (26.9%) had SBP with 20 (71.4%) of them presenting with CNNA, 8 (28.6%) were culture positive as5(17.8%) had classical SBP, and 3(10.8%) had MNB. Among the culture-positive SBP, Gram-negative isolates were more common (75%) than Gram-positive isolates (25%). The most common isolate was E. coli (37.5%) followed by Acinetobacter haemolyticus, Providencia rettgeri, Pseudomonas aeruginosa, Staph epidermidis, Staph

haemolyticus (12.5% each; Table 4). Cytological and Biochemical analysis of ascitic fluid showed a significant association of Ascitic fluid cell count, Ascitic fluid absolute Neutrophils count, and INR between SBP positive and SBP negative patients (Table 5).

Table 2: Etiology in SBP Positive and SBP Negative Group

Etiology	SBP Positive		SBP Negative		Total
	N	%	N	%	
Alcohol	18	64.3	49	64.5	67
Hepatitis B	0	0	3	4	3
Hepatitis C	4	14.3	13	17	17
ALD + Hepatitis C	5	17.8	7	9.2	12
NAFLD	1	3.6	4	5.3	5
Total	28	100	76	100	104
P valve	0.618				

Table 2: Shows that there is no significant correlation between etiology and SBP (pvalue>0.005)

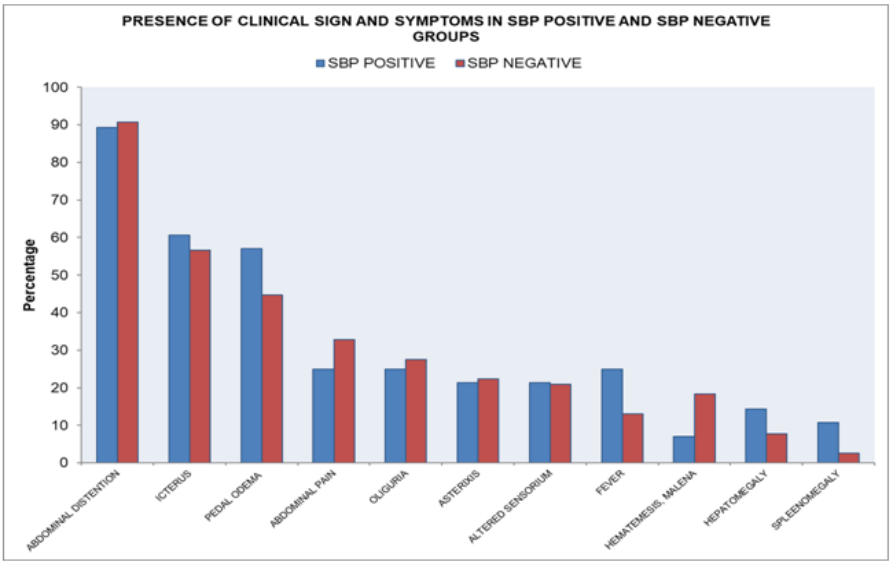


Graph 1: Shows the distribution of etiology in SBP positive and SBP negative group

Table 3: Distribution of Various Clinical Signs and Symptoms in SBP Positive and SBP Negative Group

CLINICAL PRESENTATION	SBP POSITIVE (n=28)		SBP NEGATIVE(n=76)		P-VALUE
	PRESENT n (%)	ABSENT n (%)	PRESENT n (%)	ABSENT n (%)	
ABDOMINAL DISTENTION	25 (89.3)	3 (10.7)	69 (90.8)	7 (9.2)	0.818
ICTERUS	17 (60.7)	11 (39.3)	43 (56.6)	33 (43.4)	0.075
PEDAL ODEMA	16 (57.1)	12 (42.9)	34 (44.7)	42 (55.3)	0.261
ABDOMINAL PAIN	7 (25)	21 (75)	25 (32.9)	51 (67.1)	0.439
OLIGURIA	7 (25)	21 (75)	21 (27.6)	51 (72.4)	0.788
ASTERIXIS	6 (21.4)	22 (78.6)	17 (22.3)	59 (77.7)	0.918
ALTERED SENSORIUM	6 (21.4)	22 (78.6)	16 (21)	60 (79)	0.967
FEVER	7 (25)	21 (75)	10 (13.1)	66 (86.9)	0.147
HEMATEMESIS, MALENA	2 (7.1)	26 (92.9)	14 (18.4)	62 (81.6)	0.157
HEPATOMEGALY	4 (14.3)	24 (85.7)	6 (7.8)	60 (92.2)	0.327
SPLENOMEGALY	3 (10.7)	25 (89.3)	2 (2.6)	74 (97.4)	0.087

Table 3: Shows the distribution of clinical presentation of cirrhotic patients in the SBP positive group and SBP negative group. There is no significant correlation between clinical presentation and SBP (p value>0.005)

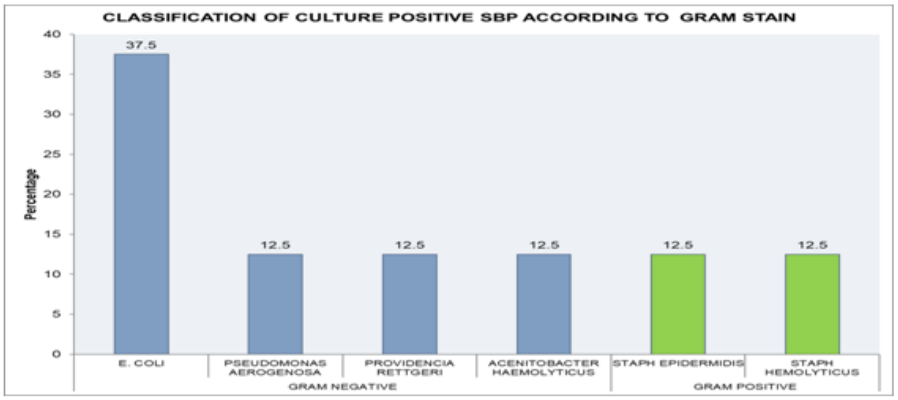


Graph 2: Shows the distribution of clinical signs and symptoms in SBP positive and SBP negative groups

Table 4: Microbiological Classification of Culture Positive SBP Patients According To Gram Stain

Gram stain	Microorganisms	Number of patients	Percentage	Total
Gram-negative	E. Coli	3	37.5	75
	Pseudomonas aeruginosa	1	12.5	
	Providencia rettgeri	1	12.5	
	Acinetobacter haemolyticus	1	12.5	
Gram-positive	Staph epidermidis	1	12.5	25
	Staph haemolyticus	1	12.5	
Total		8	100	100

Table 4: Showed that the majority of culture-positive SBP patients had gram-negative bacteria of about 75% and gram-positive was 25%. E. coli is the most pathogen (37.5%)



Graph 3: Shows the microbiological classification of culture-positive SBP patients according to gram staining

Table 5: Hematological and Biochemical Parameters in cirrhotic patients

Investigations	Outcome				P-value
	SBP Positive		SBP Negative		
	Mean	SD	Mean	SD	
Total serum bilirubin	5.16	7.525	5.38	6.388	0.881
SGOT	127.58	199.225	123.43	201.317	0.926
SGPT	99.06	284.33	54.56	45.38	0.187
Sr. Protein	28	6.9	76	6.7	0.427
Sr. Albumin	2.01	0.448	2.15	0.53	0.237
Sr. Creatinine	2.24	1.667	2.15	1.933	0.825
AF Cell count	1657.86	1334.1	294.47	182.24	<0.001
AF ANC	1156.96	1215.242	54.89	48.5	<0.001
AF Protein	1.02	0.67	1.2	0.64	0.205
AF Albumin	0.39	0.357	0.45	0.357	0.417
AF Sugar	127.91	52.14	140.34	61.826	0.346
Platelet count	1.35	0.753	1.62	0.601	0.064
INR	2.02	0.505	1.54	0.503	<0.001
MELD- Na	25.36	7.22	22.92	7.435	0.138

Table 5: Shows that among the hematological and biochemical parameters, Ascitic fluid cell count, Ascitic fluid absolute Neutrophils count, and INR had a significant correlation between SBP (p-value< 0.005)

Discussion

One of the most common bacterial infections among cirrhosis patients with ascites is spontaneous bacterial peritonitis. In individuals with liver cirrhosis, a delay in the diagnosis of SBP frequently results in death. In the current study male to female ratio was 4.7:1, which was similar to that reported by Nadagouda et al,[5] Paul et al[6]. The male predominance in this study could be due to the male individuals having a higher prevalence of alcoholic cirrhosis.The mean age of cirrhotic patients was found to be 51.5 ±12.29 years. The findings matched those of Syed et al.[7], who found a mean age of 51.1 11.7 years in their study. The majority of patients had a history of alcohol consumption as the underlying cause of cirrhosis, consistent with that reported by Nadagouda et al[5] and Chawla et al.[8] Most of the patients 68(65.3%) were in Child–Pugh's Grade C (29.4% in SBP group and 70.6% in non-SBP group), similar to a study done by Choubey PP et al[10] where 42% patients of SBP were in Child–Pugh's Grade C. In the current study, 26.9% of patients had SBP. Results similar to this study (27%) were cited in a study done by Archana Bhat et al,[10]and (25%) Bibi et al[11].Various authors reported the overall frequency of SBP as 38,[12] 47.5,[13] and 56%[14] in chronic liver disease patients. Different presenting symptoms in patients with SBP were seen in the current study, out of which abdominal distension was most common. Similar results had been reported by Paul et al.[6] In the current study, icterus was the second most common presentation (57.7%) and none of the signs and symptoms were significantly related to SBP. However, this was not observed in earlier studies.[5,6]Among the biochemical and hematological parameters ascitic fluid cell count, ascitic fluid absolute neutrophil count, and INR showa significant correlation between SBP positive and SBP negative patients. Similar results had been reported by Gharabawy et al [15] in 2018. Of 28 cases of SBP, CNNA was the most common (71.4%), followed by classical SBP (17.8%) and MNB (10.8%). The results were comparable with the study done by Zaman Aet and Bibi et al[11] where CNNA was the most common variant of SBP. The comparatively high incidence of CNNA could be due to the patients receiving an ascitic tap at an early stage, when the bacterial inoculum was still low, or possibly because of the difference in the proficiency of the culturing techniques between the different centers. The ascitic fluid culture was positive in 28.5% of SBP cases. Similar results were observed in various studies with culture positivity of 31%[13] but some studies have reported much lower rates of culture positivity, i.e., <25%.[14,17]This difference could be attributed to the different culture techniques. International literature suggests a culture positivity rate of 31 to 71%.[17] In this study, Gram-negative organisms were found to be a more common cause ofculture positives (75%) similar to that reported by Chawla et al[8]and Bibi et al.[11] Among the Gram-negative isolates, *E. coli* was the most common isolate. Similar results were cited in different studies conducted by Syed et al,[8] Chawla et al,[8]Bibi et al,[11] and Zaman et al.[16] The main reason for SBP is bacterial translocation from the gut[3]Hence the commonly isolated pathogens in SBP are usually enteric Gram-negative rods. Some of the studies have also reported the predominance of Gram-positive organisms, but that is very rare and is often due to some prophylaxis or some previous intervention.[18]Therefore all cirrhotic patients with ascites should undergo diagnostic paracentesis and ascitic fluid analysis for early diagnosis and better selection of antibiotics to

prevent antimicrobial resistance which leads to better outcome of cirrhotic patients.

Conclusion

SBP being the problem in cirrhosis with ascites, all cirrhotic should be screened for SBP. Diagnostic paracentesis should be performed at the time of hospitalization so that infection can be detected early and treated promptlyas they have a poor prognosis and high mortality if not treated early

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