ORIGINAL RESEARCH PAPER

General Medicine

MICROBIOLOGICAL PROFILE OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH CIRRHOSIS OF LIVER IN SOUTHERN ASSAM.

KEY WORDS: Ascites, Ascitic fluid, Liver cirrhosis, Peritonitis, SBP

Dr Madhusmita Khakholary Postgraduate Trainee Department Of Medicine, Silchar Medical College

Dr Dipankar Deb Professor and HOD Department of Medicine, Nagaon Medical College

Dr Prithwiraj Bhattacharjee Professor and HOD Department of Medicine, Silchar Medical college.

ABSTRACT

Liver cirrhosis is a common disorder which can have a wide range of aetiologies. Anatomically, it is characterised as a widespread process of nodule formation and fibrosis in the liver. Without any obvious intra-abdominal source of infection, spontaneous bacterial peritonitis (SBP) is characterised by infection of the previously sterile ascitic fluid (AF). SBP is a primary cause of death in decompensated liver disease and requires quick identification and care. In recent years, Assam has seen an increase in the prevalence of alcoholic liver disease and associated complications. **Aims and Objectives:** This study was undertaken with an idea to evaluate the significance of AF analysis with AF culture and sensitivity to determine microbiological profile and prognosis in cirrhotic patients with SBP in this region. **Materials and Methods:** Patients admitted with liver cirrhosis with ascites were studied during the period from June 2021 to May 2022. All patients included in the study were confirmed liver cirrhosis by ultrasound. Basic demographics, symptoms and clinical signs of patients were recorded. Patients with the history of antibiotic use within last 3 days or any intra-abdominal source of infection were excluded. Diagnostic paracentesis was done for ascitic fluid detailed report and culture. **Results:** Out of 100 SBP patients, 60 (60%) had culture negative neutrocytic ascites and 40 (40%) had bacterascites. Fever, abdominal tenderness and constipation were common in SBP patients. Ascitic fluid culture was positive in 26 (52%) patients. E. coli (28%) was the predominant pathogen followed by Klebsiella species (8%), Staphylococcus aureus (2%) and acetinobacter (2%). 33 (82.5%) cases showed sensitivity to cefotaxim. In rest 17.5% cases, organism is mildly sensitive or resistant to 3rd generation cephalosporins.

INTRODUCTION

An advanced stage of a progressive hepatic ailment, cirrhosis is a fatal cause of liver disease. Alcohol and hepatitis B, C, and other infections are the most common causes of the condition [1-6]. As more people with this illness seek treatment for cirrhosis-related problems [1,4,6-8], emergency departments (EDs) are seeing a rise in the number of these patients[6-9]. Cirrhosis is of 2 types: Compensated cirrhosis and decompensated cirrhosis. Decompensated cirrhosis is associated with a 10-fold increase in mortality [1-5] when cirrhotics are compared to the general population. Compensated cirrhosis is defined as the absence of a severe cirrhosis-related complication. There are frequently no symptoms at all in compensated cirrhosis. Portal hypertension, increased cardiac output, plasma volume expansion, and an imbalance of biochemical substances such vasoconstrictors, vasodilators, vascular endothelial growth factors etc are among the complications of cirrhosis[8–10].

Complications such as jaundice, ascites, spontaneous bacterial peritonitis (SBP), or bleeding have a substantial impact on the mortality.

Spontaneous Bacterial Peritonitis

In patients with cirrhosis who present with a variety of symptoms, spontaneous bacterial peritonitis (SBP) is a frequent and frequently fatal bacterial infection of the ascites. The diagnosis is made in the absence of an intra-abdominal source of infection or inflammatory process because it is separate from secondary peritonitis. Krencker was the first to define SBP in 1907, followed by Caroli in 1958 and Kerr and associates in 1963[11-13]. In 1964, Conn used the term "spontaneous bacterial peritonitis" to describe a state of bacteremia and peritonitis in Laennec's cirrhosis without a known source of infection[14]. SBP affects cirrhosis due to a varied spectrum of aetiology and not simply alcohol, and further study has shown variables that contribute to the aetiology, such as the translocation of gut bacteria to lymph nodes. Sodium and water retention and fluid overflow into the peritoneal cavity are caused by portal hypertension, splanchnic vasodilation, and activation of the renin-angiotensin cascade[15]. The ascites is usually transudative fluid with low opsonic activity, which creates an optimal environment for bacterial development. SBP seldom develops in the absence of cirrhosis, although there have been reports of cardiac[16], renal[17], malignancy[18], portal vein thrombosis[19], and autoimmune[21], [22]related infection of ascites.

Based on the polymorphonuclear cell count, ascitic fluid culture findings, and clinical conditions, ascitic fluid infection is divided into five types:

- Classic culture positive SBP
- Culture-negative SBP or culture-negative neutrocytic ascites (CNNA)
- Mono-microbial
- Poly-microbial bacterascites and
- Secondary peritonitis.

Gram-negative flora in the intestine is the main cause of SBP. Many factors, including the pathophysiological hallmark of bacterial translocation in an immunocompromised host, are linked to the development of SBP. Most of the time, one organism from the intestinal group is cultured from the ascitic fluid[26]. Blood cultures frequently yield the same bacterium. The majority of patients pass away from infection itself, its sequelae, and other cirrhosis-related risks such bleeding varices or the hepatorenal syndrome.

In patients who are hospitalised, the incidence of SBP varies from 10% to 30% [23] and the mortality rate varies from 10% to 46% [24,25].

The symptoms of spontaneous bacterial peritonitis include a rapid onset of fever, chills, chills-accompanied abdominal pain, rebound discomfort over the abdomen, absence of bowel sounds, and leucocytosis. Cloudy ascitic fluid with a high number of WBCs, primarily polymorphonuclear cells, are seen during paracentesis (PMN). It's possible that none of the symptoms of the full-blown syndrome—or maybe just one—are present. It can occasionally manifest as an

encephalopathy with unknown causes. Hence, in cirrhotics, inexplicable fever, hypothermia, hypotension, encephalopathy, abdominal discomfort, or even unexplained clinical deterioration should be taken into consideration as reasons for diagnostic paracentesis for the diagnosis of SBP[26].

All cirrhotics should be evaluated for SBP with at least an ascitic fluid PMN cell count and ascitic fluid culture because SBP is an issue in cirrhosis with ascites.

Alcohol consumption is at an all time rise in India. Northeast India faces a huge brunt of alcohol and substance abuse. Every year, more cirrhotic patients visit the Silchar Medical College and Hospital (SMCH) due to the rising prevalence of alcoholic liver disease in this region of the country. The entire Barak Valley, Manipur, Tripura, and Mizoram are all included in the coverage region of SMCH, the only tertiary care facility in Southern Assam.

The purpose of this study is to determine the microbiological profile of the patients with SBP in liver cirrhosis and significance of AF analysis in their prognosis.

Study Design

This is a hospital based prospective, single centred, observational study.

MATERIALS AND METHODS

Our study was carried out in patients admitted to the medicine ward, SMCH, Silchar, Assam. Patients admitted for decompensated Chronic liver disease and its complications were studied for the period from June 2021 to may 2022. Hepatic cirrhosis was confirmed by ultrasonography. All patients with hepatic cirrhosis and ascites were recruited in the study.

Criteria for diagnosing SBP:

- AF PMN leukocytes count >250 cells/mm3.
  or
- AF total cells count >500 cells/mm3 with >50%neutrophils.and
- Absence of a primary source of infection.

100 patients fulfilling the criteria were studied and the results were compared with similar studies. Investigations appropriate for CLD patients were performed with special importance given to Ascitic fluid analysis- cytology, biochemistry and culture/sensitivity.

Ascitic Fluid Analysis

Before administering any antibiotics or subjecting the patients to invasive procedures like endoscopy, therapeutic aspiration, or liver biopsy, ascitic fluid was aspirated for study as soon as the patients were admitted. The right lower abdomen quadrant is the preferred location for an ascitic tap, which is most frequently performed 15 cm laterally to the umbilicus and carefully performed to prevent enlargement of the liver or spleen. It is important to take care of the inferior and superior epigastric arteries, which run just lateral to the umbilicus and towards the mid inguinal point. 40 ml of ascitic fluid should be drawn for diagnostic purposes (ideally using a syringe with a blue or green needle). Ascitic fluid tap that were contaminated or bloody were excluded from the study.

- The automated blood culture vials at the patient's bedside were immediately inoculated with 10 ml of ascitic fluid for safe transportation to the microbiological laboratory.
- A sterile test tube containing 10ml of ascitic fluid was used to send it to the lab for conventional culture.
- 20 cc of ascitic fluid were sent for cytological and biochemical analysis. All patients' ascitic fluid was examined to determine the cell count and type of cells present. To detect the presence of pathogenic organisms, ascitic fluid was cultured.

Patients' clinical presentation, test results, therapy response, prognosis, and hospital stay outcomes were all carefully examined. Patients were treated with iv Cefotaxime 2g 8 hourly.

Ultrasonography of the whole abdomen: ultrasonography was done by a senior radiologist using 3.5MWmechanical probe USG machine.

RESULTS

Total 100 patients of age group >12 years, diagnosed as SBP were studied thoroughly with regards to both history and clinical examination. The majority of patients (65%) were alcoholics, and 8% tested positive for HBsAG. 27% of patients' aetiologies could not be identified; they may be cryptogenic.

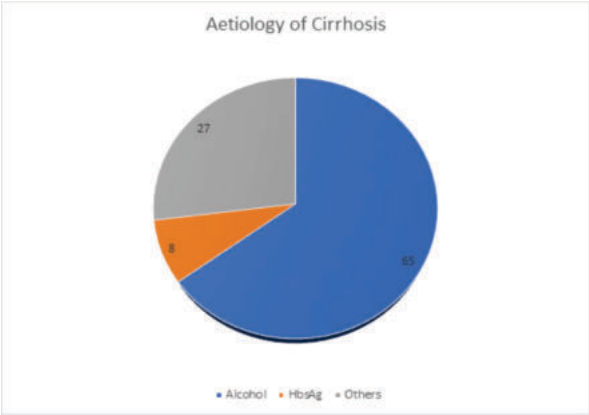

Fig 1. Pie Diagram Showing Aetiology Of Cirrhosis.

Outcome: With a 29% mortality, the outcome was dire. The majority of patients died from SBP and hepatic encephalopathy, but some also passed away from hematemesis, hepatorenal syndrome, and other cirrhosis-related sequelae.

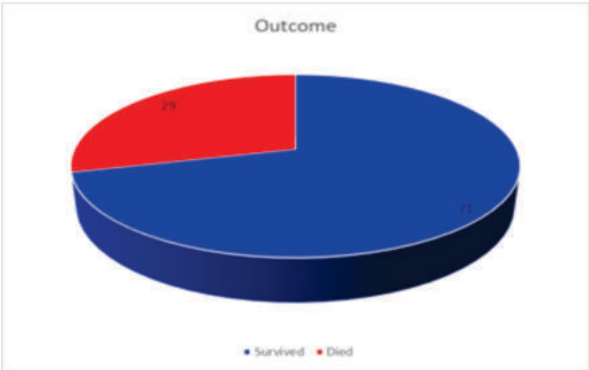

Fig 2. Pie Diagram Showing Outcome In Studied Patients

Ascitic Fluid Culture

Table 1. Ascitic Fluid Culture In Present Study Showed:

Ascitic fluid Culture	Number	Percentage
No Growth	60	60
E.Coli	28	28
Klebsiella Pneumoniae	8	8
Acinetobacter	2	2
Staph. aureus	2	2
Total	100	100

In the survivor group, 56% exhibited no growth while 15% cases were positive for ascitic fluid culture. While 11% of the patients who died during the course of treatment were positive for ascitic fluid culture, 18 % showed no growth.

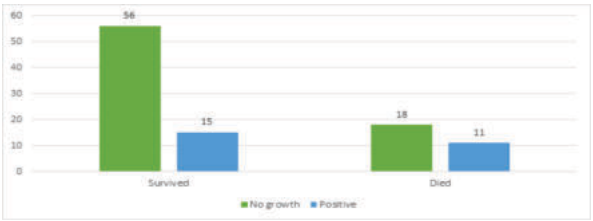

Fig 3. Ascitic Fluid Culture -survived And Died

Sensitivity

Sensitivity was tested for Cefotaxime, Norfloxacin, ciprofloxacin Amikacin, amoxycillin and clavulanic acid, linezolid, meropenem and piperacillin and tazobactam. Out of 40 cases that showed positivity in cultures, in 33 instances the isolated organism showed sensitivity to cefotaxime.

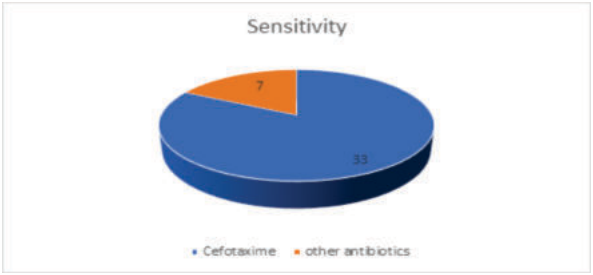

Fig 5. Pie Diagram Showing Sensitivity To Antibiotics In Ascitic Fluid C/s.

Ascitic Fluid Analysis

The average ascitic fluid protein level was 1.21mg/dl.

Good prognosis was associated with a progressive decline in ascitic fluid cell PMN count at 24 hours, 48 hours, and 5 days as compared to ascitic fluid cell count at the time of diagnosis.

Table 2. Comparison Of Ascitic Fluid (PMN) Cells Count Between The Patients Who Died And Survived.

Investigations Ascitic fluid Cells (PMNs)	Outcome				P Value
	Survived		Died		
	Mean	SD	Mean	SD	
0 Hours	492.76	215.96	1721.68	1740.25	<0.05
24 Hours	555.84	800.75	1437.344	1201.10	<0.05
48 Hours	311	76.42	1235.75	1336.72	<0.05
5 Days	79	77.75	435.5	591.27	<0.05

Table 3. Comparison Of Ascitic Fluid Protein Between The Patients Of SBP – Died And Survived

Investigations	Outcome				P Value
	Survived		Died		
	Mean	SD	Mean	SD	
Ascitic fluid Protein	1.29	0.33	1.086	0.3	<0.05

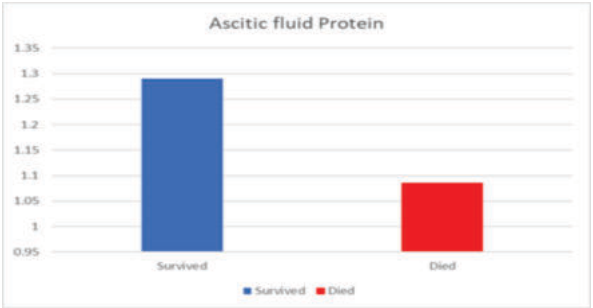

Fig 6. Ascitic Fluid Protein – Survived And Died

DISCUSSION

About 100 patients of SBP was studied, diagnosed by above-described guidelines, result of present study are compared with other studies as follows:

Ascitic Fluid Culture And Sensitivity

In the current series, 60% of the patients showed no growth and 40% were culture positive. In culture positive patients E.coli was the most prevalent bacteria isolated (28%). The Filik L, Unal S[28] investigation's ascitic fluid culture revealed 25.4% gram-negative organisms, with the most frequently identified organism accounting for 76.2% of the sample. Four out of seven patients in the DN Amarapurkar[27] series showed positive ascitic fluid cultures, with 75% of them displaying E. coli growth and one (25%) patient displaying Acinetobacter growth. In another study by A P Jain et al., 44.4% of patients had coagulase-positive Staphylococcus aureus, which was isolated from 88.8% of the patients, with the remaining cultures revealing Pseudomonas, Klebsiella, and E. coli.

In the current study, cefotaxime sensitivity was found in 82.5% of isolated organisms in ascitic fluid culture. Third generation cephalosporin treatment results in a cure rate of more than 80% of patients, according to Guarner C. et. al[28].

Ascitic Fluid Biochemistry

The development of SBP in these patients is significantly influenced by AF protein. Individuals who have an AF protein level below 1 g/dl commonly have SBP. Patients in the Runyon et al.[16] series who had AF protein levels below 1 g/dl were more likely to develop SBP. The mean AF protein in individuals with SBP was 0.78 0.24 g/dl in Amarapurkar's series[27]. In the present series the mean AF protein was 1.086±0.3g/dl indicating the role of low AF in developing SBP.

Low AF protein was significantly related to mortality

Ascitic Fluid Cytology

An ascitic fluid cell count of fewer than 200/dl was associated with a better outcome after the start of the treatment. According to Krishnamurthy MS and Patil NC 2008[26], a drop in ascitic fluid cells below 250 can be used as a benchmark for determining how long SBP patients should receive antibiotic therapy.

CONCLUSION

SBP should be actively treated because it has a very high fatality rate. Once SBP has been diagnosed, repeat ascitic fluid cell count should be done to monitor treatment because it aids in prognosis. E. coli has been found to be the most common organism in SBP with a culture-positive result in the current study. In most cases of culture positive patients, cefotaxime is the most sensitive medication. Cefotaxime is also recommended as an empirical treatment for SBP in this area. It is observed in the present study that low ascitic fluid protein is related to a bad prognosis and good prognosis is associated with decline in ascitic fluid cell count. Although the scope of this study is rather broad, more extensive research with more patients and longer-term follow-up is required to draw a firm conclusion.

REFERENCES

1. Murray CJ, Atkinson C, Bhalla K, et al. The state of US health, 1990–2010: burden of diseases, injuries, and risk factors. JAMA 2013;310(6):591–608.
2. Gines P, Quintero E, Arroyo V, et al. Compensated cirrhosis: natural history and prognostic factors. Hepatology 1987;7:122–8.
3. Asrani SK, Larson JJ, Yawn B, et al. Underestimation of liver-related mortality in the United States. Gastroenterology 2013;145:375–382.e2.
4. Singal AK, Anand BS. Recent trends in the epidemiology of alcoholic liver disease. Clin Liver Dis 2013;2(2):53–6.
5. Ichai P, Samuel D. Epidemiology of liver failure. Clin Res Hepatol Gastroenterol 2011;35(1):610–7.
6. Liou IW. Management of end-stage liver disease. Med Clin North Am 2014;98:119–52.
7. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W, Practice Guidelines Committee of the American Association for the Study of Liver Diseases, Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal

hemorrhage in cirrhosis. Hepatology 2007;46(3):922–38.
8. Mathews Jr RE, McGuire BM, Estrada CA. Outpatient management of cirrhosis: a narrative review. South Med J 2006;99(6):600–6.
9. Nusrat S, Khan MS, Fazili J, et al. Cirrhosis and its complications: evidence based treatment. World J Gastroenterol 2014 May 14;20(18):5442–60.
10. Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. Dig Dis 2016;34:382–6.
11. Krencker E. Bacterium coli commune als Sepsiserreger in 2 fallen von abdominaler krankungen. Munchen Med Wschr 1907; 54: 2095.
12. Caroli J, Platteborse R. Portocaval septicemia; liver cirrhosis & septicemia caused by colibacillus. Sem Hop 1958; 34: 472–87.
13. Kerr DNS, Pearson DT, Read AE. Infection of ascitic fluid in patients with hepatic cirrhosis. Gut 1963; 4: 394–8.
14. Conn HO. Spontaneous peritonitis and bacteremia in Laennec's cirrhosis caused by enteric organisms. A relatively common but rarely recognized syndrome. Ann Intern Med 1964; 60: 568–80.
15. Schrier RW, Arroyo V, Bernardi M, et al. Peripheral arterial vasodilation hypothesis: a proposal for the initiation of renal sodium and water retention in cirrhosis. Hepatology 1988; 8: 1151–7.
16. Runyon BA. Spontaneous bacterial peritonitis associated with cardiac ascites. Am J Gastroenterol 1984; 79: 796.
17. Kato A, Ohtake T, Furuya R, et al. Spontaneous bacterial peritonitis in an adult patient with nephritic syndrome. Intern Med 1993; 32: 719–21.
18. Makharia GK, Sharma BC, Bhasin DK, et al. Spontaneous bacterial peritonitis in a patient with gastric carcinoma. J Clin Gastroenterol 1998; 27: 269–70.
19. Kurtz RC, Bronzo RL. Does spontaneous bacterial peritonitis occur in malignant ascites? Am J Gastroenterol 1982; 77: 146–8.
20. Murray L, Lee YT. Primary peritonitis: an unusual operative diagnosis. Am Surg 1989; 55: 710–3.
21. Lipsky PE, Hardin JA, Schour L, et al. Spontaneous peritonitis and systemic lupus erythematosus. Importance of accurate diagnosis of gram-positive bacterial infections. JAMA 1975; 232: 929–31.
22. Skau T, Tegner Y. Spontaneous peritonitis and rheumatoid arthritis–a case report. Acta Chir Scand 1986; 152: 317–8.
23. Hurwich DB, Lindor KD, Hay JE, et al. Prevalence of peritonitis and the ascitic fluid protein concentration amoung chronic liver disease patients. Am J Gastroenterol 1993; 88: 1254–7.
24. Rimola A, Garcia-Tsao G, Navasa M, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis a consensus document. J Hepatol 2000; 32: 142–53.
25. Guarner C, Runyon BA. Spontaneous bacterial peritonitis: pathogenesis, diagnosis, and management. Gastroenterologist 1995; 3: 311–28.
26. Krishnamurthy MS, Patil NC 2008; serial ascitic fluid analysis in treatment of SBP. RUGHS
27. Amarapurkar DN, Viswanathan N, Parikh SS, Kalro RH, Desai HG :Prevalence of spontaneous bacterial peritonitis. J Assoc Physicians India. 1992 Apr;40(4):236-8
28. Filik L, Unal S: Clinical and laboratory features of spontaneous bacterial peritonitis. East Afr Med J.; 2004 Sep; 81(9):474-9.