FREQUENCY OF ASYMPTOMATIC SPONTANEOUS BACTERIAL PERITONITIS IN OUTDOOR PATIENTS WITH LIVER CIRRHOSIS

Maryum Khalid, Raja Samiullah, Shahid Raza Khalid

Military Hospital Rawalpindi

ABSTRACT

Objective: The objective of this study was to the incidence of silent SBP in asymptomatic cirrhotic patients of Military Hospital out patient department.

Study Design: Prospective study.

Place and Duration of Study: Gastroenterology Department, Military Hospital Rawalpindi from July 2013 to Dec 2013.

Material and Methods: Prospective exploration for evidence of SBP in asymptomatic cirrhotic patients due to any etiology with ascites. Clinical and laboratory features of consecutive outpatients with cirrhotic ascites undergoing paracentesis were recorded between July 2013 and December 2013 and ascitic fluid analysis was carried out.

Results: The frequency of spontaneous bacterial peritonitis in the population of 80 cirrhotic outpatients as determined by neutrocytic ascites (absolute neutrophil count >250 cells/mm) was 10%. Of the 8 patients with neutrocytic ascites, none was culture positive. The patients with absolute neutrophil count > 250 cells/mm were treated with antibiotics for seven days. Repeat diagnostic paracentesis showed marked improvement in absolute neutrophilic count. None of the patients developed hepatorenal syndrome or hepatic encephalopathy or recurrent SBP during 3 months follow up.

Conclusion: Incidence of silent SBP in asymptomatic cirrhotic patients' cases is significantly high. Antibiotic treatment in these patients ensures no further complications. However, a larger population may be studied to know the exact prevalence of silent SBP in our country.

INTRODUCTION

Burden of chronic liver diseases are on the rise worldwide[1-2]. In Europe an estimated 0.1% of the total population suffers from cirrhosis, the deadly complication of chronic liver disease[3]. Every year 14-26 new cases are per 100,000 population are being reported[3]. According to the latest survey by European Association for the Study of the Liver (EASL), chronic viral hepatitis is one of the four major causes of chronic liver disease[3]. Globally, the end stage complications of liver disease are in most instances attributed to chronic viral hepatitis, accounting for 57% cases of cirrhosis and 78% cases of hepatocellular carcinoma that is an alarmingly high percentage. Interestingly it is one of the preventable causes of hepatic damage[4]. Cirrhosis, in great majority of cases, leads to ascites[5] which in turn, may lead to spontaneous bacterial peritonitis (SBP) which is a potentially life threatening complication particularly in hospitalized patients[6-7] possibly leading to renal failure, worsening of liver disease, sepsis, hepatic encephalopathy, recurrent SBP and reduced survival[6]. In hospitalized patients, prevalence of SBP is 10-30%[8]. The prevalence, natural history and the outcome of SBP in outdoor patients with cirrhosis are unknown, as it may remain silent. Recurrent SBP has been reported in 34% of the cases in one of the studies[9].

An early diagnosis of SBP can help foresee the complications like sepsis, worsening of liver disease, hepatorenal syndrome (HRS) and hepatic encephalopathy (HE) that can be exploited to intervene earlier. For this reason, analysis of ascitic tap for SBP has been made mandatory in every patient undergoing ascitic fluid tap, with or without suspicion of SBP[10]. In developing countries, financial and procedural limitations have hindered this practice and incidence of silent SBP in cirrhotic patients with chronic viral hepatitis remains unknown[11]. We aimed to explore the incidence, characteristics and natural history of silent SBP in cirrhotic

Correspondence: Dr Maryam Khalid, Department of Gastroenterology, MH Rawalpindi
Email: econtactmaryum@gmail.com
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patients with chronic viral hepatitis so that a recommendation can be tailored according to local statistics with cost benefit ratio for the local population.

MATERIAL AND METHODS

This was a prospective study carried out at Gastroenterology department of Military Hospital Rawalpindi from July 2013 to Dec 2013. The protocol of the study was approved by Ethical committee of the hospital. Informed consent was taken from all participants. The diagnosis of cirrhosis was made on clinical, laboratory and radiological parameters. Severity of cirrhosis was assessed on Child-Pugh and Model of End Stage Liver Disease (MELD) score.

Inclusion Criteria

Outdoor patients with cirrhosis & asymptomatic ascites irrespective of etiology

Exclusion Criteria

Clinical symptoms of infection (fever, abdominal pain and tenderness), hepatic encephalopathy, upper GI bleed within the last four weeks, deranged renal profile within last four weeks, antibiotic treatment at admission and in the last 2 weeks, past history of SBP.

Prior to paracentesis, detailed physical examination was carried out to look for stigmata of chronic liver disease, presence of ascites and hepatic encephalopathy. Routine investigations including complete blood picture, C-reactive proteins, ESR, ALT, AST, ALP, Gamma GT, bilirubin, albumin, prothrombin time, INR, serum electrolytes (Na, K, Cl), renal function tests were performed. Diagnostic paracentesis was performed using standard aseptic technique without ultrasound guidance. 30 milliliter of ascitic fluid was drawn for total and differential cell count, total protein and albumin, aerobic and anaerobic cultures. Bedside inoculation of ascitic fluid into the blood culture bottles was done and the samples were immediately transported to the laboratory for further tests.

The diagnosis of SBP was based on the standard criteria of absolute neutrophilic count >250/mm3 (Neutrocytic ascites) in the absence of intra-abdominal source of infection. Culture positive with absolute neutrophilic count >250/mm3 were labeled as (culture positive neutrocytic ascites) while culture negative with absolute neutrophilic count >250/mm3 were labeled as culture negative neutrocytic ascites. Culture positive with absolute neutrophilic count < 250/mm3 were termed as Bacterascites.

Statistical Analysis

The data are expressed in mean values with standard error medians as range. The difference between the groups was determined by student t test using graph pad prism software. *p* value of less than or equal to 0.05 was considered to be significant.

RESULTS

Of 150 patients presented to outpatient department of Military Hospital from July to Dec 2013, 80 patients fulfilled the inclusion criteria. All the patients were males. Mean age was 61.15 years (58.5 ± 2.5 for SBP positive and 60 ± 3.1 for SBP negative patients). Etiology of cirrhosis was HBV in 10 (12.5%) and HCV in 70 (81.5%) patients. The Child-Pugh: 12 (17.14%) patients of class B and 58 (82.85%) patients of class C. There was no significant difference between cirrhotic outpatients with and without SBP in age, etiology of cirrhosis and prothrombin time. The mean total ascitic protein was significantly lower in SBP group (0.8 ± 0.02 g/dL) as compared to patients without SBP (1.75 ± 0.1). Out of 80 patients, 8

Table-1: Various characteristics of the SBP positive and negative patients.

	SBP status	Mean age	S. Albumin (g/dL)	PT (s)	Asc. Fluid Proteins (g/dL)	S. Bilirubin mMol/L	Child class C (N)	Child class B (N)	TLC (x10⁹/L)	ESR (mm/h)	CRP (mg/L)
	Positive (N=8)	58.5±2.5	28.5±1.6	30±1.8	0.8±0.002	47±0.9	8	0	8±0.02	46±1.6	60±13
	Negative (N=72)	60.5±6.8	30.1±2.8	28±1.6	1.75±0.1	53±2.3	50	12	11±0.25	33±1.8	53±21
P value	0.005	0.09	0.4	0.08	0.04	0.06	0.1	NA	0.09	0.09	0.1

patients (10%) were found to have spontaneous bacterial peritonitis evident by absolute neutrophilic count >250/mm^3. However cultures were negative in all of these patients (Culture Negative Neutrocytic Ascites CNNA). All 8 patients had child class C cirrhosis indicating advanced liver disease. The inflammatory markers like TLC, ESR and CRP were not significantly different in patients with and without SBP. (Table, Fig)

Three months outcome of SBP positive patients

The antibiotic treatment was stopped after 07 days and these patients were followed up in OPD for 3 months. There was no reported evidence of hepato-renal syndrome, hepatic encephalopathy or recurrence of SBP in these patients without any mortality.

DISCUSSION

The incidence of spontaneous bacterial peritonitis or its variants in hospitalized patients with cirrhosis has been reported to be between 20-50% in different studies[12-14]. So far few studies have evaluated incidence of asymptomatic SBP in outdoor patients[10,15-17]. In these studies its prevalence has been found to be low. In our study 8 out of 80 were found to meet the criteria of SBP i.e. absolute neutrophilic count. 250/mm3, which is found to be slightly higher than the previously conducted trials. In our study all the 8 patients diagnosed with SBP had culture negative neutrocytic ascites. Previously published studies reported majority of the patients to be culture positive with a predominant number of patients having gram positive organisms[15,17]. A possible explanation for this can be the fact that ours was a study conducted exclusively in outdoor patient department whereas previous studies were carried out both in outdoor as well as indoors. Moreover, some of the patients did report taking antibiotics 2 weeks prior to the evaluation that may have an impact on the culture outcome.

The difference between the SBP positive and negative patients with regards to the inflammatory markers was not significant in our study such as TLC, ESR, CRP levels. Whereas these markers have been reported to be reliable predicators of SBP in some of the studies[15,17], our results show that even their absence cannot rule out the incidence of SBP, and that ascitic fluid count is the only reliable way to rule out the infection. Though mortality in CNNA is less than culture positive, it still leads to significant mortality (8.4%)[18].

Advance liver disease and low ascitic fluid concentration have been identified as important risk factors for SBP. In our study, All 8 patients with SBP were of child class C and ascitic fluid total protein were significantly low (0.8 ± 0.002 g/dL) in SBP positive patients as compared to the SBP negative patients which confirms that risk of SBP is increased in advanced liver disease and low ascitic fluid protein level[17].

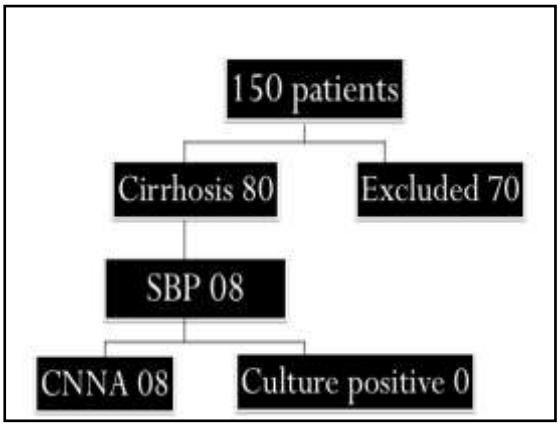

Figure-1: Schmatic representation of the results obtained in the study.

All patients diagnosed with SBP in our study with seven days course of antibiotics and follow up ascitic fluid analysis was done which showed significant improvement in their absolute neutrophilic count. These patients were followed up in OPD for three months. None of the patients died and none developed hepatorenal syndrome, hepatic encephalopathy, worsening of liver disease, sepsis or recurrent SBP. This shows that asymptomatic SBP is a less sever disease with no grave consequences as compared to symptomatic SBP[15,17].

The number of asymptomatic patients with SBP in our study is higher than previously reported but it is still too small to make a

recommendation and to determine the exact prevalence of SBP in our country and to identify its risk factors. Moreover long term follow up of these patients is required to predict the mortality and incidence of complications like HRS, sepsis, HE, deterioration of liver disease and recurrent SBP.

CONCLUSION

This study reports a high frequency of SBP in asymptomatic patients with cirrhosis. Prophylactic antibiotic treatment led to an uneventful three months follow up. However longer follow up of these patients should be done to see if any complications occur in these patients. Moreover these patients should be compared with the patients with silent SBP without antibiotics. In view of these results it can be suggested that diagnostic paracentesis should be carried out in asymptomatic outdoor patients with cirrhosis in order to detect the silent cases of spontaneous bacterial peritonitis.

CONFLICT OF INTEREST

The authors of this study reported no conflict of interest.

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