Section: General Medicine

Original Research Article

STUDY OF ASCITIC FLUID PROTEIN LEVEL AND SAAG IN SPONTANEOUS BACTERIAL PERITONITIS WITH CHRONIC LIVER DISEASE.

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ABSTRACT

Background: Spontaneous bacterial peritonitis is a common and potentially lethal complication of cirrhotic ascites. Spontaneous infections in cirrhosis account for 33% of all bacterial infections in cirrhosis. Cirrhotic patients with an ascitic fluid total protein concentration <1 g/dl are prone for spontaneous bacterial peritonitis (SBP). The present study was designed to study the relation between spontaneous bacterial peritonitis and serum ascites albumin gradient (SAAG) in chronic liver disease patients. **Aim of the study**: To study the ascitic fluid protein and SAAG in SBP patients with chronic liver disease (CLD).

Materials and Methods: This was a prospective study conducted for a period of 1year from 1st June 2022 to 31st May 2023. A total of 80 patients more than 18years of age with chronic liver disease with ascites were included in this study. Patients having had a peritoneal paracentesis with in last 2 weeks for cardiac reasons, malignancy, tubercular peritonitis, pancreatic ascites, congestive heart failure, acute viral hepatitis and secondary peritonitis were excluded. Detailed history, examination and relevant investigations were done. Around 10ml of ascitic fluid was sent for analysis for all patients. Based on investigations, patients were divided into two groups: Group A-without SBP and Group B-with SBP. The SAAG was calculated by subtracting the serum albumin level from the ascites fluid albumin level. Data was collected, recorded and statistical calculation was done using in Microsoft excel 2007.

Results: Out of 80 patients, 43 (53.75%) patients belonged to group A and 37 (46.25%) patients belonged to group B. In group A, 41 (95.34%) were male and 2 (4.65%) were female and in group B, 35 (94.59%) were male and 2 (5.40%) were female. The mean age of the patients in group A was 52 ± 4 years and in group B was 53 ± 6 years. The most common risk factor in both groups was alcohol followed by NASH, hepatitis B and hepatitis C. The most common clinical presentation in both groups was distension of abdomen followed by yellowish discoloration of eyes and swelling of feet. The serum albumin levels in Group B were lesser than group A with the values of 2.54±0.33 g/dl and 3.35±0.36 g/dl, which was statistically significant with p value of 0.0026. The ascites albumin levels were also lower in group B compared to group A with values of 0.43±0.23 g/dl and 0.91±0.31 g/dl, which was statistically very significant with p value of <0.001. But SAAG value was higher in group A compared to group B (2.45±0.01 and 2.09±0.47). This difference was statistically significant (p 0.0016). The mortality rate was higher in group B compared to group A (56.75% v/s 18.60%).

Conclusion: The development of spontaneous bacterial peritonitis in chronic liver disease patients is directly proportional to ascitic fluid albumin and SAAG ratio. The mortality rate was higher among patients who developed SBP. As patients with low ascitic fluid albumin are prone for SBP, it can be prevented by prophylactic use of antibiotics and diuresis.

Keywords: Chronic liver disease, SAAG, Spontaneous bacterial peritonitis.

INTRODUCTION

Chronic liver disease (CLD) is one of the major causes of morbidity and mortality throughout the world. Ascites is the most frequent complication of cirrhosis. About half the patients with cirrhosis develop ascites during 10 years of observation. Patients with ascites are at risk for developing spontaneous bacterial peritonitis (SBP) - a severe complication associated with high mortality. The incidence of SBP in cirrhosis has been reported to be 20% on an average, the mortality rate related to this complication being more than 50%.[1] Spontaneous bacterial peritonitis is characterized by spontaneous infection of ascitic fluid in the absence of any intra-abdominal source of infection. Majority of SBP infections have been caused by aerobic gram-negative organisms (50% of these being Escherichia coli). The remainder has been due to aerobic gram-positive organisms (19% Streptococcal species). A study describes 34.2% incidence of Streptococci, ranking in second position after Enterobacteriaceae. Viridians group streptococci (VGS) accounted for 73.8% of these streptococcal isolates.[2] Nowadays the most important analysis of SBP is quantitative cell count, fluid culture and sensitivity and calculation of serum ascites albumin gradient (SAAG) which reflects the differences in oncotic pressure and correlates with portal venous pressure. The serum ascites albumin gradient is a calculation to help determine the cause of ascites. SAAG less than 1.1gm/dl implies exudate. Total protein concentration is lower in spontaneously affected ascitic fluid compared to sterile fluid obtained from different patients. The opsonic activity of ascitic fluid correlate closely with the fluid's protein concentration. Fluids with protein less than 1 g/dl have been reported to have essentially no opsonic activity and therefore no protection from bacterial infection.[3] By calculating SAAG, we can assess the chance of occurrence of SBP in ascitic patients. Hence the present study was designed to see how SAAG affects development of SBP in sterile ascites of cirrhotic patients.

MATERIAL AND METHODS

This was a prospective study conducted from 1st June 2022 to 31st May 2023 in a tertiary care hospital. A total of 80 patients more than 18years of age with chronic liver disease with ascites were included in this study. Patients having had a peritoneal paracentesis with in last 2 weeks for cardiac reasons, malignancy, tubercular peritonitis, pancreatic ascites, congestive heart failure, acute viral hepatitis and secondary peritonitis were excluded.

Detailed history examination and relevant investigations such as Complete hemogram, serum albumin, RBS, liver function test, serum creatinine, ascitic fluid examination, ultrasonography whole abdomen, HBsAg Elisa, anti HCV were done. Serum ascites albumin gradient was calculated by subtracting the ascitic albumin from serum albumin. Based on investigations patients were divided into two groups, group A as Non-Spontaneous bacterial peritonitis (Non-SBP) and group B as Spontaneous bacterial peritonitis (SBP). Data was collected, recorded and statistical calculation was done using in Microsoft excel 2007. The result was considered statistically significant if the p value <0.05.

Aim of The Study

1. To study the ascitic fluid protein in CLD patients.
2. To study the SAAG in SBP patients with CLD.

RESULTS

The present study included 80 patients of chronic liver disease. Out of 80 patients, 76 were males (95%) and 4 were females (5%). These 80 patients were divided into SBP group and Non SBP group based on ascitic fluid analysis. Out of 37 SBP group, 35 (95%) were males and 2 (5%) were females. Out of 43 Non SBP group 41 (95%) were males and 2 (5%) were females. The mean age of patients in SBP group was 53 ± 6 years and Non SBP group was 52 ± 4 years. Alcohol (82%) was the most common risk factor in both SBP and Non SBP group followed by NASH (8%), hepatitis B (6%) and hepatitis C (4%).

The most common clinical presentation in both SBP and Non SBP group was distension of abdomen (48% versus 34%), followed by yellowish discoloration of eyes (48% versus 40%), peripheral edema (48% versus 43%), fever (35% versus 23%), and abdominal tenderness (32% versus 23%). SBP group had very high-grade fever of more than 100F. 13 patients from SBP group had hepatic encephalopathy and 7 patients from Non SBP group had hepatic encephalopathy (35% versus 16%).

The serum albumin level in SBP group ranged from 2.0 to 3.0g/dl. Out of 37 patients 18 (48%) had serum albumin level in the range of 2.0 to 2.5g/dl and 19 (51%) had in the range of 2.51 to 3.0g/dl, whereas the serum albumin level in Non SBP group ranged from 2.5 to 4.0g/dl. Out of 43 patients 10 (23%) had serum albumin level in the range of 2.5 to 3.0g/dl and 17 (39%) had in the range of 3.1 to 3.5g/dl and 16 (37%) had in the range of 3.51 to 4.0g/dl. The mean serum albumin level in SBP group was 2.54 ± 0.33g/dl and Non SBP group was 3.35 ± 0.36g/dl, which was statistically significant with p value 0.0026.

The ascitic albumin level in SBP group ranged from 0.0 to 1.0g/dl. Out of 37 patients 21 (57%) had ascitic albumin level in the range of 0.0 to 0.5g/dl and 16 (43%) had in the range of 0.51 to 1.0g/dl, whereas the ascitic albumin level in Non SBP group ranged from 0.5 to 1.5g/dl. Out of 43 patients 28 (65%) had serum albumin level in the range of 0.51 to 1.0g/dl and 15 (35%) had in the range of 1.1 to

1.5g/dl. The mean ascitic albumin level in SBP group was 0.43 ± 0.23g/dl and Non SBP group was 0.91 ± 0.31g/dl, which was statistically significant with p value <0.001.

The SAAG gradient in SBP group ranged from 1.5 to 3.0g/dl. Out of 37 patients 10 (27%) had SAAG gradient in the range of 1.5 to 2.0g/dl and 24 (65%) had in the range of 2.1 to 2.5g/dl and 3 (8%) had in the range of 2.51 to 3.0g/dl whereas the SAAG gradient in Non SBP group ranged from 2.0 to 3.0g/dl. Out of 43 patients 20 (47%) had SAAG gradient in the range of 2.1 to 2.5g/dl and 23 (53%) had in the range of 2.51 to 3.0g/dl. The mean SAAG gradient in SBP group was 2.09 ± 0.47g/dl and Non SBP group was 2.45 ± 0.01g/dl, which was statistically significant with p value 0.0016.

The mortality rate was higher in group B compared to group A (56.75% v/s 18.60%).

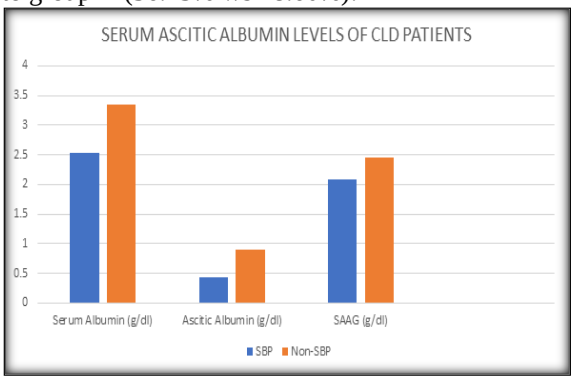

Table 1: Serum Ascitic Albumin Levels of CID Patients

Table 1: Basic Characteristic Features of CLD Patients

Characteristics		Non- Spontaneous bacterial peritonitis Group	Spontaneous bacterial peritonitis Group
Total no. patients (80)		43	37
Sex	Male	41	35
	Female	2	2
Age (years)		52 ± 4	53 ± 6
Serum Albumin (g/dl)		3.35 ± 0.36	2.54 ± 0.33
Ascitic Albumin (g/dl)		0.91 ± 0.31	0.43 ± 0.23
SAAG Gradient (g/dl)		2.45 ± 0.01	2.09 ± 0.47

Table 2: Risk Factors in Group A and Group B

Risk Factors	Group A (NON SBP)	Group B (SBP)
Alcohol	33	33
NASH	4	3
Hepatitis B	4	1
Hepatitis C	2	0

Table 3: Presenting Clinical Features in Group A and Group B

Clinical features	Group A (NON SBP)		Group B (SBP)	
	No of patients	%	No of patients	%
Temp>100F^0	10	23	13	35
Chills	3	7	3	8
Distension of abdomen	15	34	18	48
Peripheral edema	21	48	16	43
Jaundice	21	48	15	40
Abdominal tenderness	10	23	12	32
Rebound tenderness	0	0	9	24
Decreased bowel sounds	0	0	1	2
Hepatic encephalopathy	7	16	13	35

Table 4: Mortality in Group A and Group B

Mortality	Group A (NON SBP)	Percentage (%)	Group B (SBP)	Percentage (%)
	08	18.60	21	56.75

Table 5: Total Serum Albumin Levels in Group A and Group B

Groups	Serum albumin (g/dl)			
	2.0-2.50	2.51-3.0	3.1-4.0	
Group A (NON SBP)	0	10	33	p-value = 0.0026
Group B (SBP)	18	19	0	

Table 6: Total Ascitic Albumin in Group A and B

Groups	Total ascitic albumin (g/dl)			
	<0.50	**0.51-1.0**	**1.1-1.5**	
Group A (NON SBP)	**0**	**28**	**15**	**p-value < 0.001**
Group B (SBP)	**21**	**16**	**0**	

Table 7: Serum Ascites Albumin Gradient (SAAG) In Group A and Group B

Groups	Serum ascites albumin gradient(g/dl)			
	1.5-2.0	2.1-2.5	2.51-3.0	
Group A (NON SBP)	0	20	23	p-value =0.19
Group B (SBP)	10	24	3	

DISCUSSION

SBP can occur in adults and children. In children, it most commonly occurs in neonates and those around five years of age. It is most common in patients with cirrhosis. However, it can occur as a complication of any disease that results in the accumulation of ascitic fluid, such as liver disease, Budd-Chiari syndrome, congestive heart failure, systemic lupus erythematosus, renal failure, or cancers, and has a poor prognosis. Additionally, the risk of developing SBP increases with age, the use of proton-pump inhibitors (PPIs), and when undergoing SBP prophylaxis, such as selective intestinal decontamination.18

SBP has previously been described more frequently among males, at percentages ranging from 72.8% to 83.7%, which was similar to what was found in this study.19 Out of 37 SBP group, 35 (95%) were males and 2 (5%) were females. The mean age of patients in SBP group was 53 ± 6 years and Non SBP group was 52 ± 4 years. Alcohol (82%) was the most common risk factor in both SBP and Non SBP group followed by NASH (8%), hepatitis B (6%) and hepatitis C (4%).

In a study conducted by Verma RK et al, 55 patients of chronic liver disease, 20 patients were diagnosed to have spontaneous bacterial peritonitis (36.4%) based on clinical features and ascitic fluid investigations. Rests of the patients, i.e. 35 patients were found to have sterile ascites (63.6%).10 In the present study of 80 patients of chronic liver disease, 37 patients were diagnosed to have spontaneous bacterial peritonitis (46.25%) based on clinical features and ascitic fluid investigations and 43 patients were found to have sterile ascites (53.75%). The prevalence of SBP depends on severity of liver dysfunction, being higher in advanced liver disease.

The majority of patients with SBP will present with fever, chills, and abdominal pain, although some patients may be asymptomatic, and SBP is an incidental finding. Temperature is the most common symptom encountered in patients with SBP, which is a particularly useful clinical symptom as patients with cirrhosis are typically hypothermic. Additional signs and symptoms include diarrhea, paralytic ileus, new-onset or worsening encephalopathy (e.g., altered mental status) without any other identifiable cause, new-onset or worsening renal failure, or presence of ascites that does not improve with the use of diuretic medications. So one should have a high index of suspicion for SBP in all patients presenting with ascites, and this is especially true if the patient has an acute history of clinical deterioration. In a study conducted by Jain AP et al, most common presenting symptoms of SBP patients were increasing ascites refractory to treatment (90%), followed by peripheral edema (80%). Jaundice and hepatic encephalopathy was found in 75% and 65% respectively.[12] Mihas et al reported fever in 54% pain in abdomen in 57%, and hepatic encephalopathy in 67% Patients.[13] In other study, Pelletier et al, found 89% of patients were having fever, UGI bleed (42%) 53% patients had pain abdomen, and 50% cases had hepatic encephalopathy.[14] In this study, most common presenting symptoms of SBP patients were increasing ascites refractory to treatment (48%), followed by peripheral edema (43%). Jaundice and hepatic encephalopathy was found in 40% and 35% respectively. Clinical features were more common in SBP group in comparison to patients with Non SBP group. Therefore, if any patient with SCA developing temperature more than 100F with chills, increasing ascites, abdominal tenderness, upper GI bleed, hepatic encephalopathy, we should suspect that patient is developing SBP. However, according to one study it is to be noted that one third or more of patients with SBP may have no symptoms or signs directly referable to abdomen.[5] These clinical features are important as prognosis of CLD patients could be improved by early identification of these clinical features of SBP.

The ascitic total protein concentration has been used to determine whether ascitic fluid was a transudate or exudate. But now it has been found that the opsonic activity of ascites fluid has been shown to correlate closely with the fluids protein and albumin concentration. Decrease level of albumin and protein in fluid decreases opsonic activity and therefore no protection from bacterial infection.4 In a study by Huang CH et al, using the cut off point for serum albumin level of 2.85 g/dl as a predictor for recurrence of SBP, the sensitivity was 70.2% and the specificity was 76.3%.[15] Weinstein MP, et al studied 28 cases of spontaneous bacterial peritonitis over a period of 5 years and found that mortality was considerably higher in patients with serum albumin lower than 2.5 g/dl.[16] In this study SBP patients had lesser serum albumin compared to Non SBP patients with Mean±SD of serum albumin of 2.54±0.33 and 3.35±0.36 g/dl respectively which was statistically significant (p value < 0.001). The patients with SBP were found to have significantly lower ascitic fluid albumin in comparison to patients with Non SBP with mean of 0.43±0.23 and 0.91±0.31 g/dl respectively which was statistically significant (p value <0.001).

SAAG, which was first proposed by Hoefs et al in 1981, is calculated by subtracting the ascites albumin concentration from the serum albumin concentration. SAAG is used to determine the

various causes of ascites. Spontaneous bacterial peritonitis (SBP) develops in patients with portal hypertension, defined by serum-ascites albumin gradient (SAAG) > 1.1 g/dL. SBP is unlikely if SAAG is < 1.1 g/dL. The ascitic leukocyte count of 5-10k should prompt consideration of secondary peritonitis.[20] The serum-ascites albumin gradient (SAAG) helps determine whether peritoneal fluid is a transudate or exudate. Theoretically, it might also be helpful in the diagnosis of SBP, as the ascitic fluid would normally be expected to have a relatively high protein level.[21] Lichoska-Josifovikj F et al study included 70 patients who were divided into two groups, 35 patients with SBP and 35 non-SBP. The average value of SAAG in SBP was 19.0±4.6, and in non-SBP it was higher 23.2±5.5. The difference between the mean values was statistically significant for $p<0.05$ (t-test = 3.46512; p=0.000992). The univariate analysis of SAAG in prediction of SBP showed that SAAG <20 g/L significantly increased the chance of SBP by five time.[17] In our study there was a significant difference found between SBP and Non SBP group in relation to SAAG ratio. The Mean±SD of SAAG for Non SBP and SBP group was 2.45+0.01 and 2.09+0.47 g/dl respectively. The p value for this was 0.0016 which was statistically significant. This suggests that occurrence of SBP increases by decrease in SAAG gradiant.

Approximately 10 to 25% of patients with ascites will develop SBP, and the condition is associated with a 20% in-hospital rate of mortality.[18] In our study, the mortality rate was higher in group B compared to group A (56.75% v/s 18.60%).

CONCLUSION

The development of spontaneous bacterial peritonitis in chronic liver disease patients is directly proportional to ascitic fluid albumin and SAAG ratio. SAAG is a good predictor of association of SBP in CLD. The mortality rate increases with development of SBP. These patients not only need to be treated for the acute infection but also the primary disorder causing the fluid build-up. As patients with low ascitic fluid albumin are prone for SBP, it can be prevented by prophylactic use of antibiotics and diuresis.

REFERENCES

1. Rimola A, García-Tsao G, Navasa M, Piddock LJ, Planas R, Bernard B, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. International Ascites Club. J Hepatol. 2000;32(1):142-53.
2. Almdal TP, Skinhoj P. Spontaneous bacterial peritonitis in cirrhosis: incidence, diagnosis and prognosis. Scandinavian J Gastroenterol. 1997;22(3):295-300.
3. Lichoska-Josifovikj F, Grivceva-Stardelova K, Todorovska B, Andreevski V, Nikolov F, Adem D. the value of serum-ascites albumin gradient as a predictor of spontaneous bacterial peritonitis in patients with liver cirrhosis and ascites. Georgian Med News. 2022 Sep;(330):23-25. PMID: 36427835.
4. Xiol X, Castellvi JM, Guardiola J, Sese E, Castellote J, Perello A, Cervantes X, Iborra MJ (1996) Spontaneous bacterial empyema in cirrhotic patients: a prospective study. Hepatology 23(4):719–723.
5. Runyon BA. Patients with different ascitic fluid opsonic activity are predisposed to spontaneous bacterial peritonitis. Hepatol. 1986;5(5):1139.
6. Fernandes SR, Santos P, Fatela N, Baldaia C, Tato Marinho R, Proença H, Ramalho F, Velosa J (2016) Ascitic calprotectin is a novel and accurate marker for spontaneous bacterial peritonitis. J Clin Lab Anal 30(6):1139–1145.
7. Kline MM, McCallum RW, Guth PH. Clinical value of ascitic fluid culture and white blood cell count: studies in alcoholic cirrhotics. Gastroenterology 1976; 70408-412.
8. Runyon BA, Montano AA, Akriviadis EA, Antillon MR, Irving MA, Mchutchison JG. The serumascites albumin gradient is superior to the exudatetransudate concept in the differential diagnosis of ascites. Ann Intern Med. 1992; 117:215-20.
9. Lichoska-Josifovikj F, Grivceva-Stardelova K, Joksimovikj N, Todorovska B, Trajkovska M, Lichoski L. predictive potential of blood and ascitic fluid laboratory parameters for spontaneous bacterial peritonitis in patients with cirrhosis. Georgian Med News. 2021 Dec;(321):69-75. PMID: 35000911.
10. Verma RK, Giri R, Agarwal M, Srivastava V. To study the relation between spontaneous bacterial peritonitis and serum ascitis albumin gradient in chronic liver disease patients. Int J Res Med Sci 2017; 5:3654-8.
11. Huang LL, Xia HH, Zhu SL. Ascitic Fluid Analysis in the Differential Diagnosis of Ascites: Focus on Cirrhotic Ascites. J Clin Transl Hepatol. 2014 Mar;2(1):58-64. doi: 10.14218/JCTH.2013.00010. Epub 2014 Mar 15. PMID: 26357618; PMCID: PMC4521252.
12. Jain AP, Chandra LS, Gupta S, Gupta OP, Jajoo UN, Kalantri SP. Spontaneous bacterial peritonitis in liver cirrhosis with ascites: J Assoc Physicians India. 1999;47(6):619-21.
13. Mihas AA, Toussaint J, Hsu HS, Dotherow P, Achord JL. Spontaneous bacterial peritonitis in cirrhosis: clinical and laboratory features, survival and prognostic indicators. Hepatogastroenterol. 1992;39(6):520-2.
14. Pelletier G, Lesur G, Ink O, Hagege H, Attali P, Buffet C, et al. Asymptomatic bacteriocytes, is it spontaneous bacterial 1991;14(1):112-5. peritonitis? Hepatol.
15. Huang CH, Lin CY, Sheen CY. Recurrence of spontaneous bacterial peritonitis in cirrhotic patients non-prophylactically treated with norfloxacin: serum albumin as an easy but reliable predictive factor. Liver Int. 2011;31(2):184-91.
16. Weinstein MP, Iannini PB, Stratton CW. Spontaneous bacterial peritonitis. A review of 28 cases with emphasis on improved survival and factors influencing prognosis. American J Med. 1978;64(4):592-8.
17. Lichoska-Josifovikj F, Grivceva-Stardelova K, Todorovska B, Andreevski V, Nikolov F, Adem D. THE VALUE OF SERUM-ASCITES ALBUMIN GRADIENT AS A PREDICTOR OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH LIVER CIRRHOSIS AND ASCITES. Georgian Med News. 2022 Sep;(330):23-25. PMID: 36427835.
18. Oey RC, de Man RA, Erler NS, Verbon A, van Buuren HR. Microbiology and antibiotic susceptibility patterns in spontaneous bacterial peritonitis: A study of two Dutch cohorts at a 10-year interval. United European Gastroenterol J. 2018 May;6(4):614-621.
19. Thanopoulou AC, Koskinas JS, Hadziyannis SJ. Spontaneous bacterial peritonitis (SBP): clinical, laboratory, and prognostic features. A single-center experience. Eur J Intern Med. 2002;13(3):194-8.
20. Complications of end-stage liver disease:Can Fam Physician. 2016 Jan; 62(1): 44–50. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4721840.