

## ORIGINAL ARTICLE

## EVALUATION OF MODEL FOR END-STAGE LIVER DISEASE SCORE CUT OFF VALUES IN PATIENTS WITH HEPATIC ENCEPHALOPATHY

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**Background:** Model for End Stage Liver Disease (MELD) is scoring system used for prioritization of patients waiting liver transplantation. Patients with decompensated chronic liver disease (DCLD) with higher MELD score and hepatic encephalopathy (HE) have poor outcome. We planned to note association between short term mortality and various cut-off values of at admission MELD score in HCV related DCLD patients presenting with HE. **Methods:** In this descriptive case series, 208 Hepatitis C (HCV) related chronic liver disease (CLD) patients with HE were included. At admission serum bilirubin, creatinine and INR were sought to calculate MELD score. Patients who improved were discharged and kept under regular follow up. Outcome was categorized into alive or expired in 3 months after admission. Based on MELD score cut off values of >15, >20, >25 and >30, association with outcome was determined using Chi-square test. **Results:** One hundred and six (51%) patients were female. Mean patient age was 55.3±10.6 years. Outcome wise, 128 (61.5%) were alive and 80 (38.5%) expired. Mean MELD score of expired was 22.17±9.14. 55 (51%) patients with MELD score >15, 44 (65.7%) patients with >20, 30 (73.2%) patients with >25, and 21 (72.5%) patients with >30 expired. MELD score >20 had strongest association with outcome, *p* value less than 0.01. **Conclusion:** At admission MELD score >20 are most significantly associated with poor outcome in DCLD patients with HE.

**Keywords:** HCV, Chronic liver disease, Hepatic encephalopathy, MELD score

J Ayub Med Coll Abbottabad 2015;27(4):886-9

## INTRODUCTION

Hepatitis C virus (HCV) infection is a common and major source of liver disease worldwide.<sup>1</sup> HCV is important cause of morbidity and mortality in Pakistani scenario.<sup>2</sup> Patients with HCV related chronic liver disease (CLD) may develop complications like hepatic encephalopathy (HE), ascites, gastrointestinal bleeding, spontaneous bacterial peritonitis, and hepatocellular carcinoma. CLD is termed decompensated chronic liver disease (DCLD) when any of these complications develop.

Model for End Stage Liver Disease (MELD) is a scoring system which is being used for prioritization of patients waiting liver transplantation. This score is based on mathematical calculations employing bilirubin, creatinine and international normalized ratio (INR) values. MELD score ranges from 6-40. Least score of 6 indicates mild disease while highest score of 40 indicates severe disease.<sup>3</sup>

Many studies are available which have focused on association of MELD with short-term mortality in CLD patients.<sup>4</sup> Hepatic encephalopathy is not included in MELD and its association with patient survival has not yet received considerable attention.<sup>5</sup> Outcome in DCLD patients with HE who have higher MELD score is poor.<sup>6-8</sup> MELD score evaluation in the context of HE in HCV related CLD patients has however not been focused on much. Similarly cut off values of MELD score suggestive of

poor outcome are not well defined. This study was planned to note association of various cut off values of MELD score with short term mortality in patients with HE complicating HCV related DCLD.

## MATERIAL AND METHODS

This descriptive case series was conducted at the Department of Medicine, Holy Family Hospital, Rawalpindi for a period of one year after approval from Departmental Ethical Committee, Holy Family Hospital, Rawalpindi.

HCV related CLD patients with HE were included consecutively. Sample size was based on results of Pakistani studies focusing mortality in HCV related liver disease suffering from HE.<sup>8-10</sup> Considering that 16% patients with HE will have poor outcome, sample size of 208 was calculated with 95% confidence interval and 5% absolute precision. We included 208 patients in the study. Informed written consent was taken in each case from attendant or patient, wherever appropriate, depending on clinical scenario.

Diagnosis of CLD was based on clinical features, ultrasonographic findings (coarse liver and dilated portal vein etc.) and or liver biopsy if available. All patients tested positive for anti-HCV antibody and or PCR for HCV. Non HCV related CLD patients were excluded. Diagnosis and grading of HE was based on West Haven criteria.<sup>11</sup>

At admission, serum bilirubin, creatinine and INR of each patient were sought. MELD score was calculated according to the formula, i.e.,  $9.57 \times \log_e \text{creatinine (mg/dl)} + 3.78 \times \log_e \text{bilirubin (mg/dl)} + 11.20 \times \log_e \text{INR} + 6.43$ . Values more than 40 were given a score of 40. Each patient was managed for HE and CLD. Patients who improved were discharged and kept under regular follow up through OPD visits and telephonic communications. Outcome was categorized into alive or expired at 3 months of admission.

Age, gender, grade of HE, bilirubin, INR, creatinine, MELD score, and outcome were noted on a *pro forma*. Based on the MELD score, patients were divided into 4 groups: 1) MELD score  $\leq 15$ / $>15$ , 2) MELD score  $\leq 20$ / $>20$ , 3) MELD score  $\leq 25$ / $>25$ , and 4) MELD score  $\leq 30$ / $>30$ . For continuous variables like age, bilirubin, INR, creatinine, and MELD score mean $\pm$ SD was calculated. For categorical variables like gender, grade of HE, and outcome frequency and% were calculated. Independent Samples *t*-test and Chi-square test were used as tests of significance in the case of continuous and categorical variables respectively. Data was analysed using SPSS version 15.0.

**RESULTS**

Of the 208 patients, 106 (51%) were females. Mean patient age was 55.32 $\pm$ 10.64 years; 37 (17.8%) patients were in Grade-I HE, 61 (29.8%) in Grade-II, 60 (28.4%) in Grade-III, and 50 (24%) in Grade-IV HE. Mean bilirubin level was 3.67 $\pm$ 5.23 mg%. Mean INR was 2.23 $\pm$ 3.62, mean creatinine was 1.74 $\pm$ 1.4 mg%, and mean MELD score was 18.17 $\pm$ 8.58. Outcome wise, 128 (61.5%) were alive at the end of 3 months while 80 (38.5%) had expired.

Comparison of age, gender, bilirubin, INR, creatinine, and MELD score with reference to outcome are detailed in table-1. Mean creatinine and MELD score had statistically significant association with outcome. Twelve (32.43%) patients in Grade-I HE (p value 0.41), 17 (27.86) patients in Grade-II HE (p value 0.04), 21 (35%) patients in Grade-III HE (p value 0.52), and 30 (60%) patients in Grade-IV HE (p value 0.0004) expired. Correlation of outcome with MELD Groups is given in table-2.

**Table-1: Outcome: stratified by age, gender, bilirubin, INR, creatinine and MELD Score**

	Outcome		p-value
	Alive	Expired	
Age	55.10 $\pm$ 10.55	55.67 $\pm$ 10.84	0.71
Male	60	42	0.42
Female	68	38	
Bilirubin mg%	3.52 $\pm$ 5.48	3.92 $\pm$ 4.83	0.6
INR	2.06 $\pm$ 3.84	2.5103 $\pm$ 3.25	0.3
Creatinine mg%	1.37 $\pm$ 0.92	2.35 $\pm$ 1.784	0.000
MELD score	15.67 $\pm$ 7.18	22.17 $\pm$ 9.14	0.01

**Table-2: Outcome by MELD Score groups**

MELD score group	Outcome		
	Alive	Expired	p-value
$>15$ $\leq 15$	53 (49%) 75 (75%)	55 (51%) 25 (25%)	0.000
$>20$ $\leq 20$	23 (34.3) 105 (74.4%)	44 (65.7%) 36 (25.6%)	0.000
$>25$ $\leq 25$	11 (26.8%) 117 (70.1%)	30 (73.2%) 50 (29.9%)	0.000
$>30$ $\leq 30$	8 (27.5%) 120 (67.1%)	21 (72.5%) 59 (32.9%)	0.000

**DISCUSSION**

Higher MELD scores are not only associated with mortality in patients waiting for liver transplant but also in CLD patients.<sup>4,10,13</sup> Outcome wise our patients who expired had significantly higher MELD. Two important findings which were noted: 1) MELD score  $\leq 20$  and  $>20$  had most significant association with outcome, and 2) among MELD constituents mean creatinine levels had significant association with outcome.

Various cut off values of MELD score have been investigated as predictor of mortality in CLD patients. Wiesner *et al*, used MELD score to assess short term mortality in pre-transplant patients with CLD.<sup>4</sup> In this study, mortality in patients with MELD score  $<9$  was 1.9 % compared to 71.3 % in patients with MELD score  $\geq 40$ . In another study, Okonkwo *et al* noted that MELD score  $>15.5$  was associated with poor outcome.<sup>12</sup> MELD as a predictor of mortality in HCV related CLD patients with HE has been studied as well. In one study mortality in similar patients with MELD score  $\geq 25$  was significantly higher.<sup>7</sup> More hospitalizations were noted in CLD patients with MELD score  $>20$  in another study.<sup>14</sup> This study did not focus on outcome in terms of alive or expired. We tested a number of cut off values of MELD, i.e.,  $>15$ ,  $>20$ ,  $>25$ , and  $>30$ . Although all of these values correlated significantly with outcome but  $>20$  was strongest predictor of outcome.

Derangement of creatinine in patients with CLD can be due to various reasons. It may be elevated because of sepsis, hepato renal syndrome, and medications like diuretics. It also varies according to age, gender, and muscle mass. As far as constituents of MELD score are concerned, poor outcome in our study was significantly associated with higher creatinine levels. Association between creatinine and mortality in CLD patients has been inconsistent. Creatinine has been noted as an independent predictor of mortality in patients with cirrhosis.<sup>15</sup> In some studies however it did not have relation with survival.<sup>16, 17</sup>

Mortality in CLD patients with HE is variable. HE is attributed as cause of death in 30% patients of CLD.<sup>12</sup> Many factors play important role in this regard that include, aetiology of liver disease,

extent of liver dysfunction, precipitating factors, and pre-existing illnesses etc. In a Pakistani study focusing precipitating factors for HE conducted at Liaquat University Hospital Hyderabad/Jamshoro, 25.4% mortality was noted.<sup>18</sup> Mortality in our patients was comparatively high, i.e., 38.5%. Main reason for higher mortality in our study is the fact that it was assessed at end of three months rather than at discharge from or expiry in hospital.

Various grades of HE are noted in up to 60% of CLD patients.<sup>19</sup> Relationship exists between advance HE grade and outcome in patients with CLD. Short and long term mortality in these patients increases with higher grade of HE. In a study conducted by Stewart et al, which focused HE as a predictor of outcome in patients with end stage liver disease, patients with grade III HE had poor survival when compared with patients with HE grade 0.<sup>20</sup> Similar findings have been noted in literature reviews pertaining to the same subject.<sup>21</sup> Our patients with advance HE stage also had poor outcome.

In addition to HE and MELD which are alone or in combination important prognostic indicators, various factors have relation with outcome in patients with DCLD. These include; age, ascites, albumin, bilirubin, PT, and Child-Pugh score.<sup>21-24</sup> MELD score is objective based and does not include clinical criteria like ascites and encephalopathy. Change in absolute value also has more importance compared to single value.<sup>25</sup> Clinical scenario and precipitating factors also alter outcome in patients with HE complicating DCLD. We did not focus on the cause of death in our patients. Modified versions of MELD, i.e., MELD NA and delta were not employed by us. These all are short comings and or limitations of studies like ours which should be kept in mind while drawing inference. It should however be noted that with simple statistical analysis relationship between mortality and various cut of values of MELD was noted by us.

In patients with DCLD, HE is common cause of hospital admissions in Pakistan.<sup>26</sup> In our scenario liver transplantation facilities are available to very few patients. Protocols for prioritization of such patients are important as these can help in efficient management of patients with advance/severe disease. Based on results of our study, DCLD patients with HE who have higher at admission MELD score (>20) should be more energetically managed in order to improve outcome.

## CONCLUSION

Mortality in hepatitis C related DCLD patients presenting with HE is significantly higher in patients with at admission MELD score >20. Higher

creatinine levels and grade of HE also have association with poor outcome in these patients.

**Financial Disclosure:** Authors have no financial interests related to the material in the manuscript.

## AUTHOR'S CONTRIBUTION

All the authors contributed equally.

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