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ORIGINAL ARTICLE

Frequency of Patients Eligible for Liver Transplant According to MELD-Na Score in Chronic Liver Disease due to Chronic Hepatitis B and C

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Abstract

Objective: This study aimed to evaluate the frequency of liver transplant in hepatitis B and C patients according to the MELD-Na score.
Methodology: A cross-sectional study on 260 patients of CLD secondary with hepatitis B and C were performed on Liver Transplant Unit of Dow University Hospital Karachi. Patients of CLD with positive hepatitis B or C, age of ≥ 18 years, and illness of ≥ six months were selected by consecutive sampling during the period of Six months from 21st November 2020 to 21st May 2021. MELD-Na score was calculated by using the international normalized ratio (INR), serum creatinine and bilirubin. MELD-Na score of ≥ 14 was used for liver transplant eligible patients.
Results: Out of 260 CLD patients, there were 143 males (55.0%) and 117 females (45.0%), with a mean age of 49 ± 12 years (18-60 years). Majority of CLD patients were reported with chronic hepatitis C 203 (78.1%) and the remaining 57 (21.9%) CLD patients with chronic hepatitis B. Mean of MELD-Na score in CLD patients was 15.6 ± 6.1 (7-37). MELD-Na score was ≥ 14 in 194 (74.6%) CLD patients that makes them eligible for liver transplant, out of which 48 (84.0%) were hepatitis B while 146(71.9%) were hepatitis C.
Conclusion: Study concludes that the rate of MELD-Na score was significantly high in patients of CLD with chronic hepatitis B and C that makes them eligible for liver transplant.
Keywords: Chronic liver disease, Therapeutic, Hepatic transplantation, Mortality.

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Introduction

Chronic liver disease (CLD), a disease of progressive worsening of liver function that persists at least for six months. It is a persistent process of inflammation, demolition and reconstruction of liver parenchymal cells resulting in fibrosis and cirrhosis.[1,2] Cirrhosis is the last and worse phase of CLD that results in liver architecture disruption, nodule and fibrosis formation, vascular reorganization, neo angiogenesis and extracellular matrix deposition. Most commonly identified etiologies of CLD are; alcoholic liver disease (ALD), non-alcoholic fatty liver disease (NAFLD), chronic viral hepatitis (B, C and D), genetic causes (Alpha-1 antitrypsin deficiency (ALD), hereditary hemochromatosis and Wilson disease).[1-3]

Chronic liver disease is a very common and serious health disorder, increasing morbidity and mortality throughout the world. It is also one of the major causes of hospital admission and increased mortality in Pakistan.[4,5] A recent study report that approximately 1.5 billion peoples throughout the world are suffering from CLD, among which 60.0% are reported due to NAFLD,

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29.0% due to hepatitis B virus (HBV), 9.0% due to hepatitis C virus (HCV) and 2.0% due to ALD. Cirrhosis is the most commonly reported complication that accounts for 1.2 million deaths followed by liver cancer with 790,000 deaths. Approximately 3.5% of deaths in the world are reported due to CLD.[6]

Approximately 90.0% of CLD patients were reported with HBV or HCV or coinfection.[2] According to World Health Organization (WHO), approximately 296 million and 58 million people are suffering from chronic hepatitis B and C respectively. [7,8] HBV and HCV are responsible for 820,000 and 290,000 deaths respectively throughout the world. Prevalence of HBV is high in western pacific region (116 million) followed by African region (81 million), eastern Mediterranean region (60 million), south-east Asia region (18 million), European region (14 million) and American region (5 million), whereas prevalence of HCV is high in eastern Mediterranean region and European region (12 million in each) followed by South-East Asia and Western Pacific Region (10 million in each), African Region (9 million) and) and American region (5 million). [7,8]

Pakistan is among the countries that have the highest burden of morbidity and mortality due to CLD secondary to chronic hepatitis B and C. These patients create a large proportion of admissions in the hospitals. Approximately 5% of total hepatitis C cases are reported in Pakistan.[9] On national levels, the data suggests a prevalence of 2.5% for hepatitis B and 4.9% for hepatitis C in different areas of Pakistan.[9,10]

Liver transplant is the only method to increase the survival rate in patients with end-stage CLD as well as enhance the quality of life. [11] MELD (Model for End-stage Liver Disease) score was first developed in the year 2000 and then modified for better outcomes in identification of potential CLD patients for a liver transplant. A modified form of MELD score formula was developed by United Network of Organ Sharing (UNOS) in the year 2002, using international normalized ratio (INR), serum creatinine and bilirubin values.[12] In 2016 January serum Sodium incorporated in MELD equation for liver graft allocation.[13]

Health care system of low-income countries like Pakistan is very poor that fails to provide the standard of health care and increases the risk of failure of therapy, worsening of chronic diseases and decreases the quality of life. By increasing the use of MELD score in CLD patients, we can predict the severity of CLD and enlist the patients for liver transplant according to severity and prognosis of disease. Therefore, current study was designed and focused on evaluation of frequency of liver transplant in hepatitis B and C patients according to MELD-Na score.

Material and Methods

A cross-sectional study was performed on Liver Transplant Unit of Dow University Hospital Karachi. Two hundred and sixty patients were enrolled from Liver Transplant Unit by consecutive sampling. Study duration was six months from 21st November 2020 to 21st May 2021.

Any patient suffering from chronic liver disease (CLD) with a duration of ≥ six months having age of ≥ 18 years and having positive hepatitis B or C were selected for study. Patients of acute hepatitis, fulminant hepatic failure, drug-induced liver failure, alcoholic liver disease, autoimmune hepatitis, Wilson's disease, alpha-1 antitrypsin deficiency, hemochromatosis or hepatocellular carcinoma were excluded from the study.

A patient of liver disease with a duration of ≥ six months with presence of ≥ three decompensated features of liver disease was labeled chronic liver disease.[13] Decompensated features of liver disease were; jaundice (yellowness of sclera with serum bilirubin > 1 mg/dL), abnormal prothrombin time (PT) (> two seconds over control or INR > 1.3), abnormal albumin (< 3 gm/dL), low platelets (<100000/cmm), ascites (presence of dullness or fluid on clinical examination and ultrasound), splenomegaly (spleen > 12 cm on ultrasound), liver encephalopathy (Glasgow Coma Scale (GCS) < 15 along with ammonia level > 60 mg/dL), varices (dilated veins that makes > 30% esophagus lumen on endoscopy of the upper gastrointestinal tract (GIT)) and fibrosis and nodules presence on liver biopsy. A patient of chronic liver disease with a positive test of hepatitis B (HbsAg) or hepatitis C (anti-HCV) was labeled as chronic hepatitis B and C respectively. MELD-Na score of ≥ 14 was used for liver transplant eligible patients and calculated by using the following formula[13];

$$\text{MELD-Na score} = \text{MELD} + 1.32 \times (137 - \text{Na}) - [0.033 \times \text{MELD}^{*}(137 - \text{Na})]$$

Equation 1: MELD-Na Score Formula

Before commencement of research, permission of the study was obtained from ethical committee of Dow

university Hospital Karachi. Informed consent was also obtained from patients after explaining the study protocol, benefits and potential risks of study. Selected patients were evaluated for clinical signs and symptoms and then sent to a clinical laboratory for hepatitis B and C tests. After confirmation of hepatitis, each selected patient was further evaluated for platelets count, creatinine level, serum sodium, PT/INR, abdominal ultrasound and upper GIT endoscopy. MELD-Na score was calculated by using the above-mentioned formula and data was collected on predesigned and pre-approved proforma. Data interpretation was performed with a statistical package for social sciences (SPSS) version 25.

Results

Two hundred and Sixty patients of CLD were enrolled from Liver Transplant Unit and evaluated for hepatitis B and C followed by MELD score for confirmation of their eligibility for a liver transplant. Out of 260 CLD patients, there were 143 males (55.0%) and 117 females (45.0%). Mean age of CLD patients was 49 ± 12 years (18-60 years). Most of the patients 139 (53.5%) affected with CLD were in age group of 46-60 years, followed by 99 (38.1%) CLD patients in age group of 31-45 years and 22 (8.5%) CLD patients in age group of 18-30 years. Mean duration of CLD disease was 26 ± 7 months (6-144 months). Most of the patients 210 (80.8%) were suffering from CLD from > 12 months followed by 50 (19.2%) patients suffering from CLD from 6-12 months. Most of the CLD patients 203 (78.1%) were diagnosed with hepatitis C and 57 (21.9%) CLD patients were diagnosed with hepatitis B (Table-I).

Table I: Demographic and Characteristics of CLD Patients.

Variables	Frequency	Percentage
Gender		
Male	143	55.0
Female	117	45.0
Age (Years)		
Mean ± SD (Range)	49 ± 12 (18-60)	
18-30	22	8.5
31-45	99	38.1
46-60	139	53.5
Duration of CLD (Months)		
Mean ± SD (Range)	26 ± 7 (6-144)	
6-12	50	19.2
> 12	210	80.8
Hepatitis		
Hepatitis B	57	21.9
Hepatitis C	203	78.1

Mean of MELD-Na score was 15.6 ±6.1 (7-37). MELD-Na score was evaluated in CLD patients for obtaining the list of eligible patients for liver transplant. MELD-Na score was ≥ 14 (liver transplant eligibility) in 194 (74.6%) CLD patients and < 14 (non-eligibility for liver transplant) MELD-Na score in 66 (25.4%) CLD patients (Table-II).

Table II: Classification of MELD Sodium Score in CLD Patients

MELD Score Level	Frequency	Percentage
Mean ± SD (Range)	15.6 ±6.1 (7-37)	
< 14	66	25.4
≥ 14	194	74.6
Level 1 (MELD Na score ≤ 10)	48	18.5
Level 2 (MELD Na score 11-18)	147	56.5
Level 3 (MELD Na score 19-24)	38	14.6
Level 4 (MELD Na score ≥ 25)	27	10.4
Total	260	100.0

Further stratification of MELD-Na score into four subgroups was done in order to categorize the patients according to the severity of disease; 48 (18.5%) of CLD patients presented with a MELD-Na score level 1 (MELD-Na score ≤ 10), 147 (56.5%) CLD patients presented with a MELD-Na score level 2 (MELD-Na score 11-18), 38 (14.6%) CLD patients presented with a MELD-Na score level 3 (MELD-Na score 19-24) and 27 (10.4%) CLD patients presented with a MELD-Na score level 4 (MELD-Na score ≥ 25) (Table-II).

Table III: Cross-Tabulation of MELD Score in CLD Patients

Variables	MELD Score		P-value
	< 14 (n=66)	≥ 14 (n=194)	
Gender			
Male	36 (54.5%)	107 (55.2%)	0.9
Female	30 (45.5%)	87 (44.8%)	
Age (Years)			
18-30	8 (12.1%)	14 (7.2%)	
31-45	17 (25.8%)	82 (42.3%)	0.04
46-60	41 (62.1%)	98 (50.5%)	
Duration of CLD (Months)			
6-12	14 (21.2%)	36 (18.6%)	0.6
> 12	52 (78.8%)	158 (81.4%)	
Hepatitis			
Hepatitis B	9 (13.6%)	48 (24.7%)	0.06
Hepatitis C	57 (86.4%)	146 (75.3%)	

MELD-Na score was high (≥ 14) in 107 (55.2%) male and 87 (44.8%) female CLD patients whereas low (< 14) in 36 (54.5%) male and 30 (45.5%) female CLD patients (p-value = 0.9). MELD-Na score was high (≥ 14) in 98 (50.5%), 82 (42.3%) and 14 (7.2%) CLD patients and low (< 14) in 41 (62.1%), 17 (25.8%) and 8 (12.1%) CLD patients in 46-60, 31-45 and 18-30 years respectively (p-value = 0.04). MELD-Na score was high (≥ 14) in 158 (81.4%) and 36 (18.6%) CLD patients and low (< 14) in 52 (78.8%) and 14 (21.2%) CLD patients in > 12- and 6-12-months duration of CLD respectively (p-value = 0.6). MELD-Na score was high (≥ 14) in 146 (75.3%) and 48

(24.7%) CLD patients and low (< 14) in 57 (86.4%) and 9 (13.6%) CLD patients in hepatitis C and B respectively (p-value = 0.06) (Table-III).

Discussion

In low-income countries like Pakistan, who have a very low standard of health care system and very poor health care facilities, availability of liver transplant facility is not an easy task. Pakistan does not have any well-organized liver transplant center till date, although Pakistan's government established the few liver transplants centers that are doing few transplants after every few months, but no hospital is constantly undergoing for liver transplants. Still, hopes for betterment have been high because several government projects are in consideration for the establishment of a liver transplant center of excellence.

There is definitely a need to have data regarding patients requiring liver transplant on priority, for which MELD-Na scoring has been validated to determine "sickest" liver first to transplant. The study identifies the magnitude of transplant eligible CLD patients presenting to hospitals so that a protocol can be devised for the patients needing a transplant and identify the patients who require urgent liver transplant on priority and thus strengthening the case of establishment of transplant centers.

In current study, 260 patients of CLD secondary to chronic hepatitis B and C have been evaluated and results clearly demonstrated that most of these patients presented with a high MELD-Na score of ≥ 14 at the time of presentation making them eligible for a liver transplant. These observations are comparable to the different previous studies in which the MELD-Na scores of patients were included in patient's characteristics.[14-17]

In current study, patients were presented with a mean MELD-Na score of 15.6 ±6.1 which is logical when compared with previous studies related to MELD scoring. Such as studies by Oton NE et al.[18], Srikureja W et al.[19], and Gotthardt D et al.[20] who evaluated the MELD score at the time of admission in the hospital reported the mean MELD score of 15.2 ± 4.9, 14.0±9.2 and 14.2 ± 6.4 respectively. These findings are consistent with current study results and strengthen the observation that most of the patients of chronic liver disease have high MELD scores at the time of admission at hospital.

In current study, 55.38% of evaluated CLD patients were with a MELD-Na score level 2 (scores between 11 to 18), which was similar to the results of previous studies found during the literature search. A study by Sun FR et al. reported the MELD score of 10-19 in 49.0% of CLD patients[21], whereas another study by Kraja B et al. reported the MELD score of >15 in 70.0% of CLD patients.[22]

In current study, further stratification of MELD-Na score into four subgroups was done in order to categorize the patients according to severity of disease; MELD-Na score level 1 having 48 (18.5%) CLD patients, MELD-Na score level 2 having 144 (55.4%) CLD patients, MELD-Na score level 3 having 43 (16.5%) CLD patients and MELD-Na score level 4 having 25 (9.6%) CLD patients. A similar study which included such stratification was done by Perkins JD, et al. who studied the 38,800 CLD patients for MELD score and stratified them into 6 groups: 41.2% patients had MELD score of < 14 (17% with scores of 6–10 and 24.2% with scores of 11–14) and the remaining 58.8% had MELD score of >14 (29.3% with scores of 15–22, 9.8% with scores of 23–30 and 7.2% with scores of 31–40).[23] MELD score classification is very important in predicting the severity of CLD and selecting the CLD patients for a liver transplant based on their urgency.

Limitations of the study: The current study was limited to patients of CLD secondary to hepatitis B and C leaving other causes of CLD such as ALD, NAFLD, Wilson disease, etc. Another limitation of the current study was evaluation of MELD score in CLD patients for eligibility of liver transplant at the time of presentation which can predict prognosis at that particular time and not over a prolonged period.

Conclusion

It was concluded that in our local health setup, majority of CLD patients secondary to chronic hepatitis B and C present with MELD-Na score of more than 14 which is considered for a liver transplant. All of these patients are candidates needing consideration for a liver transplant as the definitive treatment for them based on their presenting MELD-Na score.

Our study findings will strengthen the calls for establishing the hospitals for liver transplants and would help in formulating a protocol for listing of these patients. It is high time that liver transplantation centers should be established in all corners of the country to improve overall morbidity and mortality due to cirrhosis.

We would definitely suggest that further studies on a national level should be carried out about MELD-Na scores with not just the frequency but also its correlation with mortality in a large study population which may include all the types of chronic liver disease.

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