EVALUATION OF MODEL FOR END STAGE LIVER DISEASE (MELD) SCORE IN SPONTANEOUS BACTERIAL PERITONITIS (SBP) IN PATIENTS WITH LIVER CIRRHOSIS

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Abstract

We determined MELD scores in patients of spontaneous bacterial peritonitis (SBP) with liver cirrhosis. All patients (n=85) had MELD scores on the basis of laboratory values of serum creatinine, serum bilirubin and PT/INR (Prothrombin Time/International Normalized Ratio). MELD scores were calculated according to the United Network of Organ Sharing (UNOS) method. The 73 (85.88%) patients presented with abdominal pain, 64 (73%) patients with fever, 25 (29%) patients with encephalopathy and 13 were having dyspnea (15.29%). The 49 (57.65%) patients had paracentesis in the past. Among 85 patients, 51 (60%) were having ascites for one year and 24 (28%) patients for more than one year. Serology for viral markers showed that 68 (80%) patients were positive for anti-HCV antibodies and 8 (9.4%) patients were positive for hepatitis B surface antigen while, 3 (3.5%) patients were positive for both B surface antigen (HBsAg) and anti-HCV antibodies. In the remaining 6 patients, 2 (2.35%) patients were due to alcoholic cirrhosis and in 4 (4.7%) patients, viral markers were negative. The 32 (37.64%) patients had a MELD score in the range of 21-25, 20 (23.52%) patients had scores of 26-30, while only 10 (11.76%) patients had MELD score > 30. Through MELD score that SBP is more associated with male patients (61%) compared to (39%) female patients. Overall, among all 85 patients, the 77 (90.59 %) patients had a high MELD score (≥16) and 8 (9.41 %) patients had a low MELD score. Therefore, in patients with liver cirrhosis who had SBP, the MELD score is found higher.

Introduction

A significant morbidity and mortality is related to the Spontaneous Bacterial Peritonitis-SBP. The identification of its 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. The objective of this cross-sectional study was to determine the frequency of a high 'Model for End-Stage Liver Disease' (MELD) score in patients of spontaneous bacterial peritonitis (SBP) with liver cirrhosis. The study conducted at Gastroenterology-Hepatology Unit, Shaikh Zayed Hospital, Lahore. A significant morbidity and mortality is found related with the Spontaneous Bacterial Peritonitis-SBP, and identification of its 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. We determined the frequency of higher MELD score in patients of spontaneous bacterial peritonitis (SBP) with liver cirrhosis. Patients with ascites and cirrhosis may develop infections and a very common is spontaneous bacterial peritonitis (SBP). The permeability to bacteria increases in cirrhosis and such leakages of bacteria lead to peritonitis. Often the immunity gives way and proliferation of bacteria goes uncontrolled and hence ascites develops. The 8-27 % patients' ascites may have SBP as highlighted by various studies. The mortality is between 20-40 % (Sleisenger and Fordtran, 1998; Sherlock and Dooley, 1997). When there is no evident abdominal infection, the infection of ascitic fluid with an already cirrhotic liver disease is referred to as SBP (Sheer and Runyon, 2005).

Cirrhosis is most commonly a result of hepatitis C virus in Pakistan (Nadeem *et al.,* 2004). Healthy population also exhibits seroprevalence of HCV infection and the range is 4-12.5 % in Pakistan and increase with age (Hashim *et al.,* 2005). The rate of hepatitis B surface antigen ranges from 1.5- 2.1% (Ijaz *et al.,* 2007). The 74 % patients with liver cirrhosis and 90 % of chronic liver disease (CLD) patients were infected with HBV (hepatitis-B virus), HCV (hepatitis-C virus) or both (Bukhtiari *et al.,* 2003). Liver cirrhosis is the most common cause of portal hypertension (PHT) all over the world (Triantos *et al.,* 2006) and portal hypertension renders the highest mortality in cirrhotic all around the world (Lowe and Grace, 2001). The infection of peritoneal fluid is usually confined by a bacterial culture and a high PMN (polymorphonuclear) leukocyte count > 250 cells/mm^3. One of the earliest indicators of ascites in such patients is asymptomatic spontaneous bacterial peritonitis and should be the first thing sought in all patients who develop ascites for the first time (Khan *et al.,* 2014). In order to diagnose SBP, the PMN count must be > 250 cells/mm^3 (Runyon *et al.,* 1988).

Owing high mortality of SBP patients, the study of factors and predisposing conditions is of greater interest. A model has been developed as a measure of risk of mortality in ESLD (end-stage liver disease) patients.

Encephalopathy and ascites, these two complications of ESLD are found to be correlated with higher MELD scores. The idea behind the MELD score is to predict the mortality and to confirm the severity of liver disease and prognosis in patient who have undergone TIPS (Transjugular Intrahepatic Portosystemic Shunt) after complicated portal hypertension (PHT). A higher MELD score alone is indicative of a higher probability of the development of SBP (Wang *et al.,* 2009). Of the 89.65 % of SBP cases had a MELD score of < 16. Patients who had no SBP had a MELD score of 64.60 % (Obstein *et al.,* 2007). In cirrhosis, there is hypochlorhydria and altered motility of the small intestine. This predisposes to an overgrowth of such microorganisms (Bauer *et al.,* 2001; Sanchez *et al.,* 2007). In a study, a comparison of bacterial overgrowth and small intestinal motility is 20 patients with SBP and another 20 patients without SBP yielded a higher bacterial overgrowth in patients with SBP (70 % as opposed to 20 %). There was significant motility disturbance in such patients also (Chang *et al.,* 1998). In another study, however, there was no association between SBP and bacterial overgrowth (Bauer *et al.,* 2001). The majority of the SBP patients usually come up with advanced cirrhosis symptoms. The risk factors which usually found associated with cirrhosis are: variceal hemorrhage, malnutrition, possibly use of proton pump inhibitors, serum total bilirubin concentration above 2.5 mg/dl, ascitic fluid total protein concentration less than 1 g/dl (<10 g/L), prior episode of SBP (Bauer *et al.,* 2001).

Materials and Methods

Study Design and Data Collection: The objective of the study was to determine the frequency of a higher Model for End-Stage Liver Disease (MELD) score in patients of spontaneous bacterial peritonitis (SBP) with liver cirrhosis. The study design was a cross-sectional survey, which was conducted for six months. Eighty five patients fulfilling the inclusion criteria were selected from Inpatient Departments: Gastroenterology-Hepatology and Gastroenterology Units of Shaikh Zayed Hospital, Lahore. The informed consents were taken from all patients. Demographic data including age, sex, etc. was obtained on the designated Proforma. All patients (n=85) had MELD scores on the basis of laboratory values of serum creatinine, serum bilirubin and PT/INR (Prothrombin Time/International Normalized Ratio). MELD scores were calculated according to the method used by the 'United Network of Organ Sharing' (UNOS) ('*http://www.unos.org'*). High MELD scores (as per operational definition) were noted in all the patients.

Sample Size and Techniques: The sample size of 85 with 95% confidence level (CI) has been considered with a 7% margin of error and expected percentage of high MELD score (≥16) i.e., 89.65% in patients with SBP and liver cirrhosis was taken. Non-probability purposive sampling technique was adopted for the patient selection. The MELD score was developed to determine the severity of liver disease based on the patient's serum bilirubin, serum creatinine, and the international normalized ratio (INR).

The MELD (Model for End-Stage Liver Disease) makes use of certain laboratory markers like serum bilirubin, serum creatinine, and the international normalized ratio (INR) for Prothrombin Time-PT to predict survival. A rising MELD score proportionality relates a severity of liver dysfunction and even at risk of death (Kamath *et al.,* 2001). The following equation was considered for MELD scoring. MELD score ≥ 16 was taken as high score (Kamath *et al.,* 2001; Biggins and Bambha, 2006). This equation describes that the predicted risk of mortality increases logarithmically (*ln*) with the increase in the MELD score. In its current application from the 'United Network for Organ Sharing' (UNOS), any laboratory values < 1 are optimized to 1 in order to prevent the generation of negative MELD scores (Kamath *et al.,* 2001; Biggins and Bambha, 2006).

"MELD Score = 10 {0.957 Ln (Serum creatinine mg/dL) + 0.378 ln (Total bilirubin mg/dL) + 1.12 ln (INR) + 0.643"

Diagnosis of spontaneous bacterial peritonitis: The diagnosis is established by a positive ascitic fluid bacterial culture and an elevated ascitic fluid absolute polymorphonuclear (PMN) leukocyte count (≥ 250 cells/mm^3) or total leukocyte count > 500cells/mm^3.

Data analysis: Data collected was analyzed by SPSS version 20. The age was presented as mean ± SD while, sex and high MELD score were presented as frequency and percentage.

Inclusion criteria: Patients with ascites (assessed clinically and ultrasonographically) secondary to liver cirrhosis due to any cause, patients with age ranging from 25-70 years of either sex, and patients who had SBP (PMN cell count ≥ 250 cells/mm^3).

Exclusion criteria: Patients exposed to antibiotics within the last two weeks (assessed on history), immunosuppressed patients like DM (BSL > 110 fasting) and diagnosed HIV-positive, patients with a history of any bleeding disorder (Thalassemia, Hemophilia, Protein C or S deficiency) and patients with prior transplantation (assessed on history).

Results

Among 85 patients, there were 52 (61%) male patients and 33 (39%) female patients. The male to female ratio was 1.57: 1. Mean age was 53.05 years (SD ±6.82) ranging 30-70 years. Table 1 shows the distribution of patients' ages, the maximum number (34%) was from the age group. 51-60 years.

Table 2 shows the frequency of symptoms of the SBP disease as follows: 73 (85.88%) patients presented with abdominal pain, 64 (73%) patients with fever, 25 (29%) patients with encephalopathy and 13 were having dyspnea (15.29%). The 49 (57.65%) patients had paracentesis in the past. Among all 85 patients, 51 (60%) were having ascites for one year and 24 (28%) patients for more than one year. The 58 (68.24%) of SBP patients had symptoms of ascites from 1-12 months, whereas, 27 (31.76%) patients had symptoms of ascites for more than a year (Table 3). Figure 1 shows a graphical representation of the frequency of the etiology of liver cirrhosis for all SBP patients. Out of 85 patients, the 66 (77.65%) patients had no previous history of SBP, while 6 (7%) patients had two episodes of SBP and 13 (15%) had one episode of SBP in the past (Table 4).

Serology for viral markers showed that 68 (80%) patients were positive for anti-HCV antibodies and 8 (9.4%) patients were positive for hepatitis B surface antigen (HBsAg) while, 3 (3.5%) patients were positive for both B surface antigen and anti-HCV antibodies (Table 5). In the remaining 6 patients, 2 (2.35%) patients were due to alcoholic cirrhosis and in 4 (4.7%) patients, viral markers were negative (Table 5). Most of the patients were anemic and among them 33 (38.8%) patients were having a hemoglobin level between 6.8-8.8 g/dl, while only 12 (14.11%) patients were having a hemoglobin level above 10.9 g/dl. Ascitic fluid analysis showed: mean WCC (White Cell Count): 677.43, PMN (Polymorphonuclear) leukocyte count: 418.21, lymphocytes count: 240.14, albumen: 0.66 g, glucose: 219.11 g and LDH (Lactate Dehydrogenase): 96.24 (Table 6).

MELD score in patients ranges from 09-36. Eight patients (9.41%) with SBP had MELD score < 15, while 15 (17.64%) patients had a score between16-20 (Table 7). Among these 8 patients who were having low MELD; 7 (8.23%) patients were having a MELD score between10-15, whereas, only 1 (1.18%) patient had a MELD score even < 10 (Table 8). The 32 (37.64%) patients had a MELD score in the range of 21-25, 20 (23.52%) patients had scores of 26-30, while only 10 (11.76%) patients had MELD score > 30 (Table 7).

Overall, among all 85 patients, the 77 (90.59 %) patients had a high MELD score (≥16) and 8 (9.41 %) patients had a low MELD score. Therefore, in patients with liver cirrhosis who had SBP, the MELD score is found higher. Figure 2 shows a graphical representation of the percentage frequency of MELD Score in SBP Patients.

Table 1. Age distribution of patients (n=85)

Age in years	No of patients	Percentages
30-40	12	14.13%
41-50	27	31.76%
51-60	29	34.11%
61-70	17	20.00%
Total	85	100.0

Table 2: Frequency of Symptoms of Disease (n=85)

Symptoms	Yes	Percentage	No	Percentages
Fever	64	75.29%	21	24.71%
Abdominal pain	73	85.88%	12	14.12%
Dyspnea	13	15.29%	72	84.71%
Paracentesis in past	49	57.65%	36	42.35%
Encephalopathy	25	29.41%	60	70.59%

Table 3. Duration of Ascites in Months (n=85)

Duration of Ascites (months)	No. of Patients	Percentage
1-12	58	68.24%
More than 12	27	31.76%

Table 4. Frequency of previous SBP in patients (n=85)

Number of Previous SBP	Number of Patients	Percentage
1	13	15.29%
2	6	7.06%
No previous SBP	66	77.65%

Table 5. Frequency of Etiology of Liver Cirrhosis (n=85)

Etiology	Number of Patients	Percentage
Anti HCV+	68	80.0%
HbsAg+	8	9.41%
Anti-HCV+& Hbs-Ag+	3	3.53%
Alcoholic Cirrhosis	2	2.35%
Unknown Cause	4	4.71%

Table 6. Ascitic Fluid Analysis

Parameters	Mean Values	Std. Deviations ±
White Cell Count	677.43	428.75
PMN Leukocyte Count	418.21	269.74
Lymphocyte Count	240.14	215.47
Albumen	0.66	0.58
Glucose	219.11	60.14
Lactate Dehydrogenase	96.24	35.74

Table 7. Frequency of high MELD score in patients with SBP (n=85)

MELD Score	Number of Patients	Percentage %
< 15	8	9.41
16-20	15	17.65%
21-25	32	37.65%
26-30	20	23.53%
>30	10	11.76%

Table 8. Frequency of low MELD score in patients with SBP (n=85)

MELD < 16	Number of Patients	Percentage
10-15	7	8.23%
<10	1	1.18%

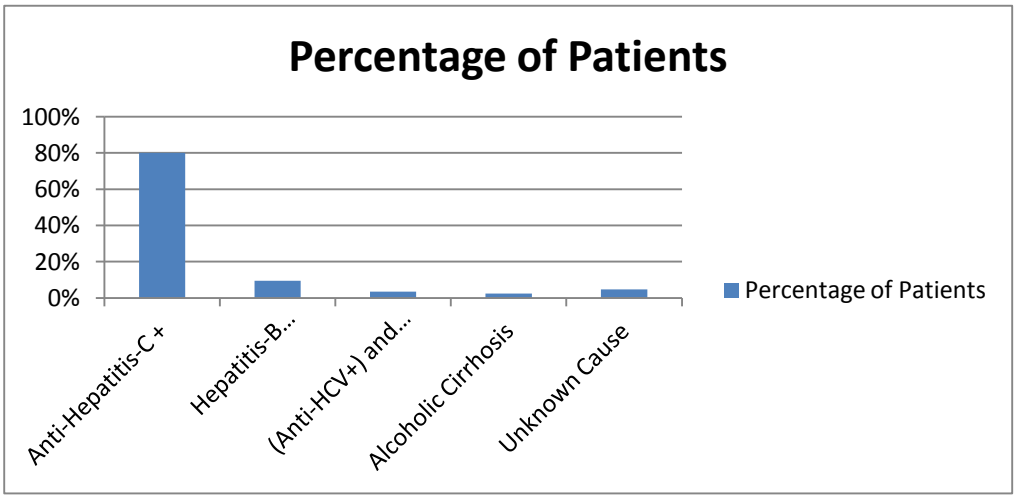

Fig. 1. Graphical Representation: Frequency of Etiology of Liver Cirrhosis for All SBP Patients

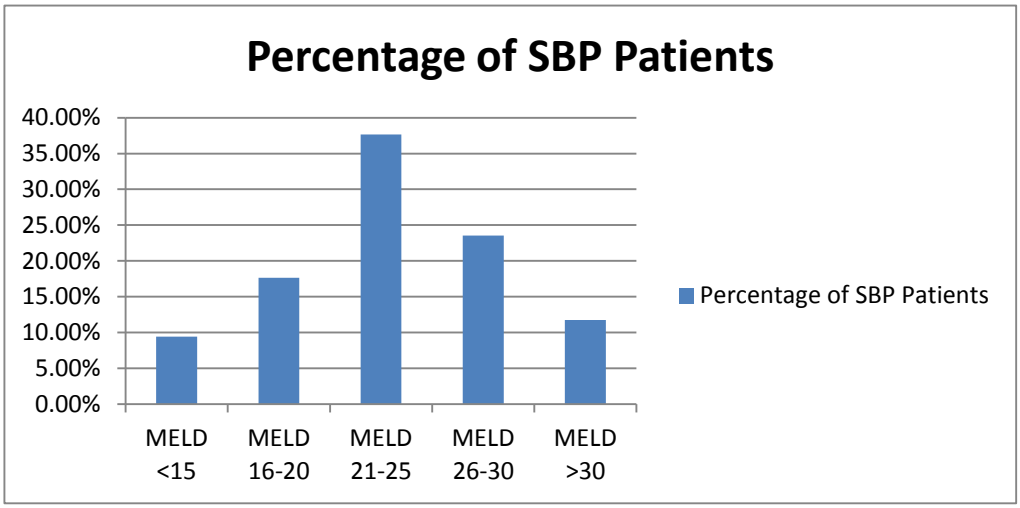

Fig. 2. Graphical representation: Percentage frequency of MELD Score in SBP Patients

Discussion

Unlikely now a day, before 1980s, there was not a definite threshold available for an early stage detection of SBPs and conditions like shock and even mortality prevailed (Runyon, 1990). Spontaneous bacterial peritonitis is a common complication in patients with liver cirrhosis followed morbidity and mortality (Zaman *et al.*, 2011). Spontaneous bacterial peritonitis was diagnosed when the total leukocyte count was > 500 cells/mm^3 or polymorphonuclear (PMN) leukocyte count > 250 cells/mm^3 or mono-microbial positive culture in ascitic fluid (Zaman *et al.*, 2011). It is profoundly known that SBP patients usually develop large ascites. Most of the spontaneous bacterial peritonitis (SBP) comes up with mixed and not obvious symptoms, in contrast to those patients who peritonitis (surgical) diagnosed lacking ascites. In our hospital, we found the most common features of SBP are: fever (69%), abdominal pain and/or tenderness (59%) and altered mental status (54%). Other symptoms include: diarrhea (32%), paralytic ileus (30%), hypotension (21%) and hypothermia (17%). The only features of SBP in some patients are leukocytosis, acidosis, or worsening renal function (Sleisenger and Fordtran, 1998; Sherlock and Dooley, 1997). Following are the indications for abdominal paracentesis in a patient with ascites: new onset ascites, at the time of each admission to the hospital, clinical deterioration, inpatient or outpatient, fever, abdominal pain, abdominal tenderness, mental status change, ileus, hypotension, laboratory abnormalities that may indicate infection, peripheral leukocytosis, acidosis, worsening of renal function and gastrointestinal bleeding (a high risk time for infection) (Sleisenger and Fordtran, 1998; Sherlock and Dooley, 1997).

We have determined the frequency of higher 'Model for End-Stage Liver Disease' (MELD) score in patients of spontaneous bacterial peritonitis (SBP) with liver cirrhosis in current research. Through MELD score, we found that SBP is more associated with male patients compared to female patients. Overall, among all 85 patients, 90.59 % patients had high MELD score (≥16) and only 9.41 % patients had a low MELD score.

Therefore, in patients of liver cirrhosis who had SBP, the MELD score is found higher. In this current study, the 80% etiology of liver cirrhosis was associated with Anti Hepatitis-C virus with major symptoms with abdominal pain (86%) and fever (75%). Maximum number (77.65%) of patients had no past history of SBP, whereas, the maximum number (68.24%) of SBP patients had symptoms of ascites for 1-12 months. The SBP has a high recurrence and up to 70% will recur in less than per year. However, quinolones like Norfloxacin (400 mg) taken orally twice a day or Ciprofloxacin (750 mg) taken once a week can prevent recurrence.

Globally, the sources of ascites are different because there is diversity of live cirrhosis prevalence and alcohol intake, etc. In Pakistan, the commonest form of liver cirrhosis is reported from hepatitis-C virus and hepatitis-B virus; however, in other parts of the world, the common reason is alcohol excess consumption (Tanwani and Ahmad, 2000). The hepatitis B surface antigen rate is 1.5- 2.1 % in Pakistani population (Majed and Qayyum 2000; Ijaz *et al.*, 2007). Further, the HCV infection's seroprevalence is 4.0-12.5 % in Pakistani and this rate increases with the adults of increase age (Hashim *et al.*, 2005). In the procedure of blood transfusion, the needle injury from non-disposal syringes is reported in the patients diagnosed with anti-HCV positive. The prevalence of hepatitis-C virus infection is found to be elevated in those patients who underwent hemodialysis persistently. In developed countries, the hepatitis-C –HCV's seroprevalence is up to 1.6% (Armstrong *et al.*, 2006) and that of the hepatitis-B –HBV is up to 0.2 % (Kim *et al.*, 2002).

In an illustrative study, mesenteric lymph nodes were obtained from 101 patients with cirrhosis and from 35 non-cirrhotic controls (Cirera *et al.*, 2001). Enteric organisms were grown from culture in only 8.6 % of controls compared to 3.4 %, 8.1 %, and 30.8 % of patients with Child class A, B, and C cirrhosis, respectively. Selective intestinal decontamination reduced the rate of positive cultures to that of non-cirrhotic patients. Other studies have shown a molecular evidence of bacterial translocation and suggested that it occurs prior to the development of clinical SBP (Runyon, 2004; Wiest and Garcia-Tsao, 2005). Lower levels of translocation of intact bacteria or pieces of bacteria may lead an activation of tumor necrosis factor (TNF), which may explain the higher levels of TNF that have been observed in patients who ultimately develop SBP compared with the controls (Such *et al.*, 2001). The presence of bacterial DNA in serum and ascitic fluid is a risk factor for death in patients with cirrhosis (Zapater *et al.*, 2007). Proton pump inhibitors have increased bacterial translocation in an animal model of SBP and also increase the risk of SBP in humans (Sanchez *et al.*, 2007; Zapater *et al.*, 2007). In this current study, we found through a MELD score that SBP is more associated with male patients (61%) compared to 39% female patients. Overall, among all 85 patients, the 90.59 % patients had a high MELD score ($\geq$16) and 9.41 % patients had a low MELD score. Therefore, in patients with liver cirrhosis who had SBP, the MELD score is found higher.

Conclusion

The outcome of this study referring an attention that SBP is a serious and challenging liver ailment to deal as it comes along with a diverse range of diagnosed or non-diagnosed symptoms. Higher MELD scores were identified in patients with liver cirrhosis who were suffering from SBP. An early diagnosis is highly recommended along with MELD scores judgment with ascitic fluid analysis. There must be proper awareness among population regarding how preventive measures along with a timely vaccinations especially for hepatitis B virus. There must be protocols and proper guidelines for staff nurses and doctors regarding diagnosis and treatment of this ailment.

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