Spectrum of Clinical Features and Risk Factor Analysis in Patient of SBP with Cirrhosis and Ascites Attended in Tertiary Care Hospital of Nepal

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ABSTRACT

INTRODUCTION: Cirrhosis and its complications like ascites and SBP are common. But studies regarding it are very few in this part of the world. So the purpose of this study is to know prevalence, presenting symptoms and risk factors of spontaneous bacterial peritonitis (SBP).

METHODS: This was a cross sectional based observational study. Data were collected consecutively from January 2014 to January 2015. A total of 90 cases of ascites with cirrhosis were chosen to include in the study. Ascites without cirrhosis, any case of secondary peritonitis were excluded in the study. Patient admitted in NAMS, Bir hospital were enrolled in this study. Ascitic fluid was analysed for diagnosis of SBP. Detail history taken, physical examination and relevant investigations had done to identify risk factors and presenting symptoms of SBP in patient of cirrhosis and ascitis.

RESULTS: During the study period of one year a total of 90 participants were included in the study. The total number of male participants were 59(66%) and females were 31(34%). Among 90 of them 29(32.22%) has SBP. Among the 29 patients of SBP 22 of them has jaundice which is 76% (p=0.58). Fever and abdominal pain presents in 15(51%, p=0.42) patients. Hepatic encephalopathy and upper gastrointestinal bleeding consists of 12(41%) and 7(24%) (with p value 0.44) respectively. Only 3 (10%) of SBP patients were asymptomatic. Among risk factors, Out of 29 patients of SBP, 22(76%) has bilirubin more than 3mg%, 12(41%) of SBP patients have history of UGI bleeding, the ascetic protein level having one or less than one was 14(48%) and 2(6%) of them have previous history of SBP.

CONCLUSION: SBP incidence among hospital attending patient was 29(32.22%) in our study. Jaundice, fever and abdominal pain were common presenting symptoms. High bilirubin, UGI bleeding and low ascitic fluid total protein were associated with SBP.

KEY WORDS: SBP, Cirrhosis, Ascites

INTRODUCTION

Cirrhosis is an anatomically a diffuse process with fibrosis and nodule formation. It is the end result of the fibrogenesis that occurs with chronic liver injury. Common causes of cirrhosis are Alcoholism, Chronic viral hepatitis B and C, Cardiac cirrhosis, autoimmune hepatitis, inherited metabolic liver disease- Hemochromatosis, Wilson’s disease, Non alcoholicsteatohepatitis, Biliarycirrhosis, Cryptogenic cirrhosis. This problem is common in Nepal and in increasing trend. Studies regarding it are very few, still ascites is very common in cirrhotic patient. So the purpose of this study is to know about spontaneous bacterial peritonitis (SBP). Among the complications, ascites with SBP is one of the common complications, having high morbidity and mortality, with significant recurrence. So the study of prevalence, presenting symptoms and risk factors of SBP in cirrhosis is very important in developing country like Nepal.

Ascites is free fluid within the peritoneal cavity. Cirrhosis is the commonest cause of ascites in the Western world (~75%), followed by peritoneal
malignancy (12%), cardiac failure (5%) and peritoneal tuberculosis (2%)\(^3\). It is one of most common symptom in clinical practice. While median survival in patients with compensated cirrhosis is around 9 years\(^4\). Once decompensation occurs, median survival decreases to 1.6 – 1.8 years\(^5\). If with ascites, mortality is about 20% per year \(^6\). So development of ascities in cirrhotic patient indicate advanced cirrhosis. Early detection and prevention of complications like SBP is the main stay of treatment.

The most common infection in cirrhosis is spontaneous bacterial peritonitis (SBP)\(^1\). It is called spontaneous because it occurs in the absence of a contiguous source of infection (e.g. intestinal perforation, intra – abdominal abscess) and in the absence of an intra – abdominal inflammatory focus (e.g. abscess, acute pancreatitis, cholecystitis)\(^1\). SBP occurs in 9% of hospitalized patients with cirrhosis and accounts for 25% of all infections\(^2\) but SBP can occur in up to 30% of individuals and can have a 25% in-hospital mortality rate \(^2\). SBP is blood - borne and in 90% monomicrobial. Bacteria of gut origin are the most commonly isolated causative organisms. Therefore, migration of enteric bacteria across the intestinal mucosa to extra intestinal sites and the systemic circulation (bacterial translocation) has been implicated in its pathogenesis\(^8\).

SBP should be suspected when a patient with cirrhosis deteriorates, particularly with encephalopathy and/or jaundice. Patients with variceal bleeding or with previous SBP are at particular risk. Pyrexia, local abdominal pain and tenderness, and systemic leukocytosis may be noted. These features, however, may be absent and the diagnosis is made following a high index of suspicion with examination of the ascitic fluid\(^1\). The diagnosis of SBP is established with an ascites polymorphonuclear count more than 250/ mm\(^3\)\(^1\). The infecting organisms are commonly Escherichia coli or group D streptococci\(^7\). With SBP, 10 – 20% of patients will die during that hospital admission. The 1 - year probability of SBP recurrence is 69% and median survival of a patient who develops SBP is 9 months\(^10\). Mortality depends on the development of renal dysfunction\(^11\) and the site of acquisition of the infection, with nosocomial infection being an important predictor of death \(^1\). SBP resolution and immediate survival are 100% in community - acquired SBP that is uncomplicated (i.e. no renal dysfunction, no encephalopathy) whether patients receive oral or intravenous antibiotics\(^12\).

So, it looks extremely important to conduct study over symptoms and risk factor analysis in cirrhotic patient with ascites regarding SBP. But the studies on this problem are not sufficient in this part of world, whatever studies were conducted, they were conducted in western countries. There are a numbers of factors social as well as economical which can influence in nature and outcome of the disease. So it needs to do study in this part of world.

 METHODS

This was a cross sectional, hospital based observational study. Data were collected from January 2014 to January 2015. A total of 90 consecutive cases of ascites with cirrhosis were chosen to include in the study. The case of liver cirrhosis defined as\(^11\): One clinical sign of hepatocellular failure + One clinical sign of portal hypertension + At least three USG findings suggestive of cirrhosis of liver and/or UGI endoscopy evidence of portal hypertension in permissible Cases. The diagnosis of SBP established with an ascites polymorphonuclear count more than 250/ mm\(^3\)\(^1\).

Ascites without cirrhosis, any case of secondary peritonitis were excluded in the study. Patient admitted in NAMS, Bir hospital were enrolled in this study. History taking, physical examinations have been done to findout relevant data. Routine blood test like CBC, blood culture and sensitivity, renal function test, PT,INR,USG, serum total protein,albumin, serum bilirubin,viral markers, urine routine etc.has been done. Ascitic fluid analysis for TC, DC, culture, total protein, albumin, sugar was done.

 Sample size calculation

\[N = \frac{(z \alpha)^2}{(p(1-p))d^2}\]

Where, \(N=\) required sample size, \(z_\alpha=\) variate corresponding to desired reliability level (1.96 for 95% reliability), \(p=\) estimated proportion in the population, \(Q=100-p\) (if \(P\) is in %), \(d=\) maximum tolerable error. An estimated 90 cases were the desired sample size to draw a valid conclusion. Data were analysed by using SPSS 17.0 and Microsoft Excel 2007 for windows. Clinical presentation and risk factors were compared using chi-square test. P value <0.05 considered as significant.
RESULTS

During the study period of one year, a total of 90 participants were included in the study. The total number of male participants was 59 (66%) and females were 31 (34%). The study population was reorganized according to their district of origin and majority of them were found to be from outside Kathmandu valley. However there were subjects from 38 out of the 75 districts of Nepal.

Patients who were enrolled in the study with the diagnosis of liver cirrhosis with various aetiologies, among 90 of them 61 (67%) were farmers, 14 (16%) were shopkeepers, 15 (17%) were various occupations including drivers, teachers, housewives. Among 90 of them 29 (32.22%) has SBP. Patients with liver cirrhosis, mean ascetic fluid protein of different group is 1.6 (SD 1) gm% in study population, 1.51 (SD + 1.2) gm% in patients of NSBP group and 1.17 (SD + 0.55) gm% in SBP group (p = 0.35). Among the patients of SBP, the ascetic protein level having one or less than one has more number which is 14 (48%). Similarly patients who has protein level between more than 1-1.5 gm% were 12 (41%) and those more than 1.5 gm% were only 3 (11%). In patients with decompensated liver cirrhosis the total bilirubin level didn’t showed any specific pattern. Although the total bilirubin level was high in SBP group, the mean total bilirubin is 9.75 mg% (SD + 9.45 mg%). Mean bilirubin level in study population was 9.41 (SD + 9.21) mg% and 9.25 (± 9.18) mg% in no SBP group (p = 0.58). Patients of cirrhosis with ascits who developed SBP, most of them have raised serum bilirubin level. Out of 29 patients of SBP, 22 (76%) has bilirubin more than 3 mg%. 7 patients (24%) has less than 3 mg% of bilirubin. Among the 29 patients of SBP 22 of them has jaundice which is 76%. Fever and abdominal pain presents in 15 (51%) patients. Hepatic encephalopathy and upper gastrointestinal bleeding consists of 12 (41%) and 7 (24%) with p = 0.44 respectively. Only 3 (10%) of SBP patients were asymptomatic.

Among risk factors, most of our patients have raised serum bilirubin level. Out of 27 patients of SBP, 22 (76%) has bilirubin more than 3 mg%. 7 (24%) patients has < 3 mg% of bilirubin. 12 (41%) of SBP patients have history of UGI bleeding. Among the patients of SBP, only 2 (7%) of them have previous history of SBP. Ascitic protein less than 1 gm% was 14 (48%).

| S.N | Parameter | No SBP mean SD Median mean SD Median p |
|-----|-----------|-------------------------------------|------------------|------------------|------------------|------------------|------------------|
| 1   | T.Bilirubin (mg/dl) | 9.25 9.18 | 6.10 | 9.75 | 9.45 | 6.00 | 0.58 |
| 2   | Conj. Bilirubin (mg/dl) | 6.04 7.09 | 3.20 | 5.83 | 6.03 | 3.40 | 0.49 |
| 3   | T.serum protein (gm/dl) (gm/dl) | 6.49 1.07 | 6.30 | 5.87 | 1.02 | 5.70 | 0.01 |
| 4   | S. Albumin (gm/dl) | 2.44 0.59 | 2.50 | 2.50 | 0.50 | 2.50 | 0.58 |
| 5   | Alkaline phosphatase | 153.16 113.91 | 107.00 | 153.22 | 131.45 | 113.00 | 0.86 |
| 6   | AST (u/l) | 80.57 58.12 | 63.50 | 80.37 | 50.61 | 71.00 | 0.98 |
| 7   | ALT (u/l) | 47.80 31.42 | 41.00 | 56.37 | 38.72 | 45.00 | 0.34 |
DISCUSSION

Nepal is a country where disease like cirrhosis is very common. Culturally consumption of alcohol is well accepted which is one of the common cause for cirrhosis. Now, coming to demographic output, among the study group of 90 patients, 59 of them were male and 31 of them were female, which constitute about 66% and 34% respectively (male predominance). In few studies like studies done by Joel J. et al14, cirrhosis and chronic liver failure, published in journal of American academy of family physician, stated that Cirrhosis and chronic liver failure together were the 12th most common cause of death in the United States in 2002, accounting for 27,257 deaths (9.5 per 100,000 persons), with a slight male predominance. The incidence of SBP in our study was 32.22%. Patients who were enrolled in the study with the diagnosis of liver cirrhosis with various aetiologies, among 90 of them 29(32 %) has SBP. This result was similar to other studies15 between 10-35% . Still our incidence was in upper limit. It may be due difference in sample size, economic status, awareness toward health and life style of the people. Male and female looks nearly equal in proportion (m: f=15:14) which is variable in different studies.

In our study, most common presenting symptom was jaundice. Among the 29 patients of SBP, 22 of them have jaundice which is 76%. Fever and abdominal pain presents in 15(51%) patients. Hepatic encephalopathy and upper gastrointestinal bleeding consists of 12(41%) and 7(24%) respectively. Only 3 (10%) of SBP patients were asymptomatic. Great variation in symptoms and signs has been reported. Minhas et al16 reported fever 54%, pain abdomen 57% and Hepatic encephalopathy 67%. In other study, Pelletier et al17, found 89% of patients were having fever, UGI bleed (42%), pain abdomen 53% and hepatic encephalopathy in 50% of cases. In our study more patients had jaundice; the cause of it may be more patient presented to the hospital at advanced stage of disease. But the result of our study is consistent with one study done by Filik L et al18, they noted that the most common clinical features were as follows: icterus (54.5%), abdominal tenderness (54.5%), hepatic encephalopathy (50.7%), abdominal pain (44.4%) and fever (38.8%).

One of the aims of this study was to evaluate the risk factors in development of SBP in cirrhotic patient with ascites. Most of our patients have raised serum bilirubin level. Out of 27 patients of SBP, 22(76%) has bilirubin more than 3mg%. Seven patients (24%) has < 3mg% of bilirubin. Our study has shown, there is strong chance of development of SBP if patient has high level of serum bilirubin. This was supported by different studies done by Follo A. et al19. we have done a detail study regarding the relation between ascitic total protein level and spontaneous bacterial peritonitis. Our study has shown that patients with liver cirrhosis, mean ascitic fluid protein of different group is 1.51(SD+ -1.2) gm% in patients of NSBP group and 1.17(SD+ -5.5) gm% in SBP group. A similar study was done by MP Agarwal, BR et al20 on 41 patients that have shown that among these patients who has SBP has mean ascitic protein 1.68 ± 0.80mg% as compared to patients without SBP having protein 1.91 ± 0.68gm%. Similar results were also seen by Dr. Abdul Rasheed et al21 in military hospital, Rawalpindi, which concluded that the mean ascitic fluid protein content was found to be low in SBP as compared to non SBP patient’s 1.41 gm% vs. 2.20 gm%. Since some of studied has shown low level of ascitic protein (<1gm %), are more susceptible for SBP, we analyzed our patients having different ascitic protein level. Among the patients of SBP, the ascitic protein level having one or less than one has more numbers which were 14(48%). Similarly patients who has protein level between more than 1-1.5mg% were 12(41%) and those more than 1.5 gm% were only 3(11%). A study was done by Luke T. Evans 22 et al in 427 cirrhotic outpatients. The mean total protein in ascitic fluid was significantly lower in the SBP group ((0.6 + _ 0.04 g/dL). El-Shabrawi MH et al.23 has done a cohort study on diagnosis of spontaneous bacterial peritonitis, ascitic fluid protein level of <= 1 gm/dl was found in 13/30 (43.3%) of studied cases. Result of our study corresponds most of other studies conducted in different parts of the world.

We tried to study relation of previous episode SBP and its relation with current episode. But only 7% of our patients have history of previous SBP. But on study done by Franca AV et al.24, SBP recurrence was observed in 44% of patients. The cause of low recurrence of SBP may be high mortality after first episode and poor recording of data of previous episodes in our country. Similarly, we analysed the risk of SBP in patient who has history of upper gastrointestinal bleeding in cirrhosis patient. 41% of them have history of UGI bleeding. But study done by Syed VA et al. 15 has different result. Patients with Upper Gastrointestinal Bleeding are 18.75% and 30.86% with SBP and without SBP respectively which doesnot support the fact that the risk factor of SBP is UGI bleeding.
LIMITATIONS
This study has done in short duration of 1 year so sample size is not large. For diagnosis of SBP, only the neutrophil counts more than 250/dl was taken. Culture was mostly negative.

CONCLUSION
SBP is a potentially treatable but life threatening condition. SBP incidence among hospital attending patient is significant in number (32.22%) in our study. Presenting symptoms and risk factors associated with SBP are similar to other part of the world. Jaundice, fever and abdominal pain were common presenting symptoms. Although this study was of short duration and included smaller number of patients, it is recommended that ascitic fluid sample should be obtained routinely in all patients admitted in hospital with cirrhosis and ascites, in addition to those who have signs and symptoms suggestive of spontaneous bacterial peritonitis. Low ascitic protein, High bilirubin level, history of UGI bleeding, previous history of SBP has high incidence of SBP. However further long term studies are needed to establish relationship.

REFERENCES