

Spontaneous Bacterial Peritonitis and its Common Pathogens in HCV Cirrhotic Patients

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ABSTRACT

Objective: To determine the spontaneous bacterial peritonitis and its common pathogens in HCV Cirrhotic patients.

Patients and Methods: This cross-sectional descriptive study was conducted at department of Medicine, Liaquat University Hospital Hyderabad/Jamshoro. This study was carried out for period of six months, i.e. from 1st March, 2009 to 31st August, 2009. Patients with liver cirrhosis caused by hepatitis C virus, ranging from 15 to 70 years of age and either gender were included in this study. Ascitic fluid was sent to Diagnostic and Research Laboratory of LUMHS within half hour of collection and ascitic fluid culture was done on blood agar media. TLC count >500-cells/ μ l or polymorph nuclear leucocyte >250-cells/ μ l were labelled as SBP positive. Growth positive on different disc was labelled with respect to the positive pathogen. All the data was entered on predesigned proforma.

Results: Total 177 cases were studied and the mean age was 50.06 ± 11.5 years with range of 20 to 70 years. Males were found in majority (78.5%) of cases, with male/female ratio of 2.3:1. Most of the patients 120(67.8%) were found having cirrhosis for 1-5 years' duration. Most of the cases 77(43.5%) presented with Child Pugh-Class B. Spontaneous bacterial peritonitis was present in 100(56.49%) patients. Among these 100 cases, 85.0% were found with positive culture, which showed Escherichia coli (most common) in 54.11% patients, followed by Klebsiella in 16.47% patients, Pneumococci in 9.41% and Enterococci in 7.0% patients.

Conclusion: It is concluded that spontaneous bacterial peritonitis was 56.49%, which is a major complication of HCV cirrhosis and E. coli is the major culprit micro-organism. Ascitic fluid culture is a sensitive method to detect the micro-organism causing spontaneous bacterial peritonitis.

Key words: HCV cirrhosis, Spontaneous bacterial peritonitis, Micro-organisms.

Author's Contribution

¹ Conception, synthesis, planning of research and manuscript writing Interpretation and discussion

² Data analysis, interpretation and manuscript writing, ³ Active participation in data collection

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Introduction

Liver cirrhosis is generally known as end stage liver disease which may develop by many causes and Hepatitis C virus is a frequent cause of chronic liver disease, all over the world including Pakistan.¹ Liver Cirrhosis results from necrosis of hepatocytes followed by formation of fibrosis and nodules.² World Health Organization stated that cirrhosis of the liver is the leading

cause of mortality (1.1%) and it was 12th most important cause of mortality in US in 2013.³ In Pakistan, accurate figure is still not known but definitely the problem seems much higher. It frequently presents with upper gastrointestinal bleed, Portosystemic encephalopathy (PSE), Spontaneous bacterial peritonitis (SBP), Hepatorenal syndrome (HRS), Hepatopulmonary syndrome and

hepatocellular carcinoma.⁴ HCV has been recognized as a major health problem over the past two decades.⁵ Cirrhosis of liver is defined as hepatic necrosis followed by fibrosis and nodule regeneration.⁶ Cirrhosis of liver is the commonest cause of mortality and morbidity throughout the world and HCV infection is rapidly increasing as a major cause of cirrhosis.⁷ Spontaneous bacterial peritonitis is a serious infection which occurs usually in cases having advanced liver cirrhosis. This disorder was defined previously as sterile ascitic fluid infection, without intra-abdominal source of infection. SBP diagnosis is based on total neutrophil count $\geq 250/\text{mm}^3$ or total leucocyte count $\geq 500/\text{mm}^3$ in ascitic fluid.⁸ All spontaneous ascitic infection incidents are symptomatic and the common clinical features are icterus (54.5%) and abdominal tenderness (54.5%) followed by hepatic encephalopathy (50.7%), fatigue (46.7%), pain of abdominal (44.4%), and fever (38.8%).⁹ SBP prevalence in cirrhotic cases by hepatitis C is 90%.¹⁰ Common isolates are *Escherichia coli* (42.8%), *Pneumococci* (28.5%), *Klebsiella* (14.28%) and *Enterococci* (7.7%).^{11,12} Severity of cirrhosis is graded in three categories as; Child-Pugh's 'A', Child-Pugh's 'B' and Child-Pugh's 'C'.¹³ Child-Pugh's classification is based on scoring of five parameters like serum bilirubin, prothrombin time, serum albumin, hepatic encephalopathy and ascites. Patients who presented with cirrhosis and ascites showed very high susceptibility to the bacterial infections.¹⁴ Spontaneous bacterial peritonitis is an ascitic fluid infection which occurs in absence of visceral perforation and lack of any focus of intra-abdominal inflammation like abscess, pancreatitis and cholecystitis. Diagnostic criteria of SBP includes: total count of polymorph nuclear leucocytes (PMN) in ascitic fluid obtained by paracentesis must exceed 250 cells/ mm^3 and from bacterial culture only one germ must be isolated.¹⁵ Very few studies are found in published literature, especially in our local setup. Therefore, this study was conducted to determine the frequency and pathogens of SBP involved in hepatitis C cirrhotic patients so that empirical therapy against most common offending agents could be started at earlier stage, in order to improve survival from this deadly complication of ascites in HCV cirrhotic patients.

Patients and Methods

This cross-sectional study was done at Department of Medicine Liaquat University of Medical & Health Sciences Jamshoro /Hyderabad. Study was carried out for period of a six months, i.e. from 1st March 2009 to 31st August 2009. All the known patients of liver cirrhosis with positive HCV antibodies who presented with ascites, ranging from 15 to 70 years of age were included. All the patients with secondary causes of peritonitis e.g. perforated gall bladder, appendix, pancreas, diverticulum, duodenal/gastric ulcer, malignant or haemorrhagic ascites and those having history of antibiotic intake within 15-days of admission were excluded. After obtaining an informed consent from patient who fulfilled selection criteria, abdominal paracentesis was done in HCV +ve cirrhotic patients, under aseptic measures. Ascitic fluid was sent to Diagnostic and Research Laboratory of LUMHS within half hour of collection. Direct microscopy was done for cells after Gram's staining; biochemical analysis was done on Cobas Mira. Ascitic fluid culture was done on blood agar media for the assessment of pathogens. All findings were recorded on a pre-designed proforma. TLC count $>500\text{-cells}/\mu\text{l}$ or polymorphonuclear leucocyte $>250\text{-cells}/\mu\text{l}$ were labelled as SBP positive. Positive growth on different discs were labelled with respect to the positive pathogen.

Sample size was calculated by using proportion (SBP in 10% to 30% patients admitted to hospital)¹⁶ with margin of error 5% and 95% confidence level, the sample size for this study was calculated as 177. Data was analysed by using SPSS version 16.00. Frequency and percentage were computed for categorical data. Mean and standard were computed for quantitative data. Chi-square test was applied to see the association of SBP with severity of liver cirrhosis and p-value <0.05 was considered as significant.

Results

Total 177 cases were studied and the mean age was 50.06 ± 11.5 years with range of 15 to 70 years. Majority of the patients 48(27.1%) were with age group of 31 – 40 years. One hundred and thirty-nine (78.5%) were males and 38 (21.4%) were females with male/females ratio of 2.3:1. Most of the patients 120(67.8%) included were having cirrhosis for the past 5 years, 52(29.4%) had

Table No. 1: Demographic Characteristics of Study (n = 177)	
Characteristic	Frequency(%)
Age Group	
15-20	14(7.9%)
21-30	22(12.4%)
31-40	48(27.1%)
41-50	40(22.6%)
51-60	25(14.1%)
61-70	28(15.8%)
Total	177(100.0%)
Gender	
Male	139(78.5%)
Female	38(21.4%)
Total	177(100.0%)
Duration of Cirrhosis	
< 1 Year	52(29.4%)
Years	120(67.8%)
>5 Years	05(02.8%)
Total	177(100.0%)
Child Pugh-Class	
A	61(34.5%)
B	77(43.5%)
C	39(22.0%)
Total	177(100.0%)
Age(Mean ± SD)	50.06±11.5 Years

cirrhosis duration less than 1 year and only 05(02.8%) had cirrhosis history more than 5 years. According to the severity of cirrhosis mostly cases 77(43.5%) were presented with Child Pugh-Class B, 39(22.0%) patients were with Child Pugh-Class C and 61(34.5%) patients were presented with Child Pugh-Class A (Table No.1). Out of 177 cases, the mean ascitic fluid protein (albumin) was 1.2 ± 0.8 g/dL whereas mean in patients with SBP was 1.54 ± 0.75 g/dL, and mean PMN cell count was 628.0±43.35 per mm³ while in SBP patients was 6770±4265 (n = 100) per mm³. Mean of WBC count was 746.1±52.97/mm³ (Table No.2).

Table No. 2 : Ascitic fluid analysis of hcv cirrhotics (n=177)	
Ascitic fluid analysis	(Mean±SD)
WBC count (/mm ³)	746.1±52.97/mm ³
PMN count (/mm ³)	628.0±43.35/mm ³
Protein (Albumin) g/dL	1.2±0.8 g/dL

Spontaneous bacterial peritonitis was present in 100 (56.49%) patients, while remaining 77(43.51%) cases were without SBP (Figure No.1).

According to the culture positivity among 100 patients of spontaneous bacterial peritonitis, positive culture was present in 85.0% cases and 15.0% were without positive culture (Fig No.2).

According to the culture positivity, Escherichia coli was most common in 54.11% patients, followed by Klebsella

Table No. 3: Frequency of different Pathogens (n=85)		
Pathogens	n	Percentage
Escherichia coli	46	54.11%
Pneumococci	8	9.41%
Klebsella	14	16.47%
Enterococci	6	7.0%
Others	11	12.94%

in 16.47% patients, Pneumococci in 9.41% and Enterococci found in 7.0% patients (Table No.3).

No significant difference was found between with and without spontaneous bacterial peritonitis according to Child Pugh classification and calculated p-value was 0.08 (Table No.4).

Table No. 4: Spontaneous Bacterial Peritonitis in relation to Severity of Child Pugh Class (n = 177)			
Child Pugh Class	With SBP	Without SBP	p-value
	n=100	n=77	
A	30(30.0%)	31(40.3%)	0.08
B	44(44.0%)	33(42.9%)	
C	26(26.0%)	13(16.9%)	
Total	100(100.0%)	77(100.0%)	

Discussion

This series revealed important aspect of the spontaneous bacterial peritonitis regarding its diagnosis and management, particularly in cases presenting with HCV cirrhosis. SBP is one of the major complication of cirrhosis with ascites, with a prevalence of about 10 – 30%.^{16,17} In Pakistan, cirrhosis is a common condition and puts economic burden on hospitals as well as on cirrhotic cases. These cases are very frequent, recurrent and related to very poor prognosis if left untreated. No such studies are available in published literature regarding the determination of risk factors in cirrhotic patients with spontaneous bacterial peritonitis and data regarding the frequency of SBP and its pathogens in HCV cirrhotic cases is scarce. Therefore, this study is focused on HCV patients with cirrhosis so that empirical therapy against most common offending agents could be started at earlier stage in our setup, in order to improve prognosis in this devastating complication of ascites.

This study was carried out to determine the different micro-organisms causing Spontaneous bacterial peritonitis (SBP). In this study the mean age of the patients was 50.06 ± 11.5 years. Consistently in the study conducted by Khan Z et al.¹⁸ in Peshawar, the mean age was 54 years. On other hand, another study conducted by Oladimeji AA et al.¹⁹ stated that mean age 62 ± 9 years of patients with range of 43-78 years, findings nearly correlate to this study.

Among the study participants, males were 78.5%, and females were 21.4% whereas Imran M et al.²⁰ reported 80% males and 20% female in their study respectively. In contrast to results of Kamani L et al.,²¹ reported 52% males in their study. This difference may be due to the fact that our study was done at tertiary care teaching hospital where most of the patients are illiterate who belong to poor socio-economic class whereas Kamani L et al.²¹ conducted their study at a private setup that is one of the most expensive hospital of the province.

In this series frequency of SBP was detected in 56.49% cases. This observation is comparable with some other local series as 54% reported by Jalbani A et al.,²² and his colleagues conducted at Chandka Medical College Larkana. Whereas in the study of Iqbal S et al.²³ conducted at Peshawar reported 51% frequency of SBP.

This study revealed mean + SD for ascitic fluid protein content in SBP patients as 1.54 ± 0.75 g/dL. These findings are comparable well with other local studies conducted in different areas of Pakistan i.e. 1.41 g/dL from Scouts Hospital Wana, South Waziristan Agency and Military Hospital Rawalpindi.²⁴ Syed VA et al.¹⁹ showed $1.18 + 0.74$ g/dL in SBP patients. In this study mean WBC count was $746.1 \pm 52.97/\text{mm}^3$ and mean PMN count was $628.0 \pm 43.35/\text{mm}^3$. On other hand, study conducted by Iqbal S et al.²³ reported mean PMN count as 1870.68 mm^3 . and Jalbani A et al.²² showed $1619.06/\text{mm}^3$ whereas Muhammad D et al.²⁶ also found comparable findings. In this study 85% cases had positive culture of ascitic fluid, out of 100 cases of SBP. Jain AP et al.²⁷ and his colleagues from India reported positive culture (81.81%) in SBP cases. Kamani L et al.²¹ showed 72.7% in their study. These results are almost same to this study.

In this study E.coli was found most common (54.11% cases) followed by Klebsiella in 16.47% and Pneumococci in 9.41% cases. These figures correlate well with other local studies of Jalbani A et al.²² and his colleagues, E.coli was present in 57.40%, Klebsiella in 18.51%, Pneumococci in 12.96%. Study of Iqbals S et al.²³ showed the frequency of E. coli as 58.13% whereas Imran M et al. reported 60% of patients having E.coli.²⁰ These findings were similar to our results as we also found E. coli as commonest pathogen followed by Klebsiella and pneumococci. Child-Pugh system is an important factor for prognostic evaluation of cirrhosis. In this study prognosis was based on cirrhosis staging (Child-Pugh's classification Pugh class A, B and C) and observed that 30% patients presented with Child-Pugh's class A grade of prognosis, 44% Child-Pugh's class B, and 26% patients presented with Child-Pugh's C. Similarly, Almani SA et al.²⁸ observed that Child-Pugh's A was in 37% cases, Child-Pugh's B in 37% and Child-Pugh's C was in 26% cases. While Yan, et al.¹³ stated that out of total cirrhotic cases Child-Pugh class A was in 22% patients, class B was in 41% and 36% cases presented with class C.¹³ In a study conducted by Yu I, Abola L et al.²⁹ conducted in Philippines, Child-Pugh's A was in 39.1%, Child-Pugh's B in 39.1% and Child-Pugh's C in 21.9% cases. These findings nearly correlate to this study.

Conclusion

It is concluded that spontaneous bacterial peritonitis was present in 56.49% cases, which is a major complication of HCV cirrhosis and E.coli was the major culprit micro-organism. Ascitic fluid culture is a sensitive method to detect the micro-organism causing SBP. Diagnosis of SBP becomes easier by paracentesis. Further long-term studies are needed to establish the relationship between spontaneous bacterial peritonitis, microbial diagnosis of ascitic fluid, and cirrhosis secondary to hepatitis C.

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