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Comparison of Ascitic Fluid Protein Levels in Cirrhotic Patients With and Without Spontaneous Bacterial Peritonitis

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ABSTRACT

Spontaneous Bacterial Peritonitis (SBP) is one of the common complications of advanced liver cirrhosis. Ascitic fluid analysis is done to diagnose SBP. Decreased Ascitic Fluid (AF) protein level is a risk factor for SBP. **Objectives:** The aim of this study was to evaluate the effect of low AF protein levels on development on spontaneous bacterial peritonitis. **Methods:** 100 patients with advanced liver cirrhosis and ascites were enrolled and their AF analysis was performed to look for SBP and protein levels to establish any relationship between the two. **Results:** Initially 100 patients with advanced liver cirrhosis and ascites, who met inclusion and exclusion criteria, were enrolled in this study (out of 113 screened). AF analysis of 41 patients showed SBP. Ascitic fluid protein levels were compared in patients who had SBP with those who did not have SBP. Data was analysed on SPSS 22. Patients with ascitic fluid protein levels less than 1.5gm/dl had a higher incidence of SBP compared with those with higher protein levels (0.98 ± 0.57 vs. 1.54 ± 0.78 $p<0.05$). Mortality was also more in patients with SBP than those who do not have SBP (31% v/s 1%). **Conclusion:** Ascitic Fluid Protein levels are significantly reduced in patients who develop SBP than in those who do not develop SBP.

Keywords: Liver cirrhosis, Spontaneous Bacterial Peritonitis, Ascitic Fluid Protein Levels.

INTRODUCTION

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, which leads to portal hypertension and end-stage liver disease[1]. Cirrhosis is the end result of liver damage caused by chronic liver disease. Common causes of chronic liver disease include hepatitis B and C and alcohol and fatty liver disease[2]. Cirrhosis is the twelfth leading cause of death by disease, accounting for 27,000 deaths each year in USA[3]. Hepatitis B is present in 4.3% and hepatitis C in 4.5-8% of general population of Pakistan[4-7].

Ascites is the most common complication of cirrhosis[8]. Spontaneous bacterial peritonitis (SBP) is a serious infection that occurs frequently in patients with advanced cirrhosis and ascites. This condition has been defined as the infection of a previously sterile ascitic fluid, without any apparent intra-abdominal source of infection. Diagnosis of SBP is based on ascitic fluid neutrophil count of $\geq$250/cmm[9,10] (and/or leucocyte count of $\geq$500/cmm) or positive bacterial culture. Its prevalence is 21% in cirrhotic patients with ascites[8]. SBP is associated with high in-hospital mortality rate ranging from 20-40%[11].

Occurrence of SBP depends on the local immune response of the ascitic fluid. Ascitic fluid protein concentration and opsonic activities are important protective factors against SBP. Liver is the main site of synthesis of proteins[12]. Cirrhosis leads to inadequate functioning of liver, which in turn leads to decreased synthesis of proteins[13]. Patients with reduced ascitic fluid protein

concentration have reduced opsonic activities. These patients have been shown to be at high risk for SBP[14].

Objective

To study comparison of ascitic fluid protein levels in cirrhotic patients with and without Spontaneous Bacterial Peritonitis.

PATIENTS AND METHODS

This was a cross sectional study done in the Department of Gastroenterology, Shaikh Zayed Hospital Lahore and study was conducted from February 2015 to July 2015.

Inclusion criteria

All male and female patients aged 18 and above with ascites secondary to liver cirrhosis

Exclusion criteria

1) Patients with non cirrhotic ascites
2) Patients with hepatocellular carcinoma
3) Patients with secondary causes of intra-abdominal sepsis

Operational definitions

Spontaneous bacterial peritonitis

Spontaneous bacterial peritonitis (SBP) was diagnosed on the basis of >250 neutrophils per mm^3 or >500 leucocytes per mm^3 or presence of bacterial growth in ascitic fluid culture.

Cirrhosis

Cirrhosis was diagnosed by presence of coarse echotexture of liver, splenomegaly and ascites as seen on abdominal ultrasound.

Study design

In this cross sectional study, 100 patients with liver cirrhosis and ascites meeting the inclusion and exclusion criteria were enrolled. All relevant baseline investigations were sent. Baseline laboratory parameters included complete blood count, liver function test, kidney function test, serum electrolyte, international normalized ratio, serum ammonia, viral markers (for hepatitis B & C) if previously unknown, and abdominal ultrasound. Ascitic fluid analysis including ascitic fluid culture was done to rule in/out spontaneous bacterial peritonitis. Written informed consent was obtained from patients before induction in the study.

Statistical analysis

One Hundred patients were inducted in this time bound study. Data was analysed by using the Statistical Package for Social Sciences (SPSS) version 22. Descriptive statistics was reported as frequency and percentages for all qualitative variables, for example sex and presence or absence of SBP. Mean and standard deviation were calculated for all quantitative variables, for example AF protein and age. Mean AF protein levels were compared between groups (with and without SBP) using t-test. P-value ≤ 0.05 was taken as significant. Stratification was done to control effect modifiers like age and gender to observe an outcome. After stratification chi-square test was applied for qualitative data and t test was applied for quantitative data. P-value ≤ 0.05 was taken as significant.

RESULTS

Screening of 113 patients with cirrhosis and ascites was done. 13 patients were excluded from the study according to exclusion criteria. 100 patients fulfilling the inclusion and exclusion criteria (mean age 41±8.9years; male/female ratio 63:37) were enrolled in the study. Ascitic fluid analysis (TLC/DLC, culture and protein level) was performed.

Etiology of liver cirrhosis was hepatitis C in 79 patients (79%), hepatitis B in 9 (9%), alcohol induced in 5 (5%), and other causes in 7 (7%).

Out of the enrolled patients, 9 (9%) patients were in CTP class B and 91 (91%) were in CTP class C. Mean CTP score was 10.7±2.8. Distribution of patients according to CTP class and SBP is described in Table 1.

Out of the 100 enrolled patients 37 were female and 63 were male.

Patients who were found to have SBP had mean ascitic fluid protein level of 0.9±0.57 g/dl. Patients without SBP had AF protein level of 1.54±0.78 g/dL.

Mortality in patients with SBP was 31%. Mortality in patients without SBP was 1%(P<0.05).

Table 1: Number of patients with and without SBP in CTP class B and C.

	SBP (41 patients)	No SBP (59 patients)
Number of patients in child class B	1	8
Number of patients in child class C	40	51

Table 2: Comparison of mean protein level in ascitic fluid in cirrhotic patients with and without SBP

Protein level in Ascitic Fluid (g/dL)	With SBP (41 patients)	Without SBP (59 patients)	p-value
Mean	0.9	1.54	<0.05
Standard Deviation	0.57	0.78	

DISCUSSION

Ascites is the most common complication in patients with decompensated cirrhosis. Approximately 50% of patients with compensated cirrhosis will develop ascites over a 10-year period[15]. Patients with cirrhosis and ascites show higher susceptibility to bacterial infections mainly because of the inadequate defense mechanisms, the most frequent and most severe being spontaneous bacterial peritonitis (SBP). Prevalence of spontaneous bacterial peritonitis in cirrhotic patients with ascites is as high as 18%, with 40–70% associated mortality[16]. Spontaneous bacterial peritonitis is probably related to several impaired defense mechanisms, such as depressed reticuloendothelial system phagocytic activity, leukocyte dysfunction, reduced serum complement and other protein, and low bactericidal activity of ascitic fluid[17]. Ascitic fluid protein concentration and opsonic activities are important protective factors against SBP. Patients with reduced ascitic fluid protein concentration and reduced opsonic activities have high risk for SBP[18]. Antibiotic prophylaxis against SBP is recommended in patients with ascitic fluid protein levels less than 1.5 g/dL[22]. This is also recommended by the AASLD and EASL guidelines[23,24].

Spontaneous bacterial peritonitis (SBP) can be a potentially life-threatening complication in patients with cirrhosis and has typically been described in hospitalized patients. The prevalence of SBP in hospitalized patients with cirrhosis and ascites is between 10% and 30%[19,20]. In our study, 41% patients with ascites were found to have SBP. Majority of patients enrolled in our study (91%) were in advanced stage of cirrhosis *i.e.* CTP class C and high child score.

This study shows that low ascitic fluid protein level is strongly associated with development of SBP. In our study ascitic fluid protein concentration in patients with SBP was 0.9±0.57 g/dl while ascitic fluid protein concentration in patients without SBP was 1.54±0.78 g/dl (p<0.05). Previously performed study by showed similar results. In his study, ascitic fluid protein concentration in the spontaneous bacterial peritonitis group (0.72±0.53 g/dl) was significantly lower (p less than 0.001) than that in the group of patients with sterile portal hypertension-related ascites (1.36±0.89 g/dl)[21]. The strength of this study is that more patients in advance stages of PSE (CTP B 9%, CTP C 91%) were studied. The limitation of the study was small sample size.

CONCLUSION

Spontaneous bacterial peritonitis is quite a common and major complication of liver cirrhosis with ascites. Ascitic fluid protein level is significantly reduced in cirrhotic patients who develop spontaneous bacterial peritonitis. Patients with liver cirrhosis and low ascitic fluid protein levels need prophylactic measures against spontaneous bacterial peritonitis.

Conflict of interest

None

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