International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319 – 6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 8; August 2017; Page No. 5682-5685
DOI: http://dx.doi.org/10.24327/ijcar.2017.5685.0778

Research article

CORRELATION BETWEEN MELD SCORE AND SBP IN PATIENTS WITH CIRRHOSIS AND ASCITES

Mayank Jain[1,2], Rajiv Baijal[1] and Sri Prakash Jaiswal[2]

[1]Department of Gastroenterology, Jagjivan Ram Hospital, Mumbai
[2]Consultants, Choithram Hospital and Research Centre, Indore

A R T I C L E I N F O

Article History:

Received 25th May, 2017
Received in revised form 13th June, 2017 Accepted 20th July, 2017
Published online 28th August, 2017

Key words:

Liver, Ascites, Infection, Mortality

A B S T R A C T

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

Material and methods: This prospective study enrolled 248 consecutive patients with cirrhosis and ascites. After excluding patients who were immunosuppressed, had history of prior antibiotic use, had previous episodes of SBP and had other confounding etiological factors for ascites, 125 patients were included in the study. SBP was defined as ascetic fluid 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).Variables like albumin, INR, creatinine, creatinine clearance and ascItic fluid analysis measurements were compared in the two groups

Results: The prevalence of SBP was 20%. The mean MELD score in SBP group was 24.92 and in the non SBP group were 19.05. Patients with MELD >25 had an odds ratio of 7(p=0.0001) for SBP as compared to patients with MELD < 15. Ascitic fluid PMN count, serum albumin, serum creatinine and creatinine clearance were significantly altered in the SBP group.

Conclusion: The prevalence of SBP was 20%. Increasing MELD score is independently associated with a greater risk of SBP. The risk of developing SBP is seven times higher if MELD score is >25 as compared to a score of < 15.

INTRODUCTION

Spontaneous bacterial peritonitis is a common complication of cirrhosis. It is considered a marker of end stage liver disease and an indication for liver transplant. MELD score is a universally accepted prognostic score to assess disease severity and survival in end stage liver disease. There is limited data that correlates MELD score and risk of SBP directly. Thus, the present study was undertaken to determine the prevalence of SBP in our setting and to determine whether patients with higher MELD score have increased risk of development of SBP.

MATERIALS AND METHODS

This is a single centre, prospective, observational and analytical study.All consecutive patients admitted at Jagjivanram Hospital, Mumbai with cirrhosis of liver and ascites from May 2008 to March 2011 were evaluated. Out of a total of 248 patients, one hundred twenty three were excluded. Reasons for exclusion were: Antibiotic use in two weeks prior to admission (73 patients) Long standing diabetes / immunosuppressant drugs (16 patients) previous history of SBP (16 patients) confounding etiology for ascites (13 patients) HIV infection (5 patients) Repeat admissions were not included.

Patients with HIV infection, diabetes, immunosuppressant drug intake 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.

Thus, one hundred and twenty five patients formed the study group. Detailed history regarding symptoms, factors leading to cirrhosis, co morbid illness and high risk behaviour was recorded. Laboratory and radiological investigations including complete hemorgram, PT/ INR, complete liver function tests, renal parameters, serum electrolytes, HIV 1 & 2, HBsAg, anti HCV, USG abdomen, ascitic fluid analysis and culture and calculation of MELD was done all patients.SBP was defined as a paracentesis yielding $\geq$ 250 neutrophils / ml of ascitic fluid. Though bed side inoculation

Corresponding author:* **Mayank Jain
Department of Gastroenterology, Jagjivan Ram Hospital, Mumbai

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 clinical presentation and natural history. Patients with ascitic fluid PMN < 250 cells/ ml were considered not to have SBP and formed the control group. Data on subsequent paracentesis in patients was not analysed. All patients with SBP are referred to as cases and those without SBP as controls in further discussion. Cases and controls were stratified into three groups based on their MELD score. The groups were MELD </= 15, 16-24 and >/= 25. The number of patients among cases and controls in each group were assessed. Outcome of cases and controls was assessed during the same admission period. Data on follow up admissions was not included.

Continuous variables were compared between the two groups using student's t test (age, MELD score, albumin, sodium, PMN count, INR, SAAG, creatinine, creatinine clearance, ascetic fluid albumin. Other variables were analysed using Chi square test (sex, MELD grouping and outcome). Correlation between MELD score and ascetic fluid PMN was made using Pearson's test and r value was calculated. Odds ratio for developing SBP with increasing MELD score was calculated among the three groups. The confidence interval was calculated for the odds ratio. Analysis was done using SPSS software. P values of < 0.05 were considered significant.

RESULTS

A total of 248 patients with cirrhotic ascites were admitted during the study period. One hundred twenty five patients fulfilled the criteria for inclusion in the study. 25 patients had SBP (cases) and 100 patients acted as controls. Table 1 shows the baseline demographic characteristics of cases and controls.

Table 1 Demographic characteristics of cases and controls

Variable	Cases	Controls	P value
No. of cases	25	100	
Age (yrs) Median (Range)	54.2(32-78)	50.1(23-78)	>0.05
Sex (%) Male Female	20(80%) 5(20%)	81(81%) 19(19%)	>0.05
Etiology Alcohol	20(80%)	66(66%)	
HCV	02(8%)	15(15%)	
Cryptogenic	02(8%)	7(7%)	
HBV	-	8(8%)	>0.05
NASH	-	2(2%)	
HBV+ HCV	-	1(1%)	
others	1(4%)	1(1%)	
AIH	01	4%	

Various laboratory parameters – INR, serum albumin, serum sodium, serum creatinine, creatitine clearance, SAAG, ascetic fluid albumin and ascetic fluid polymorphonuclear count – were compared between the two groups.(Table 2)

The mean MELD score in the cases was 24.92 while in the control group, the mean MELD score was 19.05. (p<0.01).As seen in table no.3, a total of 39 patients had MELD score less than or equal to 15. Only 7.7% (3/39) patients with MELD less than or equal to 15 had SBP. 36.8% (14/38) of patients with MELD score of more than 25 had SBP. 16.6% (8/ 48) of patients with MELD score between 16 and 24 had SBP. 56% of Cases had a MELD score of more than 25 compared to 24 % of Controls. The odds ratio for developing SBP in the MELD group 16-24 as compared to MELD less than 15 was 2.4 (X^2 =2.227, p=0.1356, CI 0.99-1.44).

Table No. 2 Comparison of laboratory parameters between Cases and Controls

Parameter	Cases Mean value+/- SD (range)	Controls Mean value+/- SD (range)	t value	p value
INR	1.50+/-0.307 (0.95-2.06)	1.463+/- 0.377 (1.02-2.52)	0.43	>0.1
Albumin (gm%)	2.49+/- 0.331 (1.9-3.33)	2.74+/- 0.476 (1.8-3.7)	2.28	<0.05
Sodium(meq/lt)	130.56+/- 6.36 (107-139)	132.97+/- 7.21 (108-147)	1.38	>0.1
Creatinine (mg/dl)	1.64+/- 1.636 (0.52-9.15)	0.825+/- 0.781 (0.29-2.48)	5.28	<0.001
Creatinine clearance (ml/min)	60.78+/-28.03 (7-147)	98.72+/- 42.53 (43-190)	3.840	<0.001
SAAG	2.05+/-0.391 (1.3-2.73)	1.83+/-0.540 (1.6-3.4)	1.76	>0.1
Ascitic fluid albumin (gm%)	0.6272+/- 0.268 (0.19-1.2)	0.605+/-0.436 (0.15-2.25)	0.22	>0.1
Ascitic fluid PMN (cells/hpf)	659.6+/- 480.76 (280-2000)	65.32+/- 48.53 (0-225)	10.27	<0.00001

Table No. 3 Classification of patients as per MELD score

MELD Score	Cases		Controls	
	No.	%	No.	%
</=15	03	12%	36	36%
16-24	08	32%	40	40%
>/=25	14	56%	24	24%

The odds ratio for developing SBP in MELD group more than 25 when compared to MELD score less than 15 was 7 (X^2=14.94, p=0.0001, CL 0.95, CI 0.02-0.36). The risk in patients with MELD score > 25 as compared to those with a score of 16-24 was 2.9 times higher (X^2 =7.064, p=0.0078, CI 0.09-0.72).Positive correlation (r=0.2, p=0.0253)was noted between ascitic fluid PMN count and MELD score.(Figure1)

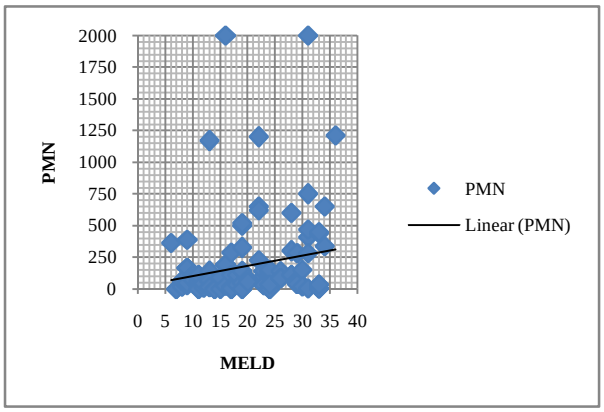

Figure no.1 correlation between MELD score and ascetic fluid PMN count

24% of patients with SBP and 12% of controls expired during the same admission (maximum duration of stay 30 days). The difference in mortality in the two groups was not statistically significant. The causes of death in cases were sepsis (3) and hepatorenal syndrome (3). The causes of death in the controls included upper gastrointestinal bleed (7), hepatorenal syndrome (3) and hepatic encephalopathy with aspiration

(2).Patients were not followed on long term basis for mortality assessment

DISCUSSION

The present study was undertaken to determine the prevalence of SBP in our setting and to determine whether patients with higher MELD score have increased risk of development of SBP. The study was done in a prospective manner. The prevalence of SBP in this study was noted to be 20%. This is as per the reported prevalence in India which varies from 20 - 30%. Studies from other countries have reported a prevalence ranging from 3- 25%. Amarapurkar *et al* from Mumbai reported a prevalence of 22% while Puri *et al* reported the prevalence to be 30% in north India.[1,2] Luke Evans *et al* reported a very low prevalence of 3.5% in outpatients without symptoms. In a study from Nepal, the prevalence of SBP was noted to be 24.69%.[3,4]

The age and sex distribution in the Case and Control groups was similar .The etiological factors for cirrhosis in the Cases included- alcohol (80%), hepatitis C (8%), cryptogenic cirrhosis (8%) and autoimmune hepatitis (4%). On the other hand, the major etiological factors in the Control group were- alcohol (66%), hepatitis C (15%), hepatitis B(8%), crytogenic(7%) and others (4%). The distribution is similar to the pattern of commonest causes of chronic liver disease in our part of the country. Alcohol (50%) is the commonest cause of chronic liver disease in adults followed by hepatitis C (12%) and B (9%).[5]

Serum creatinine levels were significantly higher in patients with SBP ($p < 0.001$). The mean creatinine clearance was significantly lower in patients with SBP ($p<0.001$). This may be due to renal impairment secondary to infection or due to advanced liver disease in the SBP group. Follo *et al* have reported renal dysfunction in 33% of patients of SBP.[6] Serum albumin levels were significantly lower in the patients with SBP. This may be secondary to advanced liver disease and renal dysfunction. Moreover, poor nutrition may also contribute to lower levels. It is highly likely that low albumin levels also increase the chances of infections like SBP in patients with chronic liver disease. The INR, SAAG, serum sodium and mean ascitic fluid albumin were comparable in both the groups and did not show a statistically significant difference.

In the study done at University of Pennsylvania, the serum creatinine values were not statistically different in SBP and non SBP group. However, the differences in serum bilirubin and INR in the two groups were statistically significant. They also reported that serum sodium is not a significant confounder for primary association between SBP and MELD score.[7]

In the present study, greater MELD score at admission was independently associated with a greater risk of SBP. 56% of Cases had MELD score of more than 25. For those with MELD $\geq$ 25, the risk of SBP was seven times higher compared to those with MELD score $\leq$ 15. This suggests that MELD score, a widely used scoring system, is also a useful tool to predict the presence of SBP. In a retrospective study done at the University of Pennsylvania, 111 patients were studied. 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 ($p=0.0003$). Patients with MELD $\geq$ 25 has an odds ratio of 9.67 for SBP compared to subject with MELD $\leq$ 15.[7] Several authors have noted increasing complications like variceal bleeding, SBP, encephalopathy and death with increasing MELD score. In the SBP group, mean MELD was 24.92 compared to MELD of 19.05 in the control group ($p<0.01$). This shows that patients with advanced liver disease have higher chances of development of life threatening complications like SBP. At the same time it should be kept in mind that SBP per se can worsen hepatic and renal function in due course and lead to higher MELD score. Three patients with MELD $\leq$ 15 also had SBP (7.7%). Thus, one cannot exclude the possibility of SBP solely on the basis of MELD score. This observation suggests 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, which tests for leukocyte esterase, are available within 90-120 seconds and may speed up treatment of SBP and improve survival.[8]

Though ascitic fluid was sent for culture in all patients, we did not make a diagnosis of SBP based on the culture reports. Since culture positive and culture negative neutrocytic ascites have similar natural history, it is unlikely this would have affected the results. [9-11] Five patients in SBP group had positive culture showing growth of E. coli. Thus, culture positivity was 20%. Various studies have reported multiple organisms as the cause of SBP- E.coli (37%), Klebsiella pneumoniae (17%), Pneumococci (12%), Streptococcus viridans (10%) and anaerobic organisms (6%).[12]

Small positive correlation was noted between MELD score and ascitic fluid polymorphonuclear cell count using Pearson's test ($r=0.2$). Pearson's r value between 0.0-0.09, 0.1-0.3, 0.3-0.5 and 0.5-1.0 denotes none, small, medium and strong correlation between two variables. Higher PMN count in ascitic fluid suggests more severe SBP. In the present study, there was small positive correlation between rising ascitic fluid PMN count and rising MELD score. This suggests that SBP is more severe in patients with higher MELD score .There is no data in literature to suggest such a correlation and further studies with larger sample size are required to confirm this finding.

24% of patients with SBP expired (6 out of 25) while 12% of controls expired during the same hospital admission. The difference in mortality in the two groups was not statistically significant.The causes of death in cases were sepsis (3) and hepatorenal syndrome (3). The causes of death in the controls included upper gastrointestinal bleed (7), hepatorenal syndrome (3) and hepatic encephalopathy with aspiration (2). As reported in literature, sepsis, hepatorenal dysfunction, gastrointestinal bleed and hepatic encephalopathy are the common modalities of death in cirrhotic patients. [12]In hospital mortality for the first episode of SBP ranges from 10-50%[13] and the one year mortality after the first episode of SBP reported to be between 31-93%. [14,15] Occurrence of SBP markedly worsens the prognosis in patients with cirrhosis and it has been proposed that a new prognostic stage of cirrhosis not reflected in the present staging system should be defined- so called "critically ill cirrhotic".[16] The present study has several strengths. Diagnostic paracentesis is routinely done for all patients admitted to our hospital with cirrhotic ascites. Therefore, we could capture all cases of SBP

in our study cohort. We excluded patients who were at a higher risk of developing SBP like those with HIV infection, long standing diabetes and immunosuppressed state, patients with prior history of SBP and on antibiotics 2 weeks prior to admission. This helped us to correctly identify the relation between MELD score and development of SBP. However, we chose not to document SBP by positive cultures. This may have lead to misclassification of early SBP cases as controls. Given the rarity of such a condition, it is unlikely to have affected our results. Sample size was small and larger, possibly multicentric studies are required to confirm our findings.

Summarising our observations, the prevalence of SBP in our setting was found to be 20 %. Higher MELD score at presentation is associated with increased chances of presence of SBP. One third of patients with MELD score >25 had SBP. The odds ratio for developing SBP when MELD score> 25 is compared to a MELD score <15 was 7.

7.7% patients with MELD < 15 also had SBP. Thus, SBP cannot be ruled out solely on the basis of MELD score. Renal dysfunction is common in patients with SBP as noted by high mean creatinine values and low creatinine clearance values. There is small positive correlation between rising MELD score and rising ascitic fluid PMN counts

To conclude, we believe that level of suspicion for SBP should be high in patients with elevated MELD score. Early ascitic tapping should be done in all such patients to establish early diagnosis of SBP and initiate treatment. This would reduce mortality in this group. Additionally, patients with a low MELD score continue to have possibility of SBP and should by no means be excluded from a diagnostic paracentesis on admission.

References

1. Amarapurkar DN, Viswanathan N, Parikh SS, Kalro RH, Desai HG. Prevalence of Spontaneous Bacterial Peritonitis. *J Assoc Physician India*. 1992; 40(4): 236−238
2. Puri AS, Puri J, Ghoshal UC, *et al*. Frequency, microbial spectrum & outcome of Spontaneous Bacterial Peritonitis. *Indian J Gastroenterol*.1996; 15(3): 86−89
3. Evans T L, Kim W.R. Joun JP, Kamath PS spontaneous bacterial peritonitis in asymptomatic out patients with cirrhotic ascites. *Hepatology* 2003:37:897-901.
4. Syed VA, Ansari JA, Karki P, Regmi M, Khanal B. Spontaneous bacterial peritonitis (SBP) in cirrhotic ascites: A prospective study in a tertiary care hospital, Nepal. *Kathmandu University Medical Journal*. 2007;5(1):48-59
5. Rajiv Baijal, H R Praveenkumar, Mayank Jain, Deepak Gupta, D N Amarapurkar. Study of etiological factors for cirrhosis. *Indian J Gastroenterol*. 2010;29 (suppl 1);abstract L2
6. Follo A, Liovet JM, Navasa M. Renal impairment after spontaneous bacterial peritonitis in cirrhosis: incidence, clinical course, predictive factors and prognosis. *Hepatology*. 1994 ;20:1495
7. Keith L Obstein, Mical S. Campbell, K. Rajinder Reddy *et al*: Association between model of End stage liver disease and spontaneous bacterial peritonitis. *Am J Gastroenterol* 2007; 2732 - 35
8. Runyon BA. Strips and tubes: improving the diagnosis of spontaneous bacterial peritonitis. *Hepatology* 2003; 37:745
9. Runyon BA. Monomicrobial nonneutrocytic bacterascites:a variant of spontaneous bacterial peritonitis. *Hepatology*.1990;12:710
10. Runyon BA, Canawati HN, Hoefs JC. Culture negative neutrocytic ascites: a variant of spontaneous bacterial peritonitis. *Hepatology* 1984 ;4:1209
11. Llovlet J, Rodriquez – Iglesias p, Moitinho E. Spontaneous bacterial peritonitis in patients with cirrhosis undergoing selective intestinal decontamination. *J Hepatol* 1997;26:88
12. Runyon BA. Ascites and spontaneous bacterial peritonitis. In Sleisinger and Fordtran's Gastrointestinal and liver diseases. 8th Edition. Saunders. volume 2:1935-1964
13. Pinzello G, Simonetti RG, Craxi A. Spontaneous bacterial peritonitis: a prospective investigation in predominantly non alcoholic cirrhotic patients. *Hepatology* 1983;3:545-9
14. Andreu M, Sola R, Sitges -Serra A. Risk factors for spontaneous bacterial peritonitis in cirrhotic patients with ascites. *Gasteroenterol* 1993;104:1133-8
15. Silvain C, Besson I, Ingrand P. Prognosis and long term recurrence of spontaneous bacterial peritonitis in cirrhosis. *J Hepatol* 1993;19:188-9
16. Arvaniti V, D'Amico G, Fede G. Infections in patients with cirrhosis increase mortality fourfold and should be used in determining prognosis.*Gastroenterology*. 2010;139:1246-56

How to cite this article:

Mayank Jain *et al* (2017) 'Correlation Between Meld Score and Sbp in Patients With Cirrhosis and Ascites', *International Journal of Current Advanced Research*, 06(08), pp. 5682-5685. DOI: http://dx.doi.org/10.24327/ijcar.2017.5685.0778

****