

Serum Bilirubin and Spontaneous Bacterial Peritonitis (SBP) in Hepatic Encephalopathy Patients

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Abstract

Introduction: Spontaneous bacterial peritonitis (SBP) is an important, frequent and a fatal complication of liver cirrhosis with ascites. Multiple factors have been found to be associated with SBP. The aim of this study is to know the association of serum bilirubin level with SBP. **Material and Methods:** Two hundred and ninety (290) patients with ascites and hepatic encephalopathy were included in this study. These patients were first checked for spontaneous bacterial peritonitis (SBP). Serum bilirubin was calculated for all these patients and its correlation with spontaneous bacterial peritonitis was then analyzed. Spearman coefficient for the significance of correlation and odd's ratio for the strength of the correlation was also calculated. **Results:** Among total 290 patients, 185 patients were having SBP, while 105 were non SBP. Male to female ratio was 1.52 and mean age was 54.7 years. While comparing the serum bilirubin levels between SBP and non SBP patients, the mean (SD) serum bilirubin level of SBP patients was 7.4 (5.5) mg/dL while that of non SBP patients was 3.6 (3.6) mg/dL. The Spearman correlation coefficient for bilirubin with SBP was significant at p value of .01. Odd's ratio of the two groups for visible hyperbilirubinemia was 5.292, showing the strength of association between SBP and hyperbilirubinemia. **Conclusion:** High serum bilirubin level is directly related to the occurrence of spontaneous bacterial peritonitis and may be used as a predictor of SBP in patients with ascites.

Keywords: Spontaneous bacterial peritonitis (SBP), hyperbilirubinemia, hepatic encephalopathy, serum bilirubin level, ascites.

1. Introduction

Spontaneous bacterial peritonitis (SBP) is a bacterial infection of ascitic fluid that develops in patients with liver failure, when there is no clear source of intra-abdominal infection, like visceral perforation [1,2]. Bacterial translocation is thought to be the primary cause of SBP, despite the fact that the exact mechanism underpinning its development is still unclear. One of the argument behind this that only a few intestinal bacteria, such as *Escherichia coli*, *Klebsiella pneumoniae*, and some other Enterobacteriaceae, are able to translocate from the lumen of the gut to the mesenteric lymph nodes and these are the bacteria that are mostly involved in SBP [3,4]. The most common presenting features of SBP are fever, abdominal pain and/or tenderness, development or worsening of hepatic encephalopathy and diarrhea [5,6]. Some cases of SBP may be asymptomatic [7]. SBP is diagnosed when the ascitic fluid neutrophil count is 250/ μ L or above and there are no other obvious infection source, such as intestinal perforation or an infectious condition in the abdominal viscera [6,8].

Spontaneous bacterial peritonitis (SBP) is among the most serious complications of liver cirrhosis and ascites. SBP is present in 10% to 30% of hospitalized cirrhotic patients with ascites [9,10]. Once being estimated as 90%, the fatality of SBP has improved with early detection and treatment as much as up to 20 to 40% in some studies [11,12]. So, it is important to identify the predictors or factors of

SBP beforehand so that preventive measures or at least early treatment can be initiated to prevent fatality.

Several factors have been identified to be associated with SBP and its related mortality, including ascitic fluid protein, high serum creatinine, low serum albumin, high child's score, high C-reactive protein, use of proton pump inhibitors, previous episode of SBP and so on [13,14]. One among these factors is high serum bilirubin level [15]. Serum bilirubin is a part of child's score which is used as predictor of outcome in cirrhotic patients, but its association with SBP has rarely been studied separately.

The objective of this study is to find out any association between serum bilirubin level with SBP, which may give a valuable information in predicting this lethal complication of liver cirrhosis and guide clinicians to take prompt actions while managing such cases.

2. Material and Methods

This research was carried out at Hayatabad Medical Complex Peshawar, Gastroenterology and Hepatology department. Two hundred and ninety (290) patients of hepatic encephalopathy with ascites were enrolled in this study, after the hospital's ethical review board approval. A standardized sample size calculator was used to determine the sample size based on the prevalence of ascites in hospitalized patients. Non-probability convenience sampling was utilized as a sampling technique. The inclusion criteria were, all the patients above 12 years of age,

having any grade of hepatic encephalopathy and having any level of ascites. The exclusion criteria were any patient with evidence of encephalopathy due to any other local brain pathology like central nervous system (CNS) infection, ischemia or hemorrhage. Hepatic encephalopathy was diagnosed on the basis of clinical features on the background of liver cirrhosis. Ascites was diagnosed by ultrasound abdomen. Spontaneous bacterial peritonitis was diagnosis by ascitic fluid neutrophil count of 250 cells/ μ L and above. Normal serum bilirubin was defined as serum bilirubin value up to 1.2 g/dL, clinically non-visible hyperbilirubinemia as serum bilirubin of 1.3 to 3 mg/dL and clinically visible hyperbilirubinemia as serum bilirubin more than 3 mg/dL. All of the patients gave their informed consent before undergoing a thorough history and clinical assessment. The ascitic fluid analysis and serum bilirubin level were performed by an experienced biochemist in a well-equipped laboratory.

The Statistical Package for Social Sciences version 22 (IBM Corporation; Armonk, NY, USA) and MS Excel

(Microsoft Corporation, Washington, USA) were used to analyze the data obtained. For continuous variables like age and serum bilirubin level frequencies, percentages, means and standard deviation were calculated while frequencies and percentages were calculated for categorical variable like gender. The significance of correlation of serum bilirubin level with spontaneous bacterial peritonitis was determined by Spearman correlation coefficient. Odds ratio was also calculated to show the strength of association between serum bilirubin level and spontaneous bacterial peritonitis. The data was presented using tables and graphs.

3. Results

Two hundred and ninety (290) hepatic encephalopathy patient with ascites from both genders (male and female) were included in this study. There were 175 males and 115 females. The age range was 15 years to 85 years with mean age of 55 years. Table 1 shows the age and gender distribution in details.

Table 1: Age and Gender Distribution

Age (Years)	Male			Female			Total		
	No. of patients	%age	Mean (S.D)	No. of patients	%age	Mean (S.D)	No. of patients	%age	Mean (S.D)
13 – 40	13	7.4%	31.08 (10.688)	24	20.9%	24.33 (10.23)	37	12.8%	26.70 (10.75)
41 – 60	93	53.1%	50.00 (6.894)	60	52.2%	48.73 (6.35)	153	52.8%	49.50 (6.69)
> 60	69	39.4%	73.58 (8.307)	31	27.0%	71.84 (8.38)	100	34.5%	73.04 (8.33)
Total	175	100.0%	57.89 (15.639)	115	100.0%	49.87 (18.16)	290	100.0%	54.71 (17.11)

Serum bilirubin value calculated for all the patients (SBP and non-SBP) ranged from 0.8mg/dL to a maximum of 25.3mg/dL. The mean (S.D) serum bilirubin value was 6.01 (5.26) mg/dL. serum bilirubin was categorized into three categories on the basis of

normal bilirubin, clinically non-visible hyperbilirubinemia (bilirubin level up to 3mg/dL) and visible hyperbilirubinemia (serum bilirubin above 3mg/dL). The detailed analysis of serum bilirubin in these patients is tabulated as Table 2.

Table 2: Serum Bilirubin Level in Patients with Ascites

Serum Bilirubin (mg/dL)	Frequency	Percentage	Mean	S.D
≤ 1.2	12	4.1%	.967	.0651
1.3 – 3	148	51.0%	2.327	.5200
> 3	130	44.8%	10.672	4.6746
Total	290	100.0%	6.012	5.2604

One hundred and eighty-five (185) patients among these ascites patients were diagnosed as having SBP on the basis of ascitic fluid neutrophil count. The

mean (S.D) serum bilirubin level in these patients was 7.4 (5.52) mg/dL, with none of them having serum bilirubin within normal range. The detailed analysis is shown in Table 3.

Table 3: Serum Bilirubin Level in Ascites Patients with of SBP

Serum Bilirubin (mg/dL)	Frequency	Percentage	Mean	S.D
≤ 1.2	0	0%	0	0
1.3 – 3	77	41.6%	2.503	.4258
> 3	108	58.4%	10.903	4.7556
Total	185	100.0%	7.406	5.5195

One hundred and five (105) patients among total 290 ascites patients, were found to be free from SBP (on the basis of ascitic fluid neutrophil count). The mean

(S.D) serum bilirubin in these patients was 3.5 (3.66) mg/dL which is significantly lower than mean bilirubin level of those with SBP (p value 0.001). The details are shown in Table 4.

Table 4: Serum bilirubin level of Ascites Patients without SBP

Serum Bilirubin (mg/dL)	Frequency	Percentage	Mean	S.D
≤ 1.2	12	11.4%	.967	.0651
1.3 – 3	71	67.6%	2.137	.5480
> 3	22	21.0%	9.541	4.1695
Total	105	100.0%	3.554	3.6659

The spearman correlation coefficient for serum bilirubin level with SBP was significant with p value of .01. Odd's ratio was found to be 5.292, showing the strength of association between for SBP and hyperbilirubinemia.

4. Discussion

In this study, we aimed to find the relation of serum bilirubin level with spontaneous bacterial peritonitis (SBP) in hepatic encephalopathy patients. One of the findings of this study was that, the number of females were significantly lesser than males (115 vs 175). Some other studies have also shown similar findings. Jessica B R et al concluded in their study that females suffer less from hepatic decompensation and hepatic related comorbidities or complications as compared to males [16]. They further added that this finding might be due to the protective effect of female sex hormones on the progression of chronic liver disease. Though the findings of the above-mentioned study regarding the gender were agreeing with ours, their findings regarding age of the female patients were contrary to our study. In our study the mean age of the male patients was significantly greater than female patients, in contrast to Jessica B R et al who reported the age of both male and female patients to be almost the same.

Spontaneous bacterial peritonitis (SBP) is one of the commonest and one of the most lethal complication of end stage liver disease and can aggravate other complication of chronic liver disease as well [17]. It is of utmost importance to find out the factors and markers that can predict SBP and its prognosis so as to institute preventive measures and early treatment. There are several factors and biomarkers associated with SBP that can be used as predictors of SBP in patients with ascites like ascitic fluid proteins, C-reactive protein, hypoalbuminemia, raised serum creatinine, proton pump inhibitors use, deranged prothrombin time (PT) etc [18 -22]. Serum bilirubin level is one of the prognostic predictors of chronic liver disease and a component of Child's Turcotte pugh score [23]. Serum bilirubin is also shown to be associated with many other conditions like cardiovascular disease, hypertension, obesity and metabolic syndrome [24,25]. Though its utility as a prognostic indicator of chronic liver disease is well established, its relation to the occurrence of spontaneous bacterial peritonitis (SBP) is not study much. Since hyperbilirubinemia is one the most prevalent biochemical abnormalities in cirrhosis patient so its relation to SBP can give a valuable information to the prediction of SBP in susceptible patients. Andreu M et al in their study found that serum bilirubin level is independently associated with the first episode of spontaneous bacterial peritonitis [11]. Though the sample size of the above-mentioned study was a bit smaller (110 patients), their findings clearly support our results. Sangram S et al deducted similar conclusions from their study stating that serum bilirubin level is significantly high

in patients with SBP [26].

In another study Ruben T et al concluded that serum bilirubin level above 4 mg/dL predict worse clinical outcome in patients with spontaneous bacterial peritonitis [27].

Although the relation of serum bilirubin with spontaneous bacterial peritonitis was hypothesized previously, the studies done previously were having smaller sample sizes and they did not study it specifically, rather it was combined with other biochemical factors like serum creatinine, serum albumin and other liver function tests [26,27].

In this study we not only established the correlation of high serum bilirubin level with spontaneous bacterial peritonitis by Spearman correlation coefficient, but also found out the strength of this correlation by odds ratio.

The main advantages of our study were the sample size, and its comparative nature which helped in establishing the strength of association.

The main disadvantage of the study was that we did not check the prognostic significance and outcome of hyperbilirubinemia in spontaneous bacterial peritonitis. Further research is needed to extrapolate and extend these finding in order to find the prognostic value of rising serum bilirubin levels in patients with spontaneous bacterial peritonitis.

5. Conclusion

Serum bilirubin level is an important prognostic indicator of chronic liver disease and a component of Child's score. Hyperbilirubinemia is a frequent finding in decompensated liver disease, ascites and spontaneous bacterial peritonitis, so it can be used as a useful predictor of spontaneous bacterial peritonitis (SBP) in such patients.

Ethics Committee Approval

MTI, Hayatabad Medical Complex, Peshawar,
Approval Number# 597/HEC/B&PSC/2021
Informed Consent

Consent taken from patient and his attorney when patient was unable to give consent.

Declaration of Interest: None

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