Original Article

Comparison of King's College Hospital Criteria (KCH) with Model for End-Stage Liver Disease (MELD) for Predicting Outcome in Patients with Acute Liver Failure

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ABSTRACT

Objective: To compare the Model for End-Stage Liver Disease (MELD) and The King's College Hospital Criteria (KCH) as early clinical prognostic indicators in patients with Acute Liver Failure.

Methodology: This descriptive Case series study was conducted in emergency medical wards of Liaquat University Hospital Jamshoro and Hyderabad from February 2008 to July 2010. This study included 76 consecutive patients with ALF defined as onset of hepatic encephalopathy occurring within 12 weeks of onset of jaundice. The patients using sedatives, anticoagulants or if any evidence of chronic liver disease were excluded. Laboratory workup was done from laboratory of University. MELD score of ≥33 and presence of positive criteria for KCH category were taken as a bad prognostic indicator. The primary end point was death during hospital stay. Continuous variables were computed as mean ± standard deviation (SD) and categorical variables as frequency and percentage.

Results: Out of 76 patients 49 were male (64.47%) and 27 (35.53%) female. The mean age of patients was 24.62 ± 10.3. Out of 76 patients a total of 59 patients (77.63%) died during the study period. The KCH criteria cut off point was reached in a total of 63 patients (out of 76) of which 50 patients died. The MELD criteria cut off point (MELD Score >33) was reached in 49 patients (out of 76) of which 46 eventually died.KCH predicted outcome with the sensitivity of 80% and Positive predictive value (PPV) of 89% (p=0.001). MELD predicted outcome with sensitivity of 82.4% and Positive predictive value (PPV) of 94%(p=0.001).Viral hepatitis B was the most common cause of Acute Liver Failure.

Conclusion: Both criteria are good predictors of the outcome in acute liver failure.

KEY WORDS: Acute liver failure, KCH criteria, MELD Score, Fulminant Hepatic Failure.

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INTRODUCTION

Acute liver failure (ALF) is a complex multisystemic illness with an ongoing high mortality rate. Most of the clinical features in patients with ALF are due to cerebral edema, coagulation disorder, severe metabolic disturbances, susceptibility to wide variety of infections and multi-organ failure (MOF) occurring as a result of severe liver injury in patients with previously normal liver.[1] ALF is classified into hyperacute (0–7 days), acute (8–28 days), and sub-

acute (more than 28 days) depending on the basis of development of encepahlopathy.[2]

In the developing world such as Pakistan viral causes predominate with infection by hepatitis B and E viruses accounting for most cases of ALF.[3] Drug-induced hepatitis is much less common in developing nations, though anti-tuberculosis therapy warrants special mention as the most common cause of drug-induced ALF in South Asia.[4]

It is difficult to predict the prognosis of ALF because of incomplete understanding of its mechanism. Massive necrosis of liver resulting from the disturbance of hepatic circulation in the evolution of the disease has been found the most important pathological finding in ALF.[5]

Prediction of outcome is very important because over the years the survival of the patients have improved gradually due to better understanding of intensive care of patients with acute liver failure rather than to the development of specific mode of therapy.[6]

Over the last two decades, a number of prognostic models have been proposed to aid in decision-making for patients with ALF to be treated either medically or by liver transplantation. The well accepted multi-variable prognostic models including the King's College Hospital (KCH) criteria and the model for end-stage liver disease (MELD) score have been improved by incorporation with other clinical and biochemical indices.[7]

Since many years "King's College Hospital (KCH) criteria" is used globally as a prognostic tool because of its simplicity as it includes easily available clinical and biochemical data such as age, duration of jaundice, bilirubin, prothrombin time, arterial PH and the etiology i.e. acetaminophen vs. non-acetaminophen. The positive predictive value of these criteria for mortality was 84% in the acetaminophen cohort and 98% in the non-acetaminophen cohort the negative predictive values were 86% and 82%, respectively.[8]

The Model for End-Stage Liver Disease (MELD) is a survival model based on a composite of three laboratory variables: serum creatinine, serum bilirubin, and international normalized ratio for prothrombin time. MELD was designed initially to assess the prognosis in patients with cirrhosis of liver for transjuglar intrahepatic Porto- systemic shunt (TIPS).[9] Now a day`s MELD is being used for assessment of prognosis in patients with ALF with good predictive values as well.[10]

The objective of the study was to compare MELD and KCH criteria as early clinical prognostic indicators in patients with Acute Liver Failure seen at our center.

METHODOLOGY

This descriptive case series study included 76 consecutive patients suffering from ALF received in Medical wards from Emergency department of Liaquat University Hospital Jamshoro and Hyderabad between February 2008 to July 2010. Patients taking sedatives, Patients taking anticoagulants and patients with Cirrhosis of liver diagnosed on the basis of clinical [reduced liver span of <8cm in midclavicular line, palpable spleen below the costal margin along with the presence of as cites], biochemical [reduced level of serum albumin <3.5 g/dl], radiological [reduced liver size of <8cm in midclavicular line, portal vein diameter of >1.3 cm and a splenic longitudinal size of >14 cm] were excluded from the study.

Informed consent was sought from patients or next of kin (as the patients were suffering from encephalopathy at the time of admission). Patients' information regarding demographic information such as age and sex, clinical presentation and laboratory workup were documented in a proforma.

Patients were diagnosed as cases of Acute Liver Failure on the basis of criteria set by O'Grady which states onset of hepatic encephalopathy occurring within 12 weeks of onset of jaundice.[11]

Encephalopathy was graded according to West Haven Grading System into: Grade 1 Altered sleep pattern (morning sleep and night time awakening); Grade 2 Disorientation to time (inability to distinguish between day and night on direct questioning) and presence of asterixis (flapping tremor of outstretched hands), Grade 3 Disorientation to place (inability to describe location where the patient is present) and presence of asterixis and Grade 4 Coma (no response to painful stimuli).[12]

During hospitalization all patients were followed for any progression in grade of encephalopathy and also the time from the appearance of jaundice to development of encephalopathy was noted.[13] King's College Hospital (KCH) Criteria for patients with nonacetaminophen ALF are either Prothrombin Time (PT) > 100 sec (or International Normalization Ratio [INR] >6.5) (irrespective of grade of encephalopathy) indeterminate or drug-induced etiologies or presence of at least 3 of 5 variables including Age < 10 or > 40 years, indeterminate or drug-induced etiologies, Duration of jaundice to encephalopathy > 7 days, PT 50 sec (INR > 3.5), Serum bilirubin > 17.5 g/dl.[14]

Table-I: Baseline characteristics of patients (n=76).

Continuous Variables	*Mean*	*Std.Devation*
Age (years)	24.62	10.329
Bilirubin (mg/dl)	21.862	8.13
Creatinine(mg/dl)	2.254	1.30
Prothrombin Time (Seconds)	86.9	64.09
INR	7.2	5,36
Categorical Variable	*Frequency*	*Percentage(%)*
Sex		
Male	49	64.47
Female	27	35. 53
KCH criteria		
Cut off point reached	63	82.89
Dead	50	65.7
MELD criteria		
Cut off point (MELD Score >33) was reached	49	64.47
Dead	46	60.5
Outcome of Patients		
Dead	59	77.63
Alive	17	22.37

MELD score was calculated according to the formula proposed by Kamath et al[9] i.e. [9.57x Logcreatinine(mg/dL)+3.78xLogbilirubin(mg/dL)+11.20xLogINR+6.43]. MELD score of ≥33 was taken as a bad prognostic indicator.[7] The presence of positive criteria for KCH category were taken as a bad prognostic indicator. The primary end point was death within seven days of hospital admission.[7] Laboratory workup included serum creatinine; Liver function tests, prothrombin time (and international normalized ratio INR) were done in Research laboratory of Liaquat University. Viral markers that were looked for included anti-HAV IgM, HBsAg, anti-HBcIgM, anti-HCV and anti-HEV IgM were done in molecular laboratory of Liaquat University Hospital Jamshoro by ELISA. History regarding drugs taken by the patients during the preceding 90 days was also taken from their relatives. Pregnancy was diagnosed by at the onset of amenorrhea, and bedside ultrasound. The Acute fatty liver of pregnancy, HELLP syndrome was considered in patients with Preeclampsia findings (hypertension, edema and proteinuria).

Statistical Analysis: Descriptive statistics of continuous data i.e., Age, Prothrombin Time, INR, Bilirubin, Creatinine and MELD Score were expressed as mean ± standard deviation (SD). Frequencies were calculated from the categorical data, i.e., gender, normal or deranged INR, Types of Viral Hepatitis, King's College Criteria and Model for End stage Liver Disease and the number of patients who died during hospitalization.

The sensitivity, specificity, positive-predictive value (PPV), negative-predictive value (NPV) and area under receiver operating characteristic (ROC)-curves for spontaneous survivors and deaths was assessed for the validity of the KCH criteria and MELD score>33. AP-value < 0.05was considered as statistically significant. Statistical package for social sciences (SPSS™) version 16 was used for data processing purpose.

RESULTS

A total of 76 patients were included in this study. The study subjects consisted of 49 males (64.47%) and 27 (35.53%) females. The mean age of patients was 24.62±10.3. Table-I shows the base line characteristics of patients

Among 76 patients 37(49%) were suffering from Hepatitis B and further 14 (18.5%) had superimposed Hepatitis D. Hepatitis E was present in 9 (12%) patients, 11(14.5%) had HELP syndrome and 5(6%) had history of anti-tubercular therapy (which included rifampicin and isoniazid in optimal doses). Out of 76 patients a total of 59

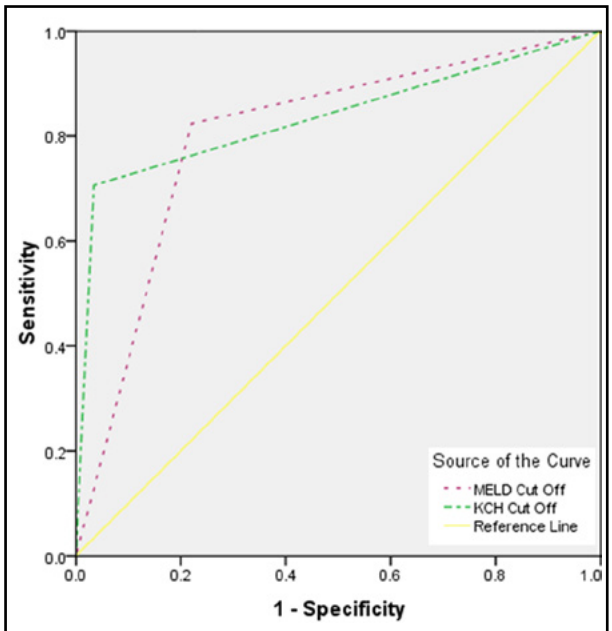

Figure-1: Comparision of MELD with KCH for the outcome patients with ALF.

patients (77.63%) died during the study period of which 32 (54.2%) were hepatitis B, 12(20.3%) hepatitis D,5(8.4%) hepatitis E, HELP syndromein 8(13.5%) patients whereas 2(3.3%) had history of antitubercular therapy. Table-II shows the causes of ALF.

The KCH criteria cut off point was reached in a total of 63 patients (out of 76) of which 50 patients died. The MELD criteria cut off point (MELD Score >33) was reached in 49 patients (out of 76) of which 46 eventually died. KCH predicted outcome with the sensitivity of 80%, specificity of 66% with Positive predictive value (PPV) of 89% and negative predictive value (NPV) of 36%(p=0.001). MELD predicted outcome with sensitivity of 82.4%, specificity of 78% with Positive predictive value (PPV) of 94% and negative predictive value (NPV) of 53(p=0.001) as shown in Table-III.

Receiver operating characteristics (ROC)-curves comparing between KCH criteria and MELD score>33 to assess death of the patient is shown in Figure-I.

Table-II: Causes of Acute Liver failure (n=76).

Cause	*Survivors (n=19)*	*Non-survivors (n=57)*	*Total*
HEV	5	4	9 (12%)
HBV	6	31	37 (49%)
HDV	2	12	14 (18.5%)
HELP syndrome	3	8	11 (14.5%)
Antitubercular drugs	3	2	5 (06%)

DISCUSSION

Fulminant hepatic failure (FHF) or acute liver failure (ALF) is a relatively rare condition, but it's quite special due a high mortality rate in spite of the advances in the field of medicine, intensive care, hepatic assist devices (HADs) and liver transplantation moreover there is no definitive therapy other than orthotropic liver transplantation (OLT).

Assessment of prognosis of this grave condition is always very crucial due to the fact that a sizeable number of the patients would need intensive care, although no facility of liver transplantation is available in this country. Because of these decision making processes it was imperative that adequate scoring systems be developed that can predict the potential of life or death, therefore simplifying the complex scenario of liver transplantation. The main prognosis predicting tools are King's College Hospital (KCH) criteria and the Model for End Stage Liver Disease (MELD) score.

As mentioned above the mortality rate of ALF is high. Classically the mortality rate before the intensive care management was around 80-90%. With the advent of liver transplantation it has been cut down to around 40%.[14]Situation in Pakistan is different because of lack of facilities liver transplant. In our study, a total of 59 (out of 76) patients (77.63%) did not survive. Sarwar S et al studied ALF in 2006 and reported mortality in 55.6% of patients. That study was done at Lahore.[15] Haroon H et al also studied the natural history of ALF at Karachi and reported that 65% of patients died during the study period.[16] The survival was poor in our study probably because of better intensive care facilities were available at Lahore and Karachi respectively.

The mean age in our my study was 24.62 years (± SD 10.3), whereas the mean age as reported by Shakil et al was 39 years.[17] Probably this huge difference in age was due to different etiologies of ALF as our study mainly consisted of patients suffering for acute viral hepatitis, whereas in that study the main cause was acetaminophen poisoning.

The very first prognostic scoring system was developed at King's College London between 1973 to 1985. Appropriately it was named after the institute. The traditional King's College Hospital criteria have been the most commonly utilized and most frequently tested of the numerous proposed prognostic criteria for ALF.[8]We sought to determine whether these criteria were applicable to the patients in our population. In our study the KCH criteria identified 63 out of 76 patients to have a poor prognosis (death). In our study KCH criteria predicted poor outcome with high sensitivity (70.6%) and PPV (89%) but lower specificity (66%) and NPV (36%). O'Grady JG and colleagues in

Table-III: Sensitivity, Specificity, PPV, NPV of KCH and MELD for the outcome of patients.

Variables	*Area*	*Sensitivity(%)*	*Specificity(%)*	*PPV(%)*	*NPV(%)*	*P value*
MELD	0.80	82.4	78	94	53	0.001
KCH	0.83	70.6	66	89	36	0.001

Abbreviations:
PPV =Positive predictive value. NPV =Negative predictive value.

their original report showed sensitivity of 91% and specificity of 90% for KCH criteria.[8] Dhiman et al from India also evaluated the prognostic potential of KCH criteria and reported 43 (out of 49) patients died during the study period (87.75%).[7] With sensitivity of 46.7%, specificity of 88.5%, PPV87.8% and NPV 48.4%. Yantorno et al from Argentina in their study comprising 64 patients with ALF observed KCH criteria predicting death in patients with ALF with sensitivity 78%, PPV 80%, NPV77%.[18] Pauwels et al reported sensitivity 80%, PPV 96% and NPV 50%.[19]

The MELD score constituting total serum bilirubin, Creatinine and international normalized ratio was initially designed as short term predictor of survival in patients admitted for transjuglar intrahepatic Porto- systemic shunt (TIPS).[20] Now a day's MELD score has been found an important predictor of survival in patients with ALF. In this study MELD score predicted poor outcome with the sensitivity of 82.4%, specificity of 78%, PPV 94% and NPV 53%.Yantornoet al in their study observed that MELD has high PPV 80.5% and low NPV 58.7% indicating that this models have the greatest applicability in predicting death rather than spontaneous survival. In this both KCH and MELD criteria were almost equal in prediction the death in patients with ALF.[18] Many studies have quoted MELD to be slightly better than KCH, but others have shown MELD to be stronger in some areas, whereas weak in other (when compared to KCH).[21,22]

Majority of our patients were suffering from acute viral Hepatitis. Among 76 patients, 37(49%) were suffering from Hepatitis B and further 14 (18.5%) had superimposed Hepatitis D and Hepatitis E was present in 9 (12%) patients. In study by Dhiman R K in 73 patients with acute liver failure, acute hepatitis B virus was present in 38 (52.1%) patients and hepatitis E virus in 12 (16.4%) patients.[7] Yantorno et al found pregnancy related acute liver failure in 8% of cases.[18] Acharya SK also found Hepatitis B in 27.3% cases and antitubercular drugs in 4.5% cases of ALF.[23] No case of hepatitis C was detected in our study which confirms reports by other researchers that hepatitis c rarely causes ALF.[24]

Limitation of the study: There are few limitations to this study. First the results of this study cannot be generalized because this is a case series study. Second a high NPV could not be achieved which make this study to predict death in patients studied rather than spontaneous survival. When this study was planned, there was no Ethics Committee in our institution, hence no Ethics Committee approval was obtained.

CONCLUSION

In summary, both MELD and KCH criteria can predict the outcome of ALF patients with precision. Both criteria have low Specificity and NPV. Further prospective studies are needed which should not only predict death without liver transplant (LT) but also to predict survival with medical treatment by means of additional prognostic indicators.

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