

Prospective study to analyze the correlation between spontaneous bacterial peritonitis and model of end stage liver disease score

Abstract

Aim: To determine whether a greater MELD score is associated with a greater risk of development of spontaneous bacterial peritonitis.

Methods: This prospective study enrolled 148 consecutive patients with cirrhosis and ascites admitted between May 2008 to March 2010. After excluding patients who were Immuno suppressed, had history of prior antibiotic use, had previous episodes of SBP and had other confounding etiological factors for ascites, sixty seven patients were included in the study. SBP was defined as ascetic fluids PMN count >250/cu.mm. The odds ratio for development of SBP associated with MELD score and grouped MELD score was calculated (<15, 16-24, >25).

Results: The prevalence of SBP was 20.9%. The mean MELD score in SBP group was 23.14+/-9.87 and in the non SBP group was 18.46+/-7.43. The odds ratio for development of SBP was 1.23 for each point rise in MELD score. (p=.0032). Patients with MELD >25 had an odds ratio of 9.52 (p=0.001) for SBP as compared to patients with MELD <15.

Conclusions: Increasing MELD score is independently associated with a greater risk of SBP. For every point increase in MELD score, the risk of developing SBP increases by 12.3%. Prophylactic antibiotics should be considered in patients with MELD score >25.

Keywords: blood culture bottles, hiv infection, diabetes, cirrhosis, comorbid illness, high risk behavior

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Introduction

Liver cirrhosis is a major cause of death all over the world. The major complications of cirrhosis include ascites, hepatic encephalopathy and hemorrhage caused by ruptured esophageal varices. Patients with cirrhosis and ascites have higher susceptibility to bacterial infections, mainly because of inadequate defence mechanisms. The most frequent infectious complications include Spontaneous bacterial peritonitis, Urinary tract infections, Pneumonia and Bacteremia. Since 1970, when SBP was first described and up to the present, the mortality rate has been decreasing from 80% to 30% due to prompt diagnosis and early initiation of adequate treatment.¹

SBP is the infection of the ascitic fluid that occurs in absence of visceral perforation and in the absence of an intra-abdominal inflammatory focus. For SBP diagnosis, the polymorphonuclear leucocyte count in ascitic fluid should exceed 250/mm³ and from bacteriological cultures, only one organism should be isolated.¹⁻⁴

Methods

The study was done at Jagjivanram Hospital, Mumbai in a prospective manner. All patients admitted with cirrhosis of liver and ascites from May 2008 to March 2010 were evaluated. Out of a total of 148 patients, eighty one were excluded. Reasons for exclusion were:

- i. HIV infection (5 patients).
- ii. Long standing diabetes/immuno suppressants (10 patients).

- iii. Antibiotic use in two weeks prior to admission (53 patients).
- iv. Confounding etiology for ascites (10 patients).
- v. Previous history of SBP (3 patients).

Repeat admissions were not included. Patients with HIV infection, diabetes, immuno suppressants like steroids and alkylating agents may have been more predisposed to develop SBP regardless of their MELD score and so were excluded. Use of antibiotics in two weeks prior to admission may have prevented development of SBP or may have rendered paracentesis insensitive to the diagnosis of SBP. All patients with documented SBP are put on antibiotic prophylaxis in our centre and were excluded in the study. Sixty seven patients formed the study group.

Evaluation of study groups

- a. Detailed history regarding symptoms, factors leading of cirrhosis, comorbid illness, high risk behaviour.
- b. Lab investigations.
 - i. Complete hemogram.
 - ii. PT/INR.
 - iii. Complete liver function tests, renal parameters, serum electrolytes.
 - iv. HIV 1 & 2, HBs Ag, anti HCV.

- v. USG abdomen.
- vi. Ascitic fluid analysis and culture.
- vii. Calculation of MELD.

SBP was defined as a paracentesis yielding ≥ 250 neutrophils/ml of ascitic fluid. Though bed side inoculation of fluid was done in blood culture bottles, a positive culture was not considered mandatory to diagnose SBP. The rationale was to capture both culture positive and culture negative neutrocytic ascites as both have similar natural history.

Patients with ascitic fluid PMN < 250 cells/ml were considered not to have SBP and found the control group. Data on subsequent paracentesis in same patients was not collected.

Results

Out of 67 patients who formed the study group, fourteen had SBP. The prevalence of SBP was 20.97%.

Demographic Characteristics

Variable	Cases	Controls
No. of cases(n=67)	14	53
# age(yrs)		
Mean	53.21	49.34
SD	10.58	9.95
Range	34-78	23-78
@Sex(%)		
Male	11(78.6)	43(81.1)
Female	03(21.4)	10(18.9)

by Student 't' Test

@Chi-Square Test

P>0.05 Not significant

In this study group age of the cases were ranging from 23-78years with mean age of 53.21years among cases and 49.34years in controls. 78.6 – 81.1% of the total cases were male in both the groups.

Profile of etiology of liver disease between the groups

Etiology	Cases(n=14)		Controls(n=53)		P value
	No.	%	No.	%	
Alcohol (42)	10	71.5	32	60.4	0.447
Crypto (07)	2	14.3	5	9.4	0.5976
HCV (07)	1	7.1	6	11.3	0.6494
AIH (01)	1	7.1	-	-	*0.0499
HBV(06)	-	-	6	11.3	0.187
HBV+HCV(01)	-	-	1	1.9	0.6045
MDS+BCS(01)	-	-	1	1.9	0.6045
NASH(02)	-	-	2	3.8	0.4605

By Chi – Square Test

P>0.05 Not significant

Among cases, 71.5% had alcoholism as etiological cause for liver disease which was more than 60.4% in controls but difference was not significant. 11.3% controls had HBV as the reason for liver disease whereas none of the cases had this cause.

Comparison of changes in mean score of MELD between the groups

Groups	Mean score of MELD	Range
	($\bar{x} \pm SD$)	
Cases	23.14 \pm 9.87	Jun-36
Controls	18.46 \pm 7.43	Jul-33
P value	0.1027	

By Chi – Square Test

P>0.05 Not significant

As per this table Mean MELD score in cases was 23.14 which were more as compared to 18.46 among controls but the difference was not significant statistically.

Profile of MELD grouping between the groups

Groups	Cases(N=14)		Controls(N=53)		P value
	No.	%	No.	%	
≤ 15 (n=24)	3	21.4	201	38.5	0.2351
16–24(n=26)	4	28.6	22	42.3	0.3505
≥ 25 (n=17)	*07	50	10	19.2	0.0194

By Chi – Square Test

P>0.05 Not significant

50% of the patients in the SBP group had MELD ≥ 25 compared to 19.2% in the SBP absent group (P 0.0194) Three patients with SBP had MELD score ≤ 15 .

12.5% patients with MELD ≤ 15 developed SBP. 41.17% patients MELD ≥ 25 had SBP (P<0.001) and 15.38% patients with MELD between 16-24 had SBP (P<0.05).

The odds ratio for developing SBP by each MELD point were 1.23, P=0.0032. Patients with MELD > 25 had an odds ratio of 9.52(3.01-33.59, P=0.001) SBP as compared to subjects with MELD < 15 .

Profile of outcome between the groups

Groups	Cases(N=14)		Controls(N=53)		p value
	No.	%	No.	%	
Survived (n=57)	10	71.4	47	88.7	0.1072
Expired (n=10)	4	28.6	6	11.3	

By Chi – Square Test

P>0.05 Not significant

This study report suggests that 88.7% SBP absent cases survived which were more than 71.4% but difference was not significant.

The mortality rate in SBP groups was nearly 30% compared to 11.3% in the SBP absent cases. The causes of death in SBP group were: Sepsis² and hepatorenal syndrome.² In the control group,

the causes of death were: UGI Bleed,³ Hepatorenal syndrome¹ and Hepatic encephalopathy and aspiration.²

Discussion

Spontaneous ascitic fluid infection is a good marker of end stage liver disease and has been proposed as an indication for transplantation in a patient who is otherwise a candidate. In the 1980s the prevalence of SBP was approximately 27% but has dropped significantly now due to measures taken to prevent SBP. With better and faster treatment modalities, the mortality rate has also reduced significantly.⁵

In the study, greater MELD score was independently associated with a greater risk of SBP. Among patients admitted with cirrhosis and ascites, with every point increase in MELD the risk of developing SBP increased by 12.3%. For those with MELD ≥ 25 , the risk of SBP was nearly ten times higher compared to those with MELD score ≤ 15 . This suggests that MELD score, a widely scoring system, is a useful tool to predict the presence of SBP.

In our group, three patients with MELD ≤ 15 also had SBP (21.4%). Thus, one cannot exclude the possibility of SBP solely on the basis of MELD score. This also substantiates the 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.⁶

The study excluded patients who were at a higher risk of developing SBP like HIV infection, long standing diabetes and immuno suppressed patients with prior history of SBP and on antibiotics within 2weeks of admission. This helped us to correctly identify the relation between MELD score and development of SBP.

In the SBP group, mean MELD was 23.14 compared to MELD of 18.46 in the control 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.

Ascitic fluid was sent for culture in all patients. Three patients in SBP group had positive culture showing growth of *E. coli*. Thus, culture positivity was 21%. Various studies have reported multiple organisms as the cause of SBP-*E. coli* (37%), *Klesiella pneumoniae*(17%), *Pneumococci*(12%), *Streptococcus viridans*(10%) and anaerobic organisms(6%). Since culture positive and culture negative neutrocytic ascites have similar natural history, it is unlikely this would have affected the results.⁷⁻⁹

In a similar retrospective study done at the University of Pennsylvania, 111 patients were included in the study. Twenty nine of 111 hospitalised patients with cirrhosis were found to have SBP. The mean MELD score for patients with SBP was 24 and for those without 18($p=0.0003$).The odds ratio for developing SBP by each MELD point was 1.11($p=.001$). Patients with MELD ≥ 25 has an odds ratio of 9.67 for SBP compared to subject with MELD ≤ 15 . None of the potential confounders substantially altered the relationship between MELD and SBP.¹⁰

Conclusion

Diagnostic paracentesis should be done in all patients with

cirrhosis and ascites to diagnoses SBP. Though patients with higher MELD score have a greater chance of developing SBP, one fifth of the patients with a MELD score of <15 developed SBP. Thus, paracentesis should be done at the earliest, preferably within one hour of admission to quickly diagnose and treat SBP.

Higher MELD score at presentation is associated with increased risk of development of SBP. Fifty percent of patients with MELD score more than 25 had SBP. The use of prophylactic antibiotics in these patients might be useful. At present, antibiotic prophylaxis is given to patients with previous documented episode of SBP or ascetic fluid albumin $<1\text{gm/dl}$. Patients with a higher MELD Score have advanced liver disease and a higher risk of complications like infection, renal failure and encephalopathy. Thus, for these patients prophylactic antibiotics may be considered even if they have not developed SBP earlier.

Our study, with its limitations, makes a point about the need of antibiotic prophylaxis in high risk group of patients with MELD score >25 . Larger studies and randomized controlled trials are required to make this a recommendation and prevent development of life threatening complications in this group.

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None.

Conflict of interest

Author declares that there is no conflict of interest.

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