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Original Article

Internal Medicine Section

To Study the Incidence, Predictive Factors and Clinical Outcome of Spontaneous Bacterial Peritonitis in Patients of Cirrhosis with Ascites

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ABSTRACT

Objective: To study the prevalence and predictive factors of spontaneous bacterial peritonitis (SBP) in patients of cirrhosis with ascites and to study the clinical characteristics and prognosis of patients with SBP.

Materials and Methods: The present study was conducted on 122 cases admitted in Department of Medicine, through emergency, in Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India. Cases of cirrhosis (irrespective of aetiology) with ascites between the ages of 18-75 years were included in this study. Ascitic fluid of every patient was aspirated under all aseptic measures, before initiation of antibiotic therapy and was sent for biochemical analysis, culture and cytological analysis.

Results: Mean age of patients enrolled was 50.30± 10.98 years. 85% were male and 15% were female. Alcohol (73.8%) was the leading cause of cirrhosis followed by HCV (37.7%) and HBV (4.9%). Of the 122 patients studied, 27 (20.4%) patients were diagnosed as having SBP and its variants. Monomicrobial Bacterascites (BA) was present in 5 patients and Culture Negative Neutrocytic Ascites (CNNA) was present in 22 patients. *Escherichia coli* were the most common isolated organism followed by *Klebsiella*. The various factors that predispose to development of SBP include low ascitic fluid protein concentration, a high level of serum bilirubin, deranged serum creatinine, high Child-Pugh score and high MELD score.

Conclusion: Ascitic fluid analysis remains the single most important test for identifying and assessing a course of SBP. Bedside inoculation of 10-20ml of ascitic fluid into culture bottle at patient bedside will yield better results. Early diagnosis and treatment will reduce the mortality rate in these patients.

Keywords: Bacterascites, Child-Pugh score, Culture Negative Neutrocytic Ascites

INTRODUCTION

Cirrhosis was named by Laennec in 1826 means orange or twany in Greek [1]. It is a diffuse process, characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules and in most if not all cases, the process follows or is accompanied by hepatocellular necrosis. WHO has estimated that cirrhosis is responsible for 1.1% of all deaths. Spontaneous bacterial peritonitis occurs in both children and adults and is a well known and ominous complication in patients with cirrhosis [2]. Of patients with cirrhosis who have SBP, 70% are Child-Pugh class C. In these patients, the development of SBP is associated with a poor long term prognosis. Fever with chills and abdominal pain or discomfort are the most common presenting complaints. The most common organisms isolated in SBP patients are *Escherichia coli* and other gut bacteria; however, gram positive bacteria including *Streptococcus viridians*, *Staphococcus aureus* and *Enterococcus sp*, can also be found [3]. A single organism is noted in 92% of cases and 8% of cases are polymicrobial.

The lab criteria for diagnosis of spontaneous bacterial peritonitis are presence of >500/mm^3 of leucocytes or presence of >250/mm^3 neutrophils in ascitic fluid [4]. Depending upon the cell count and culture of ascitic fluid, it has been further classified into its two variants i.e. Monomicrobial Nonneutrocytic Bacterascites and Culture Negative Neutrocytic Ascites. CNNA is defined as ascitic fluid leucocytes count >500/mm^3 or neutrophils >250/mm^3 with negative blood culture [5]. It may happen in as many as 50% of patients with SBP and may be the result of poor culturing techniques.BA is defined as ascitic fluid leucocytes count <500/mm^3 or neutrophils<250/mm^3 with positive ascitic fluid culture [6]. One study found that 38% of these patients subsequently develop SBP [7]. So, it may represent an early form of SBP.

OBJECTIVE

To study the prevalence and predictive factors of SBP in patients of cirrhosis with ascites and to study the clinical characteristics and prognosis of patients with SBP.

MATERIALS AND METHODS

The present study was a hospital based observational study, conducted on 122 cases from March 2012 to May 2013, admitted in medicine wards through emergency, in Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab. Cases between the age group of 18-75 years and known to have cirrhosis with ascites were included in this study. All patients with cirrhosis irrespective of aetiology of cirrhosis (alcohol, HCV, HBV, autoimmune, cryptogenic etc) were included in the study. Patients having secondary peritonitis due to appendicitis, gastrointestinal perforation, abdominal tuberculosis, septicemia, intestinal obstruction, trauma and malignancy and with history of antibiotic therapy during past ten days were excluded from the study. A detailed history of presenting symptoms, past history, drug and personal history was taken. Written consent was taken from all participating cases. The study was approved by the ethical committee of our institute.

Ascitic fluid of all cases was aspirated under all aseptic condition, before initiation of antibiotic therapy. Twenty milliliters of ascitic fluid was aspirated, out of which 10 ml of ascitic fluid was immediately inoculated at bedside into culture bottle and 10 ml of ascitic fluid was sent for biochemical and cytology examination. In biochemical

analysis ascitic fluid glucose, total protein and albumin were done. Cytology was done for the total and differential cell count. Bedside inoculation of culture bottle with 10ml of ascitic fluid was done and sent for culture and sensitivity.

The severity of disease was assessed by using Child Turcotte Pugh (CTP) and Model of End Stage Liver Disease (MELD) score. Upper GI Endoscopy was done in all cases to look for esophageal varies and was graded from I-IV.

RESULTS

Out of the total 122 cases of cirrhotic ascites, 103(85%) were male and 19(15%) were female. This high male to female ratio was due to the fact that most of the men had cirrhosis due to alcohol intake and none of the 18 female cases who participated in this study had history of alcohol consumption. Alcohol was the leading cause of cirrhosis in males followed by HCV. In females HCV was the leading cause of cirrhosis [Table/Fig-1]. All patients with alcohol related cirrhosis were males. Mean age of cases was 50.30± 10.98 years. Maximum numbers of cases (33%) were in age group of 41-50 years. The age of youngest case included in this study was 19 years and oldest case was 75 years. Twenty seven cases (22%) were less than 40 years of age and most of them had cirrhosis due to alcohol and HCV.

The presenting complaints of cases were abdominal distention in 109 (89%) followed by jaundice in 47 (39%), fever in 38 (31%), altered sensorium in 25 (20.5%), oedema feet in 23(18.9%), pain abdomen in 20(16.4%) and UGI bleed in 17 (13.9%) cases. Eighty nine (72.9%) cases were in CTP class C, 31(25.4%) in CTP class B and 2 (1.6%) in CTP class A. Eighty three (68%) cases had MELD score of >14 on admission. On admission, before starting antibiotics, AF aspiration was done in all cases. In biochemical analysis of AF, 21(17.2%) cases had AF total protein less then 1gm/dl and in cytological examination, 23(18.8%) cases had TLC more than 500cells/mm^3 [Table/Fig-2]. So out of the 122 patients studied, 25 cases (20.4%), 20 males and 5 females, were diagnosed as having SBP or its variants. Three (2.4%) cases had SBP, two (1.6%) had BA and 20 (16.39%) cases had CNNA [Table/Fig-3].

Following paracentesis, all patients were started empiric antibiotic therapy in form of Inj. Cefotaxime two gram IV every12 hours and latter antibiotics were changed according to AF Culture and Sensitivity. Three patients had *Escherichia coli* on AF culture, one had *Klebsiella* and one had *Staphococcus 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 pain abdomen and fever. Three patients had no response to treatment and kept on deterioting despite treatment and died during hospitalization.

The maximum incidence of SBP was in age group of 41–50 years and mean age of presentation was 49 years. Pain abdomen (45%), Fever (38%), Jaundice (36%), UGI bleed (10%) and Altered Sensorium (8%) were the most common presenting symptom in patients of SBP. One of the case with SBP was admitted with grade 4 hepatic encephalopathy. Out of the 25 patients diagnosed with SBP, 2 (8%) patients were asymptomatic on admission and were diagnosed as having SBP on routine ascitic fluid analysis. The mean haemoglobin in patients of SBP was 9.9 ± 1.9 g/dl and mean total leukocyte count was 12322 ± 6659/mm^3 [Table/Fig-4]. 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 > 4mg/dl was present in 12 patients. INR was significantly higher in patients with SBP compared with those without SBP. Fifteen cases of SBP had serum sodium levels of < 135 meq/l. Seventeen (68 %) of patients of SBP had serum creatinine of > 1.3 mg/dl. Out of 25 patients of SBP, 18 (72%) cases had history of significant alcohol intake, 5 (20%) cases were HCV reactive and 2 (8%) cases were HBV reactive. Incidence of SBP was highest in patients in class C of CTP score and in patients having MELD Score>14.

	Alcoholic	HCV reactive	HBs Ag Reactive	HCV Reactive & Alcoholic	HCV Reactive, HBs Ag Reactive & Alcoholic
Male	72	21	02	01	07
Female	00	15	04	00	00

[Table/Fig-1]: Distribution of all cases (n=122) according to aetiology of cirrhosis

Ascitic Fluid Analysis	No of cases (n=122)
Total Protein< 1 g/dl	21
Total Protein >1 g/dl	101
TLC <500 cells/mm^3	99
TLC >500	23
Positive AF Culture	05

[Table/Fig-2]: Ascitic Fluid analysis of cases

	AF TLC	AF Neutrophils	AF Culture
Spontaneous bacterial peritonitis (n=3)	>500/mm^3	>250/mm^3	Positive
Culture negative neutrocytic ascites (n=20)	>500/mm^3	>250/mm^3	Negative
Monomicrobial bacterascites (n=2)	<500/mm^3	<250/mm^3	Positive

[Table/Fig-3]: Ascitic Fluid analysis of cases (n=25) of SBP and its variants

No. of patients	25
Sex Female/Male	5 / 20
Hemoglobin (gm/dl)	9.9 ± 1.9
Total leukocyte count(mm^3)	12322 ± 6659
Platelet count (mm^3)	10^5 ± 0.66
International Normalization Ratio (INR)	1.6 ± 0.77
Total Bilirubin (mg/dl)	9.3 ± 8.7
Conjugated Bilirubin(mg/dl)	4.1 ± 3.9
Total proteins(g/dl)	6.2 ± 1.0
Serum albumin(g/dl)	2.3 ± 0.46
AST(IU/L)	132 ± 175
ALT(IU/l)	75 ± 53
Alkaline Phosphate (IU/l)	175 ± 106
BUN(mg/dl)	35 ± 26
Serum Creatinine(mg/dl)	2.1 ± 1.3
Serum Sodium(meq/L)	132 ± 8.6
Serum Potassium (meq/L)	4.2 ± 0.87
Random Blood Sugar (mg/dl)	164 ± 83
Child Pugh Class B/C	5/20
MELD Score	23 ± 10

[Table/Fig-4]: Clinical and Biochemical parameters of cases of SBP

DISCUSSION

All cirrhotic patients with ascites can develop SBP. The prevalence of SBP in cirrhosis patients ranges between 10%-30% [6]. Of patients with cirrhosis who have SBP, 70% are CTP Class C. In these patients, the development of SBP is associated with a poor long term prognosis. The clinical manifestations of SBP have a broad range. Most patients of SBP have symptoms and/or signs clearly suggestive of peritoneal infection, especially pain abdomen, fever and altered gastrointestinal motility. Other patients may present with development of hepatic encephalopathy or

renal failure which may be the predominant or only feature [8]. Furthermore, SBP occurrence may be asymptomatic or have minor symptoms only [9].

With the early diagnosis of the disease and prompt and appropriate antibiotic treatment, the inpatient mortality of an episode of SBP has been reduced to approximately 20% [10]. In our study, we found the incidence of SBP of 20.4 % in cirrhotic patients with a mortality of 12%. Most episodes of spontaneous bacterial peritonitis are monomicrobial and produced by enteric bacteria. Of such episodes, 67% involve gram-negative bacteria, *Escherichia coli* being the most frequently isolated organism [11].

The prevalence of SBP depends on severity of liver dysfunction, being higher in advanced liver disease [12]. Fever, high serum bilirubin, AF total protein level of < 1 g/dl and deranged renal functions are important predictors for development of SBP [13]. MELD score is another important predictors for development of SBP [14]. We found that presence of fever, pain abdomen, jaundice, renal failure, encephalopathy and MELD score > 14 are important predictors of SBP. Seventy percent of our SBP cases were alcoholics. The prevalence of SBP is higher in patients with a more advanced form of liver disease. Jain et al., reported that the prevalence of SBP was 34.92% out of 63 patients. All patients who had SBP were in child class C [7]. Two prospective studies comprising 127 patients (13 with SBP) [15] and 110 patients (28 with SBP) [16] confirmed low AF protein concentration as an independent predictor of SBP. Thus low AF protein helps us to identify cirrhotic patients at high risk for SBP.

Empiric antibiotic treatment should be started immediately after diagnosis of SBP. Third generation cephalosporins such as cefotaxim is often the treatment of choice. Administration of two gram intravenously twice a day for 10-14 days is often preferred treatment regimen. A repeat AF analysis is recommended at end of therapy to verify the declining PMN counts. Inoculation of ascitic fluid in blood culture bottles often display *Escherichia coli* and *Streptococcus* species [10], although ascites culture is negative in as many as 60% of patients, despite both clinical signs of SBP and neutrophil cell count >250 cells/µl. These patients should still be treated as having SBP [17].

Continuous oral administration of norfloxacin, 400 mg/day, is recommended in cirrhotic patients recovering from an episode of SBP. Since survival probability is very much reduced after SBP, cirrhotic patients who have recovered from an episode of SBP should be evaluated for liver transplantation. Tsung et al., found 30-day mortality in SBP patients of 24.2% and three year mortality of 66.5%.They saw a higher mortality in patients of ascites with SBP, than those without ascites. They found that Cirrhotic patients with SBP have 2.5 fold increase of 3-year mortality, compared to those without ascites [18].

We should restrict use of prophylactic antibiotics only to those patients of ascites who are at greatest risk of SBP. These include patients with upper gastrointestinal haemorrhage, high Bilirubin and low AF protein concentration. In cirrhotic patients without a past history of SBP and with a high ascites protein content (i.e. >10 g/l), long-term prophylactic administration of antibiotics is not necessary since the risk of SBP in these patients is negligible, provided adequate prophylaxis is administered if and when gastrointestinal haemorrhage develops in the course of the disease. Nonselective beta blockers increase the risk for hepatorenal syndrome and death in patients with cirrhosis and SBP [19] and should be carefully used.

LIMITATIONS OF STUDY

Analysis of 122 hospitalised cirrhotic patients may not reflect pattern of disease in the community and requires a large population study. Cases were selected from a tertiary care centre, so reference bias may be present. Though we tried our best to rule out all cases with history of antibiotic intake prior to hospitalization, but use of indiscriminate antibiotic use in community may affect the ascitic fluid culture analysis.

CONCLUSION

Spontaneous bacterial peritonitis is a serious complication of cirrhosis and all patients should be screened for it, as early diagnosis and management will help to reduce mortality in these patients. We should rule out SBP in any patient of ascites. A high index of suspicion must be kept in patients of ascites, who present with acute clinical deterioration. Any patient with cirrhosis and ascites, who present with pain abdomen, fever, jaundice, UGI bleed or hepatic encephalopathy, should undergo diagnostics paracentesis before starting antibiotics. Bedside inoculation of culture bottle would yield better results. Treatment is with a third generation cephalosporin like cefotaxime being the most commonly used antibiotic.

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ABBREVIATIONS

AF =Ascitic fluid, BA =bacterascites, CNNA= Culture Negative Neutrocytic Ascites, CTP=Child –Turcotte- Pugh, HCV=Hepatitis C Virus, HBV= Hepatitis B Virus, INR=International Normalized Ratio, MELD=Model of End-stage Liver Disease, SBP=Spontaneous bacterial peritonitis, UGI= Upper Gastrointestinal

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