Original Article

Relation of Low Ascitic Fluid Proteins with Spontaneous Bacterial Peritonitis (SBP) in Patients with Portosystemic Encephalopathy – A Comparative Study

Himayat Ullah and Ghulam Mustafa

ABSTRACT

Objective: To establish the relationship between the ascitic fluid protein level with spontaneous bacterial peritonitis (SBP).

Study Design: Comparative study

Place and Duration of Study: This study was conducted at the Department of in the Department of Gastroenterology, Hayatabad Medical Complex Peshawar, during the June 2022 to November 2022.

Materials and Methods: This study included 290 portosystemic encephalopathy patients which were divided into two groups, 1 and 2, based on the presence or absence of SBP. Ascitic fluid proteins were measured for both groups and then compared for different variables, among the groups. The collected data was put into MS Excel (Microsoft Corporation, Washington, USA) and SPSS version 22 and analyzed. Means, medians, and standard deviations were calculated. The Spearman correlation coefficient was also calculated to show the relation between ascitic fluid proteins and SBP. Odds ratios of having SBP with different ranges of ascitic fluid protein were calculated to show the strength of the relation of low ascitic fluid proteins with the occurrence of SBP.

Results: Among 290 patients, 185 patients were in group 1 (SBP) and 105 patients were in group 2 (non-SBP). Males were 118 (63.8%) and 67 (54.3%) in group 1 and 2 respectively. The mean (S.D) age was 53.4 (15.2) and 57(19.9) years in group 1 and 2 respectively. Patients having ascitic fluid proteins < 1 g/dL were 118(63.8%) and 38(36.2%) in group 1 and 2 respectively, those having 1-2 g/dL were 53 (28.6%) and 42 (40%) in group 1 and 2 respectively and those above 2 g/dL were 14 (7.6%) and 25 (23.8%) in group 1 and 2 respectively. The mean (SD) ascitic fluid proteins level was 1.07 (0.58) and 1.57 (0.74) in group 1 and 2 respectively. Odds ratio showed that low ascitic fluid protein level was an independent factor for SBP in these patients ($p < .001$).

Conclusion: Low ascitic fluid protein level is an important risk factor and future predictor for the development of SBP and can be considered for the primary prophylaxis of SBP.

Key Words: Liver cirrhosis, Spontaneous bacterial peritonitis, Ascites, Encephalopathy.

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INTRODUCTION

Ascites is the abnormal accumulation of fluid in the peritoneal cavity. It is one of the commonest complications of chronic liver disease and cirrhosis liver. It is also one of the leading causes of hospitalization in patients with chronic liver disease[1].

Department of Medicine, College of Medicine, Shaqra, Shaqra University, Saudi Arabia

Correspondence: Dr. Himayat Ullah, Assistant Professor at Department of Medicine, College of Medicine, Shaqra, Shaqra University, Saudi Arabia.
Contact No: 0333 5046792
Email: himayatullah@su.edu.sa

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According to some studies, 5 years mortality after hospitalization due to ascites reaches up to 44%[2], with few studies showing even worse prognosis of 50% 3-year mortality due to refractory ascites[3]. Though the exact mechanism is unknown, the commonest mechanism suggested to be involved in ascites development is portal hypertension which leads to vasodilation and salt, and water retention through the renin-angiotensin-aldosterone system[4]. Ascites lead to many complications including electrolyte imbalance, pressure symptoms, hepatorenal syndrome, pleural effusions, hernias, infections including spontaneous bacterial peritonitis, etc.

Spontaneous Bacterial Peritonitis (SBP) known as spontaneous is the bacterial infection and diagnosed by an ascitic fluid neutrophil count of 250/µL and above in the absence of any other cause of infection like intestinal perforation or an infective process in the abdominal viscera[5]. In up to 90% of the cases, the culture of ascitic fluid will be positive for a single type

of bacteria (mono-bacterial growth), mostly *E. coli* and Streptococci[6]. The mechanism of bacterial contamination of the sterile ascitic fluid is not clearly understood but there are proposed theories of "Transluminal" Translocation and the "Hematogenous Spread" of the bacteria[7]. Many risk factors for the development of SBP have been identified like low ascitic fluid proteins, low vitamin D, use of proton pump inhibitors (PPI) high serum bilirubin level, decompensated cirrhosis, low ascitic fluid complement levels, low serum albumins, etc.[8,9]

Although data from several studies have shown that low ascitic fluid proteins are associated with the increased risk of SBP with some older studies suggest that ascitic fluid proteins level below 1mg/dL increases the risk of SBP by 10 folds[10], there are some recent studies which are against this finding and concludes that low ascitic fluid proteins have no association with the increased risk of SBP[11].

Spontaneous Bacterial Peritonitis (SBP) is a grave complication of chronic liver disease with one-year mortality ranging from 50 to 70% in adults with cirrhosis and in-hospital mortality of up to 18% in some studies, which can be decreased to below 5% by prompt diagnosis and treatment[12,13].

The main objective of this study was to establish the relationship between the ascitic fluid protein level with spontaneous bacterial peritonitis (SBP), which is still controversial based on the results from different studies for example those mentioned above[11].

MATERIALS AND METHODS

The study was conducted from June 2022 to November 2022, at the Department of Gastroenterology, Hayatabad Medical Complex Peshawar. It was approved by the hospital ethical review committee (Reference # 597/HEC/B&PSC/2021). A total of 290 patients with portosystemic encephalopathy and ascites were selected through non-probability convenience sampling and included in the study after informed consent. The criteria for inclusion into the study was any portosystemic encephalopathy patient above 12 years of age with ascites. The sample size was calculated based on a universally accepted sample size calculator[14] keeping the confidence interval above 95% and a 5% margin of error. Portosystemic Encephalopathy was diagnosed on the basis of clinical features and after excluding any alternative diagnosis. Ascites was diagnosed clinically and confirmed by ultrasound abdomen and pelvis. All the patients were subjected to detailed history and physical examination. These patients were then divided into two groups, one with spontaneous bacterial peritonitis (Group 1 = SBP) containing 185 patients and the other without spontaneous bacterial peritonitis (Group 2 = non-SBP) containing 105 patients. Spontaneous Bacterial Peritonitis (SBP) was diagnosed by diagnostic paracentesis with an ascitic fluid neutrophil count of 250/µL or above[5]. Patients having any other cause of raised ascitic fluid neutrophils like abdominal tuberculosis or other intra-abdominal infection were excluded from the study. Ascitic fluid analysis was performed in order to measure the ascitic fluid proteins, in a reliable laboratory under the supervision of a well-qualified biochemist. The collected data was put into MS Excel (Microsoft Corporation, Washington, USA) and Statistical Package for Social Sciences version 22 (IBM Corporation; Armonk, NY, USA) and analyzed. Means, medians, and standard deviations were calculated for continuous variables like age, ascitic fluid protein levels, and frequencies and percentages for categorical variables like gender. The Spearman correlation coefficient was also calculated to show the relation between ascitic fluid proteins and SBP. Odds ratios of having SBP with different ranges of ascitic fluid protein were calculated to show the strength of the relation of low ascitic fluid proteins with the occurrence of SBP. The data were presented as tables and graphs.

RESULTS

Two Hundred and ninety (290) patients, divided into two (2) groups, containing both male and female, with portosystemic encephalopathy (PSE) and ascites were included in this study. Group 1, which consisted of patients with SBP, contained 185 patients, while group 2, which was composed of patients without SBP, was having 105 patients. In Group 1 (patients with SBP) there were 118 males and 67 females with a male-to-female ratio of 1.76, while In Group 2 (non-SBP patients) there were 57 males and 48 females with a male-to-female ratio of 1.24 (Table 1).

The mean (±SD) age was 53.4 (± 15.16) in group 1, with the youngest patient aged 16 years and the oldest one aged 85 years. Whereas in group 2, the mean (±SD) age was 57 (± 19.9) with the youngest patient aged 15 years and oldest one 85 years (Table 2).

Out of 185 patients in group 1, 118 (63.8%) were having ascitic fluid proteins below 1 g/dL, and only 14 (7.6%) patients were having above 2 g/dL. The mean (± SD) ascitic fluid proteins level in group 1 was 1.07 (± 0.58). In comparison, among patients in group 2, only 38 (36.2%) of the patients were having ascitic fluid proteins less than 1 g/dL, while the rest of 67 (63.8%) patients were having ascitic fluid proteins ≥ 1g/dL. The mean (± SD) ascitic fluid protein level in this group was 1.568 (± 0.74)). Table 3 shows that out of 39 patients in both groups 1 and 2 with ascitic fluid proteins above 2 g/dL, 14 (35.9%) were having SBP while the rest 25 (64.1%) patients were without SBP, while out of 156 patients with ascitic fluid proteins below 1g/dL, 118 (75.6%) patients were having SBP while only 38 (24.4%) patients were without SPB. Figure 1 is the bar representation comparing the percentages of patients

having ascitic fluid protein below 1 g/dL, 1 to 2 g/dL and above 2g/dL from both groups 1 and 2. Spearman correlation coefficient between ascitic fluid proteins and SBP was -0.344 (significant at .01 level), indicating ascitic fluid protein level is inversely related to the development of SBP.

Table 4 shows the risk estimates of the occurrence of SBP in different levels of ascitic fluid proteins. The odds ratio of SBP is 3.1, 0.32, and 0.26 when the ascitic fluid protein levels were < 1 g/dL, ≥ 1 g/dL, and > 2 g/dL respectively. It means that patients with ascitic fluid proteins less than 1g/dL were 9.6 times more prone to develop SBP compared to those having ascitic fluid protein level of 1 g/dL or above and approximately 12 times more prone compared to those with ascitic fluid proteins above 2 g/dL.

Table No.1: Distribution of Patients According to Gender

Gender	Patients with SBP		Patients without SBP		TOTAL	
	N	Percentage	N	Percentage	N	Percentage
Male	118	63.8%	57	54.3%	175	60.3%
Female	67	36.2%	48	45.7%	115	39.7%
Total	185	100.0%	105	100.0%	290	100.0%

Table No.2: Distribution of Patients According to Age

Age (years)	Patients with SBP (n = 185)			Patients without SBP (n = 105)		
	N	Percentage	Mean (SD)	No.	Percentage	Mean (SD)
13 – 40	14	7.6%	26.0 (10.9)	23	21.9%	27.1 (10.8)
41 – 60	121	65.4%	48.5 (6.2)	32	30.5%	53.3 (7.0)
> 60	50	27.0%	73.0 (8.4)	50	47.6%	73.1 (8.3)
Total	185	100.0%	53.4 (15.2)	105	100.0%	57.0 (19.9)

Table No.3: Distribution of Patients with SBP According to Ascitic Fluid Protein Levels

Ascitic Fluid Proteins (g/dL)	Patients with SBP (n = 185)			Patients without SBP (n = 65)		
	No.	Percentage	Mean (SD)	No.	Percentage	Mean (SD)
< 1	118	63.8%	0.73 (.1469)	38	36.2%	.776(.1584)
1 – 2	53	28.6%	1.43 (.3310)	42	40.0%	1.657(.2795)
> 2	14	7.6%	2.57 (.2455)	25	23.8%	2.620(.2598)
Total	185	100.0%	1.07 (.5781)	105	100.0%	1.568(.7440)

P value = .001

Table No.4: Risk Estimate of SBP According to Ascitic Fluid Protein Level

Ascitic Fluid Protein level (g/dL)	**Odds Ratio (Risk Estimate) of SBP (95% Confidence Interval)**		
	Value	**Lower**	**Upper**
< 1	3.105	1.887	5.111
≥ 1	.322	.196	.530
> 2	.262	.129	.531

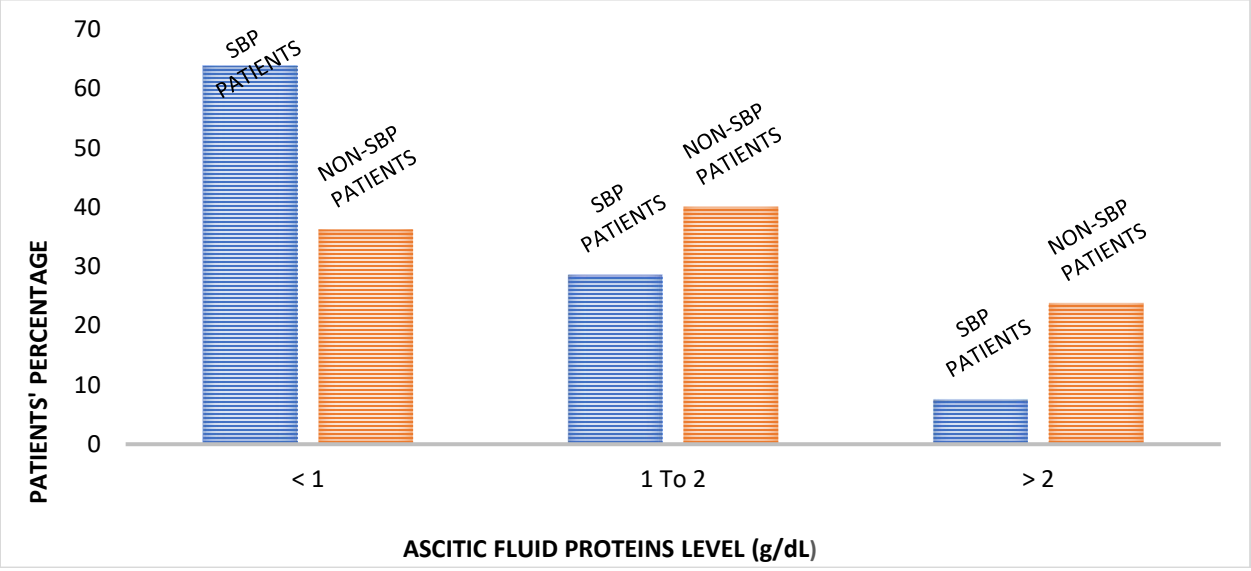

Figure No. 1: Comparison of SBP and non-SBP Patients' Percentages on the Basis of Ascitic Fluid Protein Levels

DISCUSSION

In this comparative study, the relation of ascitic fluid proteins level to the development of spontaneous bacterial peritonitis (SBP) in portosystemic encephalopathy patients, was studied. We measured the ascitic fluid protein level in patients with SBP and then compared it to the ascitic fluid protein level of non-SBP patients. Spontaneous Bacterial Peritonitis (SBP) is one of the most common complications of cirrhosis and accounts for 7 to 30% of cirrhotic patients with ascites and 4% of emergency admissions in such patients[15]. In this study, it was found that among portosystemic encephalopathy patients with ascites, 63.8% of the patients were found to have SBP. Chien-Hao H. et al in their review article stated that the prevalence of SBP in decompensated cirrhosis patients is found to be 20%[16]. In one of the similar studies done by Kavita P, et al. on liver cirrhosis patients with ascites, the frequency of SBP was reported to be 20.4%[17]. The reason for the higher prevalence of SBP (63.8%) in our study might be due to the sample selection, as our patients were suffering from portosystemic encephalopathy which has SBP as an etiologic factor. Though with a much smaller sample size, Ajayi A.O. et al inferred that hospitalized patients with cirrhosis liver and ascites have a prevalence of SBP of 67.7%[18]. Many factors have been identified to increase the risk of SBP including low ascitic fluid proteins, low vitamin D, use of proton pump inhibitors (PPI), high serum bilirubin level, decompensated cirrhosis, low ascitic fluid complement levels, low serum albumins, intestinal bacterial overgrowth, etc.[10] In this study, it was found that the vast majority of the patients were having ascitic fluid proteins level < 1 g/dL (63.8%) while those without SBP, most of them were having ascitic fluid proteins level ≥ 1g/dL (74.3%). The percentage of SBP was 81.4% in the patients of both groups having ascitic fluid proteins level below 1 g/dL. As the level of ascitic fluid protein rose above 2 g/dL, the proportion of patients with SBP falls to 35.9% which is statistically quite significant. These findings indicate that ascitic fluid protein level is inversely related to SBP which is further supported by a negative spearman correlation coefficient. This finding is somewhat consistent with the previous studies on the subject. Lata J et al., in their article, stated that patients with ascitic fluid proteins level below 1 g/dL and 10 times more prone to developing SBP than those with ascitic fluid proteins level above 1 g/dL[6].

Although there are several studies that, in one way or another, support the inverse relation of ascitic fluid proteins level with SBP, there are few that state that low ascitic fluid proteins do not predispose patients to SBP. In another study found no difference in the risk of developing SBP in 274 patients with cirrhosis whether having high or low ascitic fluid proteins[19].

Another study concluded that 50% of the patients with ascitic fluid proteins < 1.5g/dL developed SBP in one year follow-up, while those having ascitic fluid proteins level above 1.5g/dL, none of them developed SBP[20]. So, knowing the ascitic fluid protein level priorly, clinicians can decide to start prophylactic antibiotics to prevent SBP in these patients. Currently, the American Association for the Study of Liver Diseases recommends secondary prophylaxis of SBP, the primary prophylaxis of SBP is not routinely advised. It is desirable to make guidelines for the primary prophylaxis of SBP in high-risk patients, preferably in those having low ascitic fluid proteins.

CONCLUSION

Spontaneous bacterial peritonitis is a life-threatening complication of cirrhosis liver and ascites. Risk identification, prevention, and prompt management are crucial steps in decreasing the mortality of this grave complication. Strategies should be made for the primary prevention of SBP on the basis of risk factors like low ascitic fluid proteins level.

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Author's Contribution:

Concept & Design of Study:	Himayat Ullah
Drafting:	Ghulam Mustafa
Data Analysis:	Ghulam Mustafa
Revisiting Critically:	Himayat Ullah, Ghulam Mustafa
Final Approval of version:	Himayat Ullah

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