Original Article

Mortality in Cirrhotic Patients

Frequency of Mortality in Cirrhotic Patients with Acute Variceal Hemorrhage with High MELD (Model for End Stage Liver Disease) Score

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ABSTRACT

Objective: To determine the frequency of mortality in cirrhotic patients with acute variceal hemorrhage with high MELD score

Study Design: Observational study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology and Hepatology, Liaquat National hospital, Karachi from December 2015 to December 2016.

Materials and Methods: Total 193 patients of acute UGI bleeding with cirrhosis were admitted from the period. Patients with hemoglobin <7g/dl were transfused according to individual requirements and resuscitated. Esopghagoduodenoscopy was done to confirm the diagnosis and treat variceal hemorrhage by variceal band ligation for esophageal varices or cyanoacrylate injection in gastric varices within 24 hours of admission. Endoscopy was performed by well experienced and trained Gastroenterologists. Patients MELD score were calculated, those with high MELD score were observed for inhospital mortality. After discharge from hospital patients were followed up in outpatient department for a period of one month.

Results: There were 124 male and 69 female patients. The mean age was 45.94±10.44 years. The mean MELD score was 26.19±5.45. Mortality was 16 (8.3%) cases. Among mortality cases, mean MELD score was 27.08±5.46. The association of mortality was found significant with high MELD score.

Conclusion: MELD score, if high may be used as a marker for identifying and management of high risk patients of cirrhosis with variceal hemorrhage

Key Words: Mortality, Liver Cirrhosis, MELD Score

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INTRODUCTION

Portal hypertension is the hypertension in hepatic portal system, which is stated as hepatic venous gradient (HVPG) greater than 6mmHg.Cirrhoss is the most common cause of portal hypertension in adults, it is a chronic progressive disease which is manifested with a dynamic circulatory changes in the body with complications which can lead to mortality if untreated. It is a cause of residual disability worldwide and a challenge for physicians and health care system.[1,2]

Acute variceal hemorrhage is a catastrophic and life threating complication of cirrhosis, with fatality extraordinary as 20- 35%.[4] It is very difficult to estimate prognosis in these patients because outcomes is also influenced by the presence of fibrosis, which is preexisting injury in diseased liver, current synthetic function of liver status and lastly severity of hemorrhage itself.[5] Numerous factors now have been recognized which are linked to increased risk of mortality after the episode of variceal hemorrhage ,which include Child–Turcotte–Pugh score, presence of portal vein thrombosis, hepatocellular carcinoma, acute on chronic liver failure ,ongoing hemorrhage at endoscopic evaluation, aminotransferases level and severity of portal hypertension assessed by hepatic venous pressure gradient (HVPG).[6]

Variceal hemorrhage's predisposing factors are size, shape, pressure, and place of varices and also other clinical manifestations of underline diseases.[7]The varices commonly expand in distal portion of esophagus, stomach and rectum; however other parts of the gastrointestinal tract can be affected. Varices in middle portion of esophagus are formed deeply in the sub-mucosal layer and have mucosal support but in distal portion varices are more superficial and have less mucosal support, so they have more susceptibility for bleeding. Gastric varices hemorrhages are also common.[8]

These varices can be the continuation of esophageal varices in greater or lesser curvature (GOV-1=Type 1 gastroesophageal varices) or it can be isolated in fundus

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(IGV1= type 1 isolated gastric varices) with prevalence of 10% and 90% respectively.[9] The more serious chronic hepatic disease takes place with the more complications and the more mortality because of hypovolumic shock, infections, and hepatic failure. Up to now different methods are created to predict the complications and mortality rate of cirrhosis.[5, 10]

The MELD score is highly validated, it is extensively used to access disease severity, and its implications include predicting survival among cirrhotic patients undergoing surgery, intensive care unit patients with infections, highlighting and categorizing patients as those who urgently require liver transplantation. MELD score has exclusively replaced the Child-Pugh scoring system.[11] The score is extensively applied to estimate outcomes which includes post-surgical liver decompansation and unanimously validated for prioritization of cirrhotic patients for liver transplantation.[12]

Thus MELD and child Pugh scoring systems are both applicable for estimation of survival but however MELD score supremacy over child Pugh scoring system needs more validation .[13]

Therefore, this study was designed with the aim to determine the frequency of mortality and morbidity in cirrhotic patients with acute variceal bleeding with high MELD score >12.

MATERIALS AND METHODS

This Retrospective observational study was conducted at Department of Gastroenterology and Hepatology, Liaquat national hospital, Karachi from July 2015 to June 2016.

Inclusion Criteria:

1. Either gender
2. Between 18 to 60 Years
3. Decompensated Cirrhotic patients with High MELD score irrespective of Sero negative or Sero positive presenting with hematemesis or malena.
4. Patients admitted with Acute UGI bleeding within 48 hours.

Exclusion Criteria:

1. Patients with known case of tuberculosis, cardiac valvular disease, diagnosed case of malignancy.
2. Patients who did not undergo endoscopy

This retrospective observational study was conducted on 158 patients with acute upper GI bleeding admitted at the Department of Gastroenterology and Hepatology, Liaquat National Hospital Institute for Postgraduate of health Sciences, Karachi. The study was approved by ethical review committee. Informed consent was taken. In addition, MELD score was calculated based on laboratory examination. The MELD score ≥12 was considered as high score. All patients were extensively assessed which included history and physical examination by principal investigator. Patients confirming the inclusion and exclusion criteria were assessed. Blood sample was taken for laboratory examinations (Complete blood counts, liver function profile (bilirubin, aminotrasferases (AST, ALT), Creatinine, INR). Patients were resuscitated, those with hypovolemic shock were shifted in high dependency unit, stabilized, and Patients with hemoglobin less than 7 g/dl were transfused according to individual requirements. All patients received prophylactic antibiotic therapy (IV third generation cephalosporin) and intravenous octreotide 50 mcg was given bolus to reduce portal pressure and then infusion was started at 50 mcg/hour for 72 hours for suspected variceal bleeding. Endoscopy was performed within 24 hours to establish the diagnosis. All endoscopies were performed by well-trained experienced consultant gastroenterologist. Patients were classified as Variceal Bleeding Patient based on endoscopic evidence .During hospitalization patients were closely monitored and discharged when stable they were followed in outpatient department over a period of a month to observe mortality. Furthermore, patient's demographics including name, age, and gender were collected. Microsoft excel and SPSS version 20 was used.

RESULTS

Total 193 cirrhotic patients of either gender, age between 18 to 60 years with MELD score ≥12, and acute UGI bleeding within 48 hours were included in the study to determine the frequency of mortality. The results revealed, 124 male and 69 female patients, with the mean age of study subjects was 45.94±10.44 years. The frequency distribution of age is presented in Figure-I.

Figure No.1: Frequency distribution of age

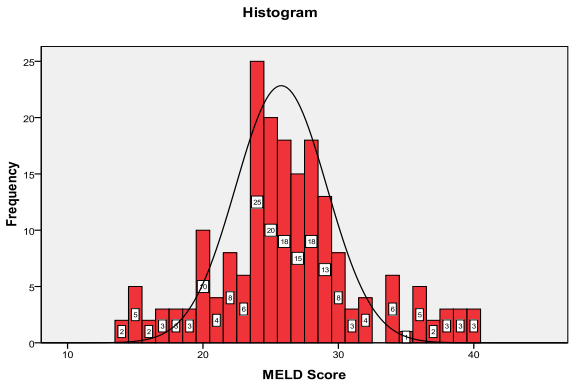

Figure No.2: Frequency distribution of meld score

The overall mean MELD score of study subjects was 26.19±5.45. As far as the outcome is concerned, mortality was observed in 16 (8.3%) cases. As shown in Table 1.

Table No.1: Discriptive statistics of age and meld score and frequency distribution of gender, mortality and cirrhosis (n=193)

	Mean ±SD	95% CI (LB – UB)	Median (IQR)	Range	Min	Max
Age (Years)	45.94 ±10.44	44.46 – 47.43	48.00 (17)	40	20	60
Meld score	26.19 ±5.45	25.41 – 26.96	26.00 (5)	26	14	40

	Frequency	Percentage
Gender		
Male	124	64.2%
Female	69	35.8%
Mortality		
Yes	16	8.3%
No	177	91.7%
Cirrhosis		
Companseted	64	33.1%
Decompanseted	129	66.9%

Table No.2: Frequency and association of mortality according to gender (n=193)

Gender	Mortality		Total	P-value
	Yes (n=16)	No (n=177)		
Female (n=69)	9 (4.7%)	60 (31.1%)	69 (35.6%)	***0.074
Male (n=124	7 (3.6%)	117 (60.6%)	124 (64.2%)	
Total	16 (8.3%)	177 (91.7%)	193 (100%)	

Table No.3: Frequency and association of mortality according to age (years) (n=193)

Age	Mortality		Total	P-value
	Yes (n=16)	No (n=177)		
≤ 45 years (n=107)	10 (5.18%)	107 (55.45 %)	127 (60.63%)	0.019
< 45 years (n=70)	6 (3.12%)	70 (36.25%)	76 (39.37%)	
Total	16 (8.3%)	177 (91.7%)	193 (100%)	

The stratification according to gender, age, cirrhosis and MELD score was done. Post stratification association mortality was observed with these modifiers using chi square test considered p ≤0.05 as significant.

The results showed that mortalities were observed in 7 (3.6%) male patients whereas in female patients 9(4.7%) mortalities were observed but the mortality was not significantly associated with gender (p=0.074). As shown in Table-II. 10(5.18%) mortalities were observed among patients with age ≤ 45 years and 6(3.12%) mortalities were observed among patients with age > 45 years. The association of mortality was significant with age (p=0.019). As shown in Table-III). As shown in Table-IV. Total 2(1%) mortalities were observed with MELD score 13-20, 4(2%) mortalities were observed with MELD score 21-30 and 10(5.3%) mortalities were observed with MELD score >30. The association of mortality was found highly significant with MELD Score (p=0.000).

Table No.4: Frequency and association of mortality according to cirrhosis (n=193)

Cirrhosis	Mortality		Total	P-value
	Yes (n=16)	No (n=177)		
Compensated (n=64)	7 (3.6%)	57 (29.5 %)	64 (33.1%)	***0.547
De-compensated (n=129)	9 (4.7%)	120 (62.2%)	129 (66.9%)	
Total	16 (8.3%)	177 (91.7%)	193 (100%)	

Table No.5: Frequency and association of mortality according to meld score (n=193)

Meld Score	Mortality		Total	P-value
	Yes (n=16)	No (n=177)		
13 – 20 (n=24)	2 (1%)	22 (11.6%)	24 (12.6%)	0.000
21 – 30 (n=132)	4 (2%)	129 (66.5%)	133 (68.5%)	
> 30 (n=36)	10 (5.3%)	26 (13.6%)	36 (19%)	
Total	16 (8.3%)	177 (91.7%)	193 (100%)	

DISCUSSION

The present study provides new insight to improve risk prediction in cirrhotic patients with acute variceal bleeding. Acute variceal hemorrhage (AVH) is a common presentation and devastating unpredictable consequence of high portal pressure in cirrhotic population and embarks significant fatality.[14] Specifically, we showed that MELD outperforms other models designed to predict prognosis in AVB, our study all concluded that patients with MELD score 30 or greater had 6 week mortality rate of 5.3%. Literature review also illustrated in hospital mortality or 6 week mortality significantly greater in patients with high MELD scores after AVB.[15] Kamath et al[16] claimed direct correlation relation between MELD score and the short term mortality rate in cirrhotic patients, and MELD score is regarded as an absolute index of residual reserve of functioning liver.

Prognostic evaluation of end stage liver disease patients is a global challenge for hepatologists. The Hepatologists from Mayo Clinic were the pioneers in proposing scoring system that is MELD score and they initially used to survey the outcomes in cirrhotic patients undergoing undertaking transjugular intrahepatic portosystemic shunt surgery (TIPSS). Later they generalized its validation to compensated, decompensated , and end stage liver disease to estimate and foresee mortality and morbidity.[18]

The MELD scoring system in another study demonstrated its preciseness, strength to prognosticate outcomes in cirrhotic patients , in other scenarios as well it proved its efficacy in foreseeing survival benefits Quarterly , half yearly then annually.[16] Furthermore MELD score and its list of benefits and its tremendous significance enlightened.[19] It was found in a largest study that, cirrhotic liver itself is potential risk factor for death , it has been established that liver disease approaching end stage liver disease along with its sequel such as hepatic encephalopathy, refractory ascites , variceal hemorrhage has subsequent rising number of deaths lately with an adjusted odds ratio of 5.65 (95% confidence interval, 3.72-8.41; $P<.001$) and 2.05 (95% confidence interval, 1.45- 2.84; $P<.001$), respectively.[3] In a study, estimated death percentage was around 20.5% in subjects with acute variceal hemorrhage , which is within known percentage in between of 20–30% during hospital stay, regardless they had hepatocellular carcinoma.[20]

In our study total 2(1%) mortalities were observed with MELD score 13-20, 4(2%) mortalities were observed with MELD score 21-30 and 10(5.3%) mortalities were observed with MELD score >30. It showed that higher the MELD score, high was the mortality rate. The association of mortality was highly significant with MELD Score (p=0.000), as compare to one previous study, highlighted that MELD scoring system accurate in estimation of risk of death optimized cut-off value of 12.9. These results were different from those of Amitrano et al.[21] who found the superiority in estimating short term survival. In their series, MELD score >15 was linked to poor survival outcomes.

The MELD-based model was not consistent and indeed over-predicted mortality for high MELD values in one of the validation sets. All of the patients in that cohort received antibiotics compared to 71% of the second validation cohort, while such information was not available for the derivation cohort.[22] The current study also didn't take into account blood transfusion requirements, which was found significant at cut-offs of 2 units.[23]

One of the series, patients with recurrent bleeding showed a convincing statistical values with difference ($p < 0.01$) among survivors and non-survivors. The occurrence of re-bleeding was significantly associated with mortality, a illustrated in of Bamba et al.[24] who reported a high significantly high MELD , ongoing active hemorrhage, increasing no of blood products transfused were indicative of early chances of mortality. These parameters also were consistent with other studies.[23]

In patients with cirrhosis and AVB, MELD scoring system simple to calculate when patient is hospitalized, it is precise validated in risk stratification and estimating survival, in hospital, short or long term. MELD could be more efficient than the other criteria for selecting high-risk patients who might benefit from more aggressive treatments. Our proposed MELD-based predictions might be useful in refining in evaluating the impact of new therapeutic strategies on patient prognosis, and in improving risk stratification in future clinical trials.

CONCLUSION

In our study we conclude that MELD score is a highly recommended tool may be used as a identification of high risk cirrhotic patients with acute variceal hemorrhage so they could be aggressively managed in high dependency units to prevent mortality.

Author's Contribution:

Concept & Design of Study:	Shahid Karim
Drafting:	Shahid Karim & Baseer Sultan Ahmad
Data Analysis:	Perzez Ashraf & Mansoor ul Haq
Revisiting Critically:	Baseer Sultan Ahmad
Final Approval of version:	Shahid Karim

Conflict of Interest: The study has no conflict of interest to declare by any author.

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