

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

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ABSTRACT

Objective: To determine the frequency of asymptomatic spontaneous bacterial peritonitis in patients of liver cirrhosis with ascites.

Study Design: Descriptive study.

Place and Duration of Study: The study was conducted at indoor and outpatient departments of Medicine, Military Hospital, Rawalpindi, Pakistan from 29th February 2008 to 28th August 2008.

Subject and Methods: One hundred and ninety five patients of liver cirrhosis with ascites were selected. To standardize the study; patients of both genders over 18 years of age, diagnosed with liver cirrhosis and ascites were included in the study after obtaining their informed consent. Patients with abdominal tenderness and fever, hepatic encephalopathy, intra-abdominal surgically treatable cause, with any co-morbid disease (hypertension and diabetes mellitus) or refusing to give consent were excluded from the study. Strict inclusion/exclusion criteria were observed to control the confounding variables. Diagnosis of spontaneous bacterial peritonitis was based on increased ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥ 250 cells / mm³) and/or positive bacterial culture.

Results: Out of 195 patients, 10 patients (5%) had neutrocytic ascites (absolute neutrophil count ≥ 250 cell/mm³). Out of these 195 patients, three patients (1.5%) were found to have positive ascitic fluid culture.

Conclusion: In our study the frequency of asymptomatic spontaneous bacterial peritonitis in patients of liver cirrhosis with ascites turned out to be 5% which is low. Therefore, analysis of ascitic fluid through diagnostic paracentesis should be reserved for inpatient or outpatient with clinically apparent new onset ascities or in cirrhotic patients with ascities whose general condition deteriorates.

Keywords: Ascitic fluid, Liver cirrhosis, Neutrocytic ascites, Spontaneous bacterial peritonitis.

INTRODUCTION

Cirrhosis is a progressive, diffuse, fibrosing and nodular condition of liver that disrupts its entire normal architecture¹. Spontaneous bacterial peritonitis (SBP) was first described by Conn in 1964². Spontaneous bacterial peritonitis is defined as an ascitic fluid infection without an evident intra abdominal surgically treatable source. The presence of infection is documented by a positive ascitic fluid bacterial culture and / or elevated ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥ 250 cells / mm³)³.

In cirrhotic patients with ascites spontaneous bacterial peritonitis (SBP) is a

common and potentially fatal complication. More than 60% of spontaneous bacterial peritonitis episodes are due to gram negative enteric bacilli. The most frequently isolated microorganisms are *Escherichia coli* and *Klebsiella pneumoniae*⁴. Spontaneous bacterial peritonitis occurs in the absence of any intra-abdominal surgically treatable source of infection. Its reported incidence in ascitic patients varies between 7-30%⁵.

In 1960s and 1970s, ascitic fluid infection was detected at an advanced stage due to low index suspicion of infection and high threshold for performing a paracentesis. As a result shock was common and mortality was high. Nowadays patients with ascites undergo surveillance paracentesis upon admission in hospital. Due to this practice spontaneous bacterial peritonitis is currently detected much earlier. The prevalence

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of asymptomatic spontaneous bacterial peritonitis in patients with cirrhotic ascites varies from 3.5% to 28%⁶. Clinical manifestations of spontaneous bacterial peritonitis are nonspecific. The most frequent signs and symptoms are fever (69%), abdominal pain (59%), signs of hepatic encephalopathy, abdominal tenderness (very rare), diarrhea, ileus, shock and hypothermia^{7,8}.

The reason to conduct this study was to determine the frequency of asymptomatic spontaneous bacterial peritonitis in patients of liver cirrhosis with ascites. If this study is able to determine that asymptomatic spontaneous bacterial peritonitis is common in cirrhotic patients with ascites then it can be logically concluded that every cirrhotic patient of ascites should undergo abdominal paracentesis to rule out spontaneous bacterial peritonitis. By adopting this practice, we would be diagnosing and treating more patients of spontaneous bacterial peritonitis and will be able to reduce the high rate of mortality associated with this disease.

MATERIAL AND METHODS

This descriptive study was conducted at indoor and outpatient departments of medicine, Military Hospital, Rawalpindi. The study was carried out over a period of six months from 29 February 2008 to 28 August 2008. Convenience non-probability sampling technique was used. One hundred and ninety five (n=195) patients of liver cirrhosis with ascites were selected. Sample size was calculated by using the formula for sample size: $[n = z^2pq/e^2]$ where: n=sample size, $z^2=3.84$, p = prevalence 15% (by taking mean of lower limit of 3.5% and upper limit of 28%), $q=(1-p)$ and e =degree of precision (0.05) with CI of 95%. To standardize the study patients of both genders who were over 18 years of age having liver cirrhosis with ascites were included in the study after obtaining their informed consent. Patients with abdominal tenderness and fever, hepatic encephalopathy, intra-abdominal surgically treatable cause, with any co-morbid disease (hypertension and diabetes mellitus) or

refusing to give consent were excluded from the study.

This study was conducted after approval from the hospital ethical committee and all the data were collected after informed consent of the patient. Diagnosis of liver cirrhosis with ascites was made on history, relevant physical examination, laboratory investigations and imaging modalities. To control the confounding variables strict inclusion/exclusion criteria were observed. Ascitic fluid total protein, lactate dehydrogenase and glucose was performed in all patients to rule out secondary bacterial peritonitis because even in case of perforation, clinical signs and symptoms of peritonitis may be lacking in up to 30% of patients owing to the separation of visceral and parietal peritoneum by ascitic fluid. Erect abdominal x-ray was performed in selected patients with history and physical findings suggestive of intra-abdominal source of infection. Once the diagnosis of liver cirrhosis with ascites was confirmed, abdominal paracentesis was carried out. Skin was cleaned by antiseptic and 1% lignocaine was infiltrated locally for anaesthesia. Large (20 ml) syringe was used and the needle was inserted in the abdominal wall in the left lower quadrant 3 cm cephalad and 3 cm medial to the anterior superior iliac spine. The syringe was advanced while aspirating until fluid was withdrawn for routine examination and culture. The syringe was withdrawn, needle was removed and sterile dressing was applied. Inoculation of blood culture bottles were done by bedside with 10 ml of ascitic fluid⁹. Diagnosis of spontaneous bacterial peritonitis was based on increased ascitic fluid absolute polymorphonuclear leukocyte (PMN) count (≥ 250 cells/mm³) and /or positive ascitic fluid bacterial culture.

All the data were collected through a performa. The data was entered and analyzed by SPSS version 12.0. Descriptive statistics was used to calculate mean \pm SD for quantitative variable i.e. age. Frequencies and percentages were calculated for qualitative variables i.e. gender, socioeconomic status, culture of ascitic fluid,

polymorphonuclear leucocyte (PMN) count (< 250/mm³ and >250/mm³) and spontaneous bacterial peritonitis.

RESULTS

During the six months study period from 29th February 2008 to 28th August 2008, one hundred and ninety five cases of liver cirrhosis with ascites were selected from indoor and outpatient departments of medicine, Military Hospital, Rawalpindi.

Out of 195 patients of liver cirrhosis with ascites, 10 patients (5%) had neutrocytic ascites (i.e there ascitic fluid absolute polymorphonuclear leukocyte count was ≥ 250 cells / mm³) and out of which 3 patients (1.5%) were found to have positive ascitic fluid culture (Table 1). The organism cultured from ascitic fluid in these asymptomatic patients was *Escherichia coli*, detail is shown in Fig 1.

While studying the distribution of age, the mean age was observed as 56±4.1 years. Majority (67%) of the patients were between 51-60 years, 27% were between 61-70 years, 5% were from 41-50 years age group and only 1% was from 31-40 years age group. Detail of distribution of cases by age is shown in Fig 2. Regarding gender 80% were males. Most patients belonged to low socioeconomic group comprising 77% (n=150) while 20% (n=39) belonged to middle socioeconomic group and 3% (n=6) belonged to upper socioeconomic status.

DISCUSSION

Spontaneous bacterial peritonitis was first reported in 1893 by Chorrin and since then many cases have been documented¹⁰. Patients with cirrhosis and ascites have 10% annual risk of ascitic fluid infection. The incidence of spontaneous bacterial peritonitis in hospitalized patient with cirrhosis varies from 7-23% in developed western countries^{11,12}.

There are four essential steps in pathogenesis of spontaneous bacterial peritonitis. Firstly, small intestinal bacterial overgrowth; secondly, increased intestinal permeability;

thirdly, bacterial translocation and lastly, immunosuppression³. These key elements are not

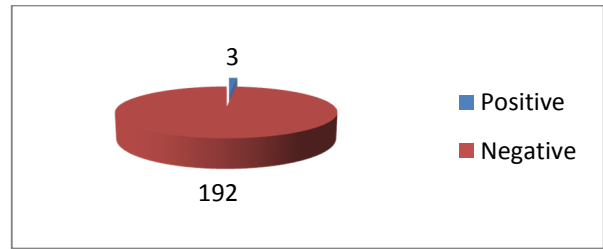


Figure-1: Results of bacterial culture.

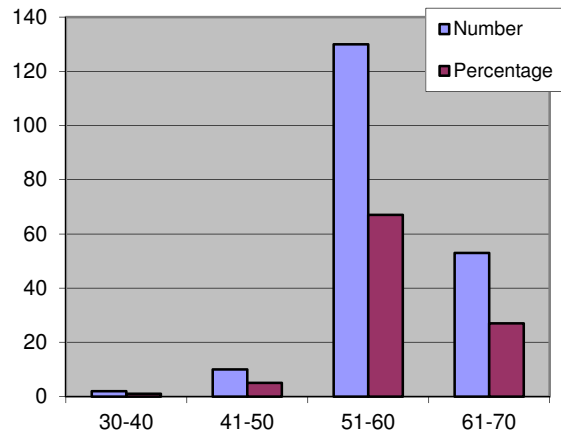


Figure-2: Distribution of patients of liver cirrhosis with ascites in four age groups.

separate, but interlinked. The main reasons for small intestinal bacterial over growth in patients affected by liver cirrhosis can be summarized as reduced intestinal passage, abnormalities in bile secretion, hypochlorhydria, abnormalities in IgA production and malnutrition¹³. In severely ill patients with liver cirrhosis, small intestinal motility is impaired. This results in bacterial overgrowth and the subsequent translocation of microorganisms through dysfunctional mucosal barrier. Portal hypertension is the main contributory factor for the increased intestinal permeability and subsequent impaired function of the intestinal barrier^{14,15}. Bacterial translocation is defined as either active or passive penetration of living microorganisms and their toxic products through the mucosal epithelial layer to the lamina propria mucosae. From there, microorganisms migrate to mesenteric lymph nodes and/or other extraintestinal sites¹³. Patients with liver cirrhosis suffer from immunosuppression due to multiple

reasons such as decreased phagocytic activity of neutrophilic granulocytes and the mononuclear phagocytic system, deteriorated humoral

ascites. In current study, 195 patient of liver cirrhosis with ascites were enrolled. Their mean age was 56.5 ± 4.1 years. This compares with a

Table-1: Summary of culture results of ascites fluid obtained from patients of liver cirrhosis with ascites.

Spontaneous bacterial peritonitis	Culture positive	Culture negative	Total
Positive (PMN count ≥ 250 cells / mm^3)	3	7	10
Negative (PMN count < 250 cells / mm^3)	0	185	185
Total number of cases of liver cirrhosis with ascites	3	192	195

PMN: Polymorph nuclear leukocyte

immunity and decreased opsonin activity of ascitic fluid¹⁶. All these interlinked factors are key elements in the pathogenesis of spontaneous bacterial peritonitis in patients of liver cirrhosis with ascites.

For the diagnosis of spontaneous bacterial peritonitis, the polymorphonuclear leucocytes (PMN) from the ascitic fluid obtained by paracentesis must exceed ≥ 250 cell/ mm^3 and from bacterial culture only one pathogenic microorganism must be isolated. If the sample of ascitic fluid contains blood then the diagnosis of spontaneous bacterial peritonitis is made by finding more than one neutrophilic granulocytes per 250 erythrocytes¹⁷. In culture negative neutrocytic ascites; fluid culture is negative and absolute PMN count is similar to that of classic spontaneous bacterial peritonitis. Both these conditions are identical from clinical as well as therapeutic approach. Therefore, the Consensus Conference of the International Ascites Club has recommended not to differentiate between these two conditions¹⁸.

Microbial spectrum in cases of spontaneous bacterial peritonitis includes mainly the gram negative aerobic flora of gut *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*^{19,20}. In our study only *Escherichia coli* was isolated. In addition patients with cirrhosis and ascites show a higher susceptibility to bacterial infections due to inadequate defence mechanisms. Other infections include urinary tract infections (20%), pneumonia (15%) and bacteremia (12%)²¹.

This study was undertaken to determine the frequency of asymptomatic spontaneous bacterial peritonitis in patients of liver cirrhosis with

study from Jalbani in which the mean age was 51 ± 12.5 years²². Out of them, 10 patient (5%) had PMN count of ≥ 250 cells per cubic millimeter which is close to the mean of two studies (5.32%). First study was done in 2008 at Division of Gastroenterology, department of medicine of University of Federal De Sao Paulo, Brazil showing a percentage of 3.5% and the second study was done at department of medicine at Military Hospital, Rawalpindi 2004 showed a percentage of 7.14% on the basis of polymorphonuclear cells^{23,24}. One study from Peshawar reported the overall frequency of in SBP cirrhotic patients with ascites due to HCV as 38 in 100 patients (38%)²⁵. In another study which was also from Peshawar reported that out of 70 cirrhotic patients, SBP was found in 26 patients (37.14%)²⁶.

Among patients of neutrocytic ascites, three patients were also culture positive (1.5%) which is close to the study published by Evans et al in 2003 showing a percentage of 1.4%^{5,27}. Out of ten patients with spontaneous bacterial peritonitis, 8 were male (80%) and two were female (20%) which is similar to the study done at Military Hospital, Rawalpindi during October 2000 to March 2002 by Hussain et al (2006)²⁸.

CONCLUSION

Although this study was of short duration but it showed that 5% of patients of liver cirrhosis with ascites having no symptoms, had spontaneous bacterial peritonitis. At the end of discussion (American Association for Study of Liver Disease (AASLD) recommends diagnostic paracentesis in patients of cirrhotic ascities whether inpatient or outpatient who develop

signs and symptoms or laboratory abnormalities suggestive of infection. Moreover some reports published state that the routine culture of ascitic fluid in asymptomatic patients only add to the treatment cost of patient with cirrhosis and should be avoided²⁹. Therefore it is recommended that the diagnostic paracentesis of ascitic fluid for detection of spontaneous bacterial peritonitis is most likely to be useful in only cases of new onset ascities, worsening of existing ascities and in condition where there is a clinical pointer that raises suspicion of spontaneous bacterial peritonitis).

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