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Original Research Article

Estimation of Prevalence of Asymptomatic Spontaneous Bacterial Peritonitis in Cirrhotic Patients with Ascites

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Abstract

Spontaneous bacterial peritonitis (SBP) is a serious and potentially life-threatening complication in patients with decompensated liver cirrhosis. The prognosis is generally improved if antibiotics are begun before the onset of shock and renal failure. Because of significant morbidity and mortality related to SBP, identifying predisposing factors is of great interest. The Model for End-Stage Liver Disease (MELD) score is a measure of mortality risk in patients with end-stage liver disease.

Method: This is a prospective study conducted for the period of 1 year. Patients with ultrasound proven ascites & cirrhosis were selected for the study. After taking informed consent 10 ml of ascitic fluid is collected and sent for various biochemical analyses like proteins and sugar along with cell count.

Results: Most of the cases were reported in the age group 41-60 years (N=28, 56%). 7 (14%) of cases were more than 60 years. The mean age of study participants was found 48.06± 13.03 years of age ranged from 14 to 85 years. Majority of cases were Male. Male female ratio was 1.94**:**1. Prevalence of asymptomatic spontaneous bacterial peritonitis in cirrhotic patients with ascites was found 16% (8 out of 50 cases). We found 12% (6 out of 50 cases) culture positive cases in cirrhotic patients with ascites, in which E. Coli was found in 50% of culture positive cases then Klebsiella (33.3%) and least number of cases show Streptococcus Viridans (16.7%). SBP was defined by Cell Count (PML) in Ascitic Fluid of cirrhotic patients with ascites, PML count of > 250/mm3, was found in 5 (10%) patients from 50, and in 45 (95 %) patients were reported cell count ≤250/mm3. Higher alcohol intake proportion was observed in SBP group which was statistically non- significant. In SBP group Statistically insignificant (P value >0.05) lower mean duration of cirrhosis was observed. Significant difference (P value <0.05) in the mean values of S. Bilirubin and INR between the presence and absence of SBP in patients. In the presence of SBP group, mean MELD was 29.88 compared to MELD of 21.81 in the absence of SBP group. All 8 patients with SBP had Meld score greater than 24. No patients with MELD score from 11-24 also had SBP, Whereas the patients in which SBP was absent, 10 patients have MELD score from 11 to 18 and 21 patients have MELD score from 19 to 24. This distribution was found statistically significant

(P value <0.001) when compared the absence and presence of SBP in patients. By ROC analysis MELD Score is a good predictor of SBP in cirrhotic patients in our study (High values of MELD predict SBP).

Conclusion: there is a low prevalence of SBPin asymptomatic individuals with ascites and liver cirrhosis. In the patient population under study, serum Bilirubin and INR concentration was found to be the accurate predictor of SBP episodes. We saw a tendency for the infection to develop more frequently in individuals with severe liver disease (higher MELD score).

Keywords: Spontaneous bacterial peritonitis, MELD score, Cirrhosis.

Introduction

Spontaneous bacterial peritonitis (SBP) is a serious and potentially life- threatening complication in patients with decompensated liver cirrhosis.[1] In the early 1970s, Harold Conn coined the term "Spontaneous Bacterial Peritonitis" and defined it as the abrupt onset of acute peritonitis and bacteremia caused by enteric organisms in decompensated cirrhotic patients.[2]

The prevalence and natural history of spontaneous bacterial peritonitis in asymptomatic patients with ascites secondary to cirrhosis is unknown. Usually, it appears to be a consequence of impaired defense mechanisms and an increased susceptibility to bacterial infections in cirrhotic patients with ascites in the absence of any intraabdominal source of infection (e.g., intestinal perforations or abscesses). SBP may be further complicated by hepatorenal syndrome or systemic sepsis and has the high recurrence rate – estimated as approximately 70% within one year of follow up. [3]

As a serious complication in cirrhosis, Spontaneous bacterial peritonitis isassociated with significant morbidity and mortality and can trigger a cascade of events in other organ systems; specifically, renal impairment in cirrhotic patients has been associated with worse prognosis.6 It occurs in both children and adults and is a well-known and ominous complication in patients with cirrhosis. [4]

Two variants of SBP have been described: (a) "classical" SBP, defined as the presence of bacteria in the ascitic fluid associated with a high ascitic fluid polymorphonuclear cell (PMN) count (with an accepted cut-off value of 250 cells/p1 and (b) culture-negative neutrocytic ascites (CNNA) in patients with increased ascitic fluid PMN count but with sterile ascites. Bacterascites (BA) is another finding and is defined as a positive ascitic fluid culture without an increased PMN count. BA is usually considered asymptomatic or "without clinical evidence of SBP"[5]

As spontaneous bacterial peritonitis has increased prevalence in patients with liver cirrhosis and ascites, it is necessary to consider bacterial inflammation in every clinically decompensated cirrhotic patient as it is recognized as an important marker of liver disease progression. Its prevalence is as high as 12% in hospitalized patients while it develops in up to 3.5% of patients that are treated as outpatients. Many other studies also suggest that 10- 30% of hospitalized patients and 3.5% of outpatients with cirrhosis and ascites have SBP. With in-hospital mortality ranging from 20-40% and an estimated prevalence of 10–30%, it accounts for 4% of cirrhosis-related emergency globally.[6]

Ascites is the most common complication of cirrhosis and is often the first sign of decompensation to appear. It occurs within 10 years of diagnosis in half of patients with

5-year mortality of 44%. The disease can be compensated or decompensated. Significant morbidity and mortality are associated with decompensation. Complications include variceal hemorrhage, ascites, increased risk of bacterial infection, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, umbilical hernia and hepatic hydrothorax. Management should be focused on the prevention of recurrence of complications.[7]

The presence of an infection in a previously sterile ascites in the absence of an intra-abdominal source of infection or malignancy is also termed as SBP. The clinical manifestation is nonspecific and variable, up to one third of patients might be asymptomatic (bacterascites) or it can quickly emerge as a fatal sepsis syndrome. Presenting signs and symptoms can include fever, changes in mental status, abdominal tenderness, gastrointestinal (GI) bleeding, chills, nausea, or vomiting. Because of the tremendous variability in presentations, and also because such presentations may overlap with other conditions often seen in cirrhosis (e.g., encephalopathy), a proper assessment is essential in diagnosis.[8]

According to the American Association for the Study of Liver Diseases (AASLD) practice guidelines, diagnosis of SBP is made in the presence of elevated ascitic fluid polymorphonuclear (PMN) leukocyte count ≥250 cells per mm^3, although infection can also be diagnosed when patients are ascitic fluid culture positive with PMN <250 cells per mm^3. [9,10]

The development of SBP is associated with a poor long-term prognosis. Fever with chills and abdominal pain or discomfort are the most common presenting complaints. The most common organisms isolated in SBP patients are Escherichia coli and other gut bacteria; however, gram positive bacteria including Streptococcus viridians, Staphococcus aureus and Enterococcus sp., can also be found.[4]

The outcome of cirrhotic patients with SBP has dramatically improved during the last 20 years. At present, the SBP resolution rate ranges between 70 and 90% and hospital survival ranges between 50 and 70%. An early diagnosis of SBP and, specially, the use of a more adequate antibiotic therapy, are the most probable reasons for the improvement in prognosis for SBP. In approximately 60–70% of the cases the organism responsible is isolated in ascitic fluid culture or in blood cultures. The remaining cases are considered asa variant of SBP and are treated in the same way as those with a positiveculture.[11]

Disease-related deaths from SBP declined significantly between the 1970s and 1990s due to increased awareness of the disease, earlier detection of the disease, and an increase in the number of antibiotics.

The prognosis is generally improved if antibiotics are begun before the onset of shock and renal failure. However, because of the severe underlying liver disease that is usually aprogenitor to the development of SBP, inpatient non–infection-related mortality rates have still been quite high at 20% to 40%. Because of significant morbidity and mortality related to SBP, identifying predisposing factors is of great interest. The Model for End-Stage Liver Disease (MELD) score is a measure of mortality risk in patients with end-stage liver disease.[12]

The MELD scoring system has been shown to predict more accurately 3- month mortality than the previous Child Pugh system. The aim of the study is to calculate the association between development of spontaneous bacterial peritonitis and the severity of liver cirrhosis (i.e. MELD Score) and estimate the prevalence of asymptomatic spontaneous

bacterial peritonitis in cirrhotic patients with ascites.

Aims and Objective

This study was undertaken -

1. To estimate the prevalence of asymptomatic spontaneous bacterial peritonitis in cirrhotic patients with ascites.
2. To calculate the association between development of spontaneous bacterial peritonitis and the severity of liver cirrhosis (i.e. MELD Score).

Methods

Study Design: Observational Study

Inclusion Criteria

1. Patients with known history of cirrhosis presenting with Ascites

Exclusion Criteria

1. Not on prophylactic antibiotics.
2. No history of fever in the past two weeks
3. No features of hepatic encephalopathy
4. No features suggestive of preexisting intra-abdominal infection.
5. No features suggestive of renal failure

Methodology

Patients with ultrasound proven ascites & cirrhosis were selected for the study. After that a fresh ultrasound is also done to rule out any active infection and other clinical conditions that can interfere with the exclusion criteria like pancreatitis. They were also filling the inclusion and exclusion criteria. After taking informed consent 10 ml of ascitic fluid is collected and sent for various biochemical analyses like proteins and sugar along with cell count.

The cell count is measured by Neubauer's chamber. Another 10 ml was taken and sent for culture and inoculated into culture tubes under aseptic precaution. Along with it a liver function test, serum amylase and prothrombin time is also done. To avoid person to person error the same people must collect the ascitic fluid. It is also sent to the same lab. Soon after the procedure, a prophylactic antibiotic course is started. With the parameters, the Child's Tourette Pugh scoring is also done. After the reports come, appropriate treatment is promptly started.

Duration Of Study

September 2021 to August 2022.

Statistical Analysis

Statistical analysis was performed using SPSS 20 software and the analyzed data was expressed in percentages. P-value equal to or less than 0.05 was significant.

Results

This is a prospective study done on 50 patients. The mean age of study participants was 48.06± 13.03 years. The age ranged from 14 to 85 years. Majority of cases were in middle age group (41-60 years) with 28 (56%) cases, followed by 15 (30%) cases in less than 40 years age group. Only 14% of cases were more than 60 years. There was male predominance with Male female ratio of 1.94:1. [Image 1]

In our study, we estimated 16% (8 out of 50 cases) prevalence of asymptomatic spontaneous bacterial peritonitis in cirrhotic patients with ascites. On cell count, 10% (5 out of 50 cases) had cell count more than 250/mm3 in ascitic fluid. On culture of ascitic fluid, 12% (6 out of 50 cases) patients were culture positive in cirrhotic patients with ascites. The most common organism isolated in culture was e coli in 6 cases followed by klebsiella in 2 cases. [Table 2].

Table 1: Age distribution of study participants

Age group	N	%
<40 years	15	30.0
41-60 years	28	56.0
>60 years	7	14.0
Total	50	100.0

The mean age of patients with spontaneous bacterial peritonitis was 45.50±17.83 while the mean age of patients without SBP was 48.55±12.12, the age was comparable in both groups. In our study, statistically insignificant (P value >0.05) was observed with lower mean age and higher male proportion. [Table 3]

On comparing various parameters between the two groups (with and without spontaneous bacterial peritonitis), there was statistically insignificant (P value >0.05) result with alcohol intake and duration of cirrhosis however, the results were significant with Meld score greater than 24 (P value <0.001).[Table 4]

On comparing laboratory investigation data between the two groups, in our study, statistically significant (P value <0.05) higher mean S.Bilirubin and INR were observed in SBP group. However, the serum sodium and serum creatinine did not show any significant result.[Table 5]

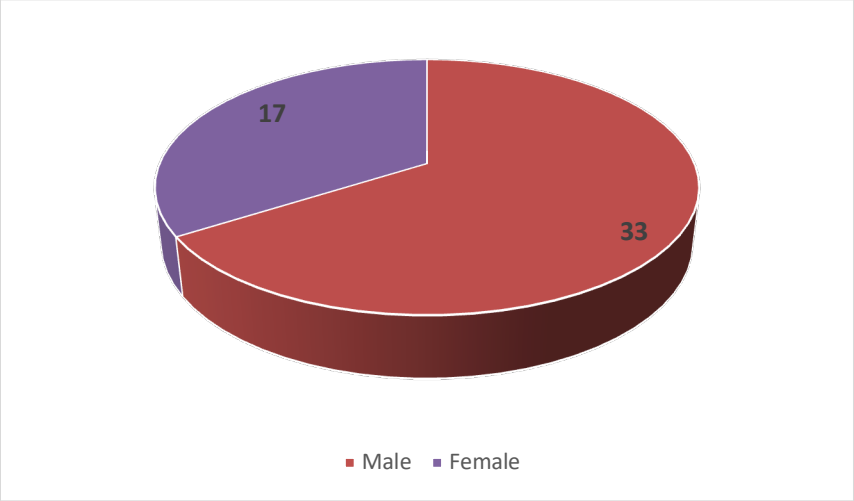

Image 1: Gender distribution of study participants

Table 2: Micro-organism in culture positive

Micro-organism	N	%
E. Coli	3	50.0
Klebsiella	2	33.3
Streptococcus Viridans	1	16.7
	6	100.0

Table 3: Age and spontaneous bacterial peritonitis

SBP	N	Mean	SD	Median	Minimum	Maximum	P value
Absent	42	48.55	12.126	48.50	14	85	0.550
Present	8	45.50	17.833	41.50	27	74	
Total	50	48.06	13.028	46.50	14	85	

Table 4: Comparison of Different Paraments with Spontaneous Bacterial Peritonitis

	Spontaneous Bacterial Peritonitis						
	Absent		Present		Total		
	N	%	N	%	N	%	
Age group							Chi-square=3.327 with 2 degrees of freedom; P = 0.155
<40 years	11	26.2%	4	50.0%	15	30.0%	
41-60 years	26	61.9%	2	25.0%	28	56.0%	
>60 years	5	11.9%	2	25.0%	7	14.0%	
Gender							
Female	16	38.1%	1	12.5%	17	34.0%	Chi-square=1.962 with 1 degree of freedom; P = 0.161
Male	26	61.9%	7	87.5%	33	66.0%	
Alcohol consumption							
No	19	45.2%	1	12.5%	20	40.0%	Chi-square = 3.001 with 1 degree of freedom; P = 0.083
Yes	23	54.8%	7	87.5%	30	60.0%	
MELD Score							
11 to 18	10	23.8%	0	0.0%	10	20.0%	Chi-square = 15.539 with 2 degrees of freedom; P <0.001
19 to 24	21	50.0%	0	0.0%	21	42.0%	
>24	11	26.2%	8	100.0%	19	38.0%	
Duration of Cirrhosis							
≤5 years	24	57.1%	6	75.0%	30	60.0%	Chi-square = 0.893 with 1 degree of freedom; P = 0.345
>5 years	18	42.9%	2	25.0%	20	40.0%	
Total	42	100.0%	8	100.0%	50	100.0%	

Table 5: Laboratory investigation and spontaneous bacterialperitonitis

	Spontaneous Bacterial Peritonitis				
	Absent		Present		
	Mean	SD	Mean	SD	P value
Serum Sodium	136.93	4.66	134.63	5.48	.218
S. Bilirubin	2.20	0.63	2.88	1.19	.023
S. Cr.	1.45	0.41	1.61	0.34	.313
INR	2.10	0.63	3.09	0.82	<0.001

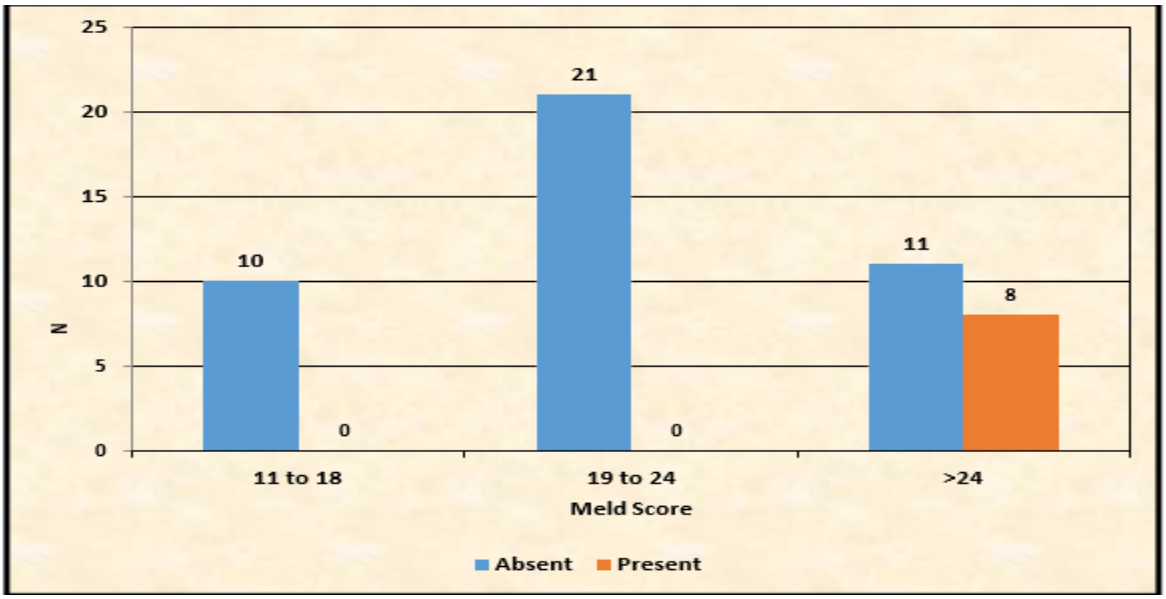

Image 2: Meld score and spontaneous bacterial peritonitis

Table 6: To predict sbp by meld score

Area	P value	95% Confidence Interval	
		Lower Bound	Upper Bound
0.926	<0.001	0.85	1

Area under Curve (AUC) - 0.926

On ROC analysis we found statistically significant (P value <0.001) value of AUC. The value of AUC is 0.926 which shows MELD Scoreis a good predictor of SBP in cirrhotic patients in our study (High values of MELD predict SBP).

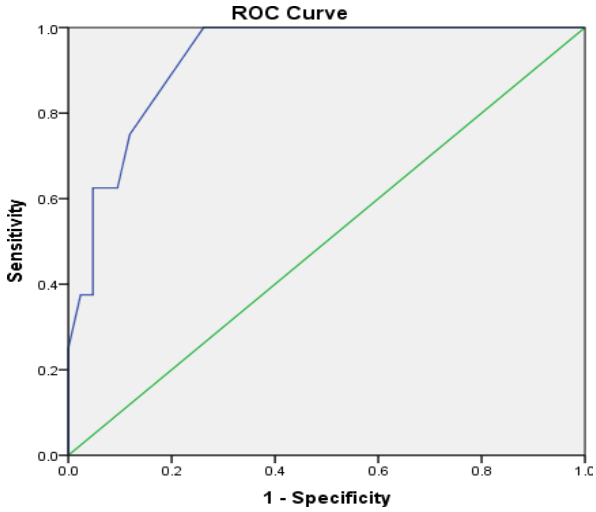

Image 3: To predict SBP by meld score

Discussion

Bacterial infections and spontaneous bacterial peritonitis (SBP), the most common and potentially fatal ascites consequence, are more common in cirrhotic patients.[13-15] In hospitalized patients with cirrhosis, SBP is common (10–30%) and has an annual recurrence incidence of about 70%.[13,15,16] SBP is linked to high mortality, and the chance of long-term survival ranges from 25 to 50 percent. [17] The prognosis for this infection is poor because of a number of serious consequences include septic shock, progressive renal failure, variceal haemorrhage, and multiple organ failure. [13,14,18]

Approximately two-thirds of SBP cases are asymptomatic;[13] thus the protocols of clinical practice set forth by the American Association for the Study of Liver Disease and EASL recommend performing analysis of ascites fluid for diagnosis of infection after each paracentesis procedure.[18] However, this approach is debatable and there are few studies that evaluate the analysis of ascitic fluid in asymptomatic patients. [17,20]

SBP is one of the most prevalent infections that patients with liver cirrhosis are vulnerable to, with a varying frequency but a high fatality rate. For this reason, it is important to find non-invasive, affordable, and simple to implement characteristics that are connected to SBP and have a predictive role.

In this study, most of the cases were reported in the age group 41-60 years (N=28, 56%), which was followed by 15 (30%) cases seen in age group less than 40 years. 7 (14%) of cases were more than 60 years. The mean age of study participants was found 48.06± 13.03 years of age ranged from 14 to 85 years. We estimated 16% (8 out of 50 cases) prevalence of asymptomatic spontaneous bacterial peritonitis in cirrhotic patients with ascites. The findings of our analysis confirm the clinical assumption that SBP is not very common in individuals who show no overt indications of illness. Likewise, our results, other studies also reported the low SBP incidence in recent outpatient-based reports of asymptomatic patients. [7,21,22]

We found 12% (6 out of 50 cases) culture positive cases in cirrhotic patients with ascites, in which E. Coli was found in 50% of culture positive cases then Klebsiella (33.3%) and least number of cases show Streptococcus Viridans (16.7%).

Similar to our results, Runyon BA, et.al was also reported that aerobic gram-negative bacilli account for more than two-thirds of all SBP cases and more than 92% of all instances are monomicrobial, with Escherichia coli followed by Klebsiella species being the most prevalent.[23] Additionally, E. coli was the main bacterium identified in the investigations of Gills *et al*.[24] E. coli was isolated in 58.13%, Streptococcus pneumoniae in 18.60%, Staphylococcus aureus in 9.13%, Klebsiella in 9.13% and Acinectobacter in 4.63% were all isolated in the 2003 research at Khyber Teaching Hospital in Peshawar.[25]

Current recommendations define SBP as an ascitic fluid PMN count > 250 cells/l. 22,24 However, a worldwide agreement year ago experimentally established these cut-off levels. [23,26] Better and evidence-based models for SBP prediction are required to direct primary prophylaxis and enhance individualized patient care in light of the adverse effect of SBP on the clinical course of patients with decompensated cirrhosis. We found that SBP might develop at anyMELD, which is consistent with recent research that found no link between MELD and the likelihood of SBP development.[27]

In our study, if SBP was defined by Cell

Count (PML) in Ascitic Fluid of cirrhotic patients with ascites, PML count of > 250/mm3 was found in 5 (10%)patients from 50, and in 45 (95 %) patients were reported cell count ≤ 250/mm3.

According to recent research by Lutz *et al*. [28] the relative A-PMNcount may serve as a measure of subclinical infection or inflammation caused by bacterial translocation into the ascitic fluid and may predict the development of SBP. Additionally, a considerably elevated risk for the development of SBP has previously been linked to an absolute PMN level of 100 cells/l. 12.[29] Additionally, it has recently been demonstrated that SBP development may be predicted by the absolute A-PMN cell count.[30] Additionally, Oey and associates noted that individuals with BA had a similar degree of hepatic impairment and a similar outcome to those with SBP.[31]

Geographical differences in the pathogenesis of liver cirrhosis exist. Inour study, alcohol intake proportion was found higher in SBP group. Hence, alcohol was seemed to be the most frequent cause in our investigation, which is comparable to a Brazilian study by Gonçalves *et al*. [32] Our results, however, were different from those of African studies, where HBV was the predominant cause. [33,34]

Our research found a significant difference in the mean values of S. Bilirubin and INR between the presence and absence of SBP in patients. In line with our results, Metwally K, et.al reported that in a group of 59 individualswith SBP from research with 300 patients with liver cirrhosis, the mean values of BT, creatinine, INR, and serum WBC were considerably higher, while the mean PLT was significantly lower.[35]

In our study, Mean of Meld Score was observed in absence and presence of SBP was found statistically significant (P value <0.001). All 8 patients with presence of SBP had Meld score greater than 24. This distribution was found statistically significant (P value <0.001) when compared the absence andpresence of SBP in patients. For those with MELD ≥25, the risk of SBP was nearly ten times higher compared to those with MELD score 11-24. In our study, by ROC analysis we found statistically significant (P value <0.001) valueof AUC. The value of AUC is 0.926 which shows MELD Score is a good predictor of SBP in cirrhotic patients in our study (High values of MELD predict SBP). This suggests that MELD score, a widely scoring system, is a useful tool to predict the presence of SBP.

In our group, no patients with MELD 11-24 also had SBP, whereas the patients in which SBP was absent, 10 patients have MELD score from 11 to 18 and 21 patients have MELD score from 19 to 24. Thus, one cannot exclude the possibility of SBP solely on the basis of MELD score. This also substantiatesthe point that all patients with cirrhosis and ascites should undergo paracentesis at the time of admission to exclude SBP. The cell count should be reviewed as early as possible, and antibiotics should be started if needed. Dipstick test results are available within 90-120seconds and may speed up treatment of SBP and improve survival.[36]

In the presence of SBP group, mean MELD was 29.88 compared to MELD of 21.81 in the absence of SBP group. This showed a trend towards significance. This shows that patients with advanced liver disease have higher chances of development of life-threatening complications like SBP. Also, SBP per se can worsen hepatic and renal function and lead to higher MELD score.

Comparable retrospective research that was conducted at the Universityof Pennsylvania comprised 111 participants. In 111 hospitalized cirrhotic patients, 29 were found to have SBP. Patients with SBP on average

had a MELD score of 24, compared to those without it at 18 (p=0.0003). Each MELD point increased the probability of getting SBP by 1.11 (p.001). When compared to those with MELD 15, patients with MELD >25 had an odds ratio of 9.67 for SBP. None of the conceivable factors significantly changed the association between MELD and SBP.[13]

Conclusion

According to the findings of our study, there is a low prevalence of SBPin asymptomatic individuals with ascites and liver cirrhosis. In the patient population under study, serum Bilirubin and INR concentration was found to be the accurate predictor of SBP episodes. We saw a tendency for the infection to develop more frequently in individuals with severe liver disease (higher MELD score).

Gram-negative bacteria predominated in the cultures from our SBP patients, suggesting alterations in the profile of the causing agents. We want to underline that our findings should be viewed cautiously and that they could only apply to a certain patient cohort. To evaluate the issue, more research is needed.

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