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Original Research Article

Clinical profile of patients presenting with mushroom toxicity in a tertiary care setup in Northeast India: with special focus on model for end-stage liver disease score as a predictor of disease outcome

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ABSTRACT

Background: Ingestion of wild mushrooms leading to toxicity is a common phenomenon every year during the rainy season in Upper Assam, India. The model for end-stage liver disease (MELD) score was developed to predict mortality in a specific group of patients with decompensated chronic liver disease. It has also been used to predict mortality in patients with acute liver failure, which is also one of the dreaded complications of mushroom toxicity. There are only a couple of studies in the world that have studied MELD score as a predictor of outcomes in patients with mushroom toxicity and to the best of our knowledge, this is the first such study done in India.
Methods: In this hospital-based observational study, 35 patients aged >13 years with an alleged history of ingestion of wild mushrooms, but no other cause of hepatic dysfunction were included in this study. Disease outcome (discharged/expired) was correlated with both MELD score and day of presentation from symptom onset.
Results: The mean age was 32.54 years with a male-to-female sex ratio of 4:5 among the study participants. Gastrointestinal symptoms, including loose stool, vomiting, pain abdomen, and jaundice, were the most common. The MELD score was significantly higher in patients who succumbed to the toxin ($p<0.05$) and positively correlated with mortality ($r=0.664$, $p<0.001$) and a later day of presentation ($r=0.226$, $p=0.123$). A later-day presentation also positively correlated with mortality ($r=0.227$, $p=0.189$).
Conclusions: The MELD score can be used as a prognostic tool in patients with mushroom toxicity.

Keywords: Mushroom toxicity, MELD score, Acute liver failure

INTRODUCTION

Mushrooms, fungal fruiting bodies, are known to mankind for over 4,600 years. The Romans thought of mushrooms as the "food of god" which has been used by mankind for food and medicinal purpose, though misused for recreational purposes as well. Out of more than 1000 species of mushrooms, 25 are considered to be edible. Contrastively, there are around 100 species that are toxic to humans, with new species being identified and added to the list every year.[2]

The incidence of mushroom poisoning varies with geographical distribution, with the incidence being high in continents, such as Europe, Asia, and Russia, where mushroom ingestion is a common practice. Although no large-scale studies were conducted to determine mortality rates of mushroom toxicity in India, these rates vary from 1-21%, though in north-eastern states they were reported at 9%.[3]

The pathophysiology of toxicity depends on the type of mushroom consumed and its toxin. False parasol (*Chlorophyllum molybdites*), also known as backyard mushroom, causes acute gastroenteritis; psilocybin-

containing species such as Psilocybe are known to evoke hallucinations; muscarine-containing species such as *Psilocybe semilanceata* are responsible for cholinergic manifestations such as sweating, diarrhea, and bronchorrhea.[4,5] Furthermore, amatoxin-containing species such as Amanita is implicated in liver failure by disrupting RNA polymerase II; Orellanine-containing toxin belonging to the genus Cortinarius (e.g., *Cortinarius orellanus*) are nephrotoxic.[6,7] In contrast, gyromitrin-containing species such as *Gyromitra esculenta* are neurotoxic and may precipitate seizures.[8]

Acute liver failure can be defined as evidence of coagulopathy, usually an international normalized ratio (INR) ≥1.5, and any degree of altered sensorium (encephalopathy) in a patient without pre-existing cirrhosis and with an illness of 26-week duration.[9] Common acute liver failure causes include paracetamol toxicity, viral hepatitis, autoimmune hepatitis, and non-paracetamol drugs and toxins, including methanol and herbal medications. Mushroom is a relatively less common cause of acute liver failure but is not uncommon in developing nations in Asia.[10] Among the mushrooms, *Amannita phalloides* is one of the common causes of acute liver failure that disrupt RNA polymerase II. Patients often present initially with gastrointestinal symptoms such as nausea, abdominal cramps, and diarrhea but later they progress to develop hepatitis and eventually multiorgan failure.[11]

Researchers at the Mayo clinic developed a scoring system called the model for end-stage liver disease (MELD) to predict mortality in patients of refractory ascites and variceal bleeding undergoing trans-jugular intrahepatic portosystemic shunt (TIPS).[12] Later it was found that MELD could predict 3-month mortality in patients with chronic liver disease awaiting liver transplant quite accurately.[13] However, recently MELD scoring has also been found to be equally or even more sensitive than King's College Hospital (KCH) criteria in patients with both paracetamol and non-paracetamol-related acute liver failure.[14,15]

Mortality in patients with mushroom toxicity is due to multiorgan failure, especially liver and kidney. However, one of the most critical factors leading to severe disease is reporting late to a healthcare facility to seek medical help. Very few studies have investigated MELD score as a predictor of outcome in mushroom toxicity and emphasized the potent influence of the day of presentation on disease outcome. The present study was carried out to evaluate the clinical profile of patients with mushroom toxicity and explore the possibility of using the MELD score as a predictor of disease outcome.

METHODS

This study was conducted at the Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, India for 16 weeks from May 2022 to July 2022. It was a hospital-based, cross-sectional prospective, observational study. The study population included all patients presenting with an alleged history of ingesting wild mushrooms.

Study participants

All patients presenting with symptoms of an alleged history of ingestion of wild mushrooms, attending the Department of Casualty or Outpatient Department, under the Department of General Medicine, at Assam Medical College and Hospital, Dibrugarh, Assam, India, during the study period and fulfilling the selection criteria were recruited to the current research.

Sample size

All the patients (n=35) with an alleged history of ingestion of wild mushrooms that presented during the seasonal outbreak between May 2022 and July 2022 were included in this study.

Inclusion criteria

All patients with an alleged history of ingestion of wild mushrooms with age >13 years were included.

Exclusion criteria

Patients who were diagnosed case of any other liver disease like cirrhosis, viral hepatitis, autoimmune hepatitis, or alcohol-induced hepatitis; history of ingestion of toxins other than mushroom-like herbal medications; and patients who were uncooperative and did not give consent were excluded.

Data extraction

The disease outcome was predicted using MELD scoring, with two defined outcomes, discharged in good health or expired to the disease. Based on this scoring, the outcome was correlated with the MELD score. The MELD score was determined on the first day of the patient's admission.

The MELD equation used to calculate the severity score is as follows.[16]

$$MELD\ score = 9.57 \times log\ e\ creatinine\ (mg/dl) + 3.78 \times log\ e\ bilirubin\ (mg/dl) + 11.20 \times loge\ INR + 6.43(constant\ for\ liver\ disease\ etiology)$$

Data analysis

The statistical analysis of data was performed using the statistical program statistical package for social sciences (SPSS), version 20.0. Chicago, SPSS Inc.) and Microsoft excel 2016. Results on continuous measurements are presented as mean±standard deviation and compared using the student's t-test. Discrete data are expressed as numbers

(%) and are analyzed using the Chi-square test. Pearson's correlation coefficient (r) was used to determine the correlation among continuous variables. The statistical significance was fixed for all analyses at a 5% level (p value <0.05).

RESULTS

The current study was performed in the Department of Medicine, Assam Medical College and Hospital, Assam, India, to study MELD score as a predictor of outcome in patients with an alleged history of ingestion of wild mushrooms.

Thirty-five (35) patients who fulfilled the selection criteria were included in the study. The following tables and figures illustrate important features and results of the study.

In our study, 45.7% of patients (n=16) were male and 54.3% (n=19) were female. The mean age of the patients was 32.54+13.8 years. The most common clinical features were gastrointestinal (loose stool, pain in the abdomen, vomiting, and jaundice) followed by hypotension, bleeding diathesis, altered behavior and uremia (Figure 1).

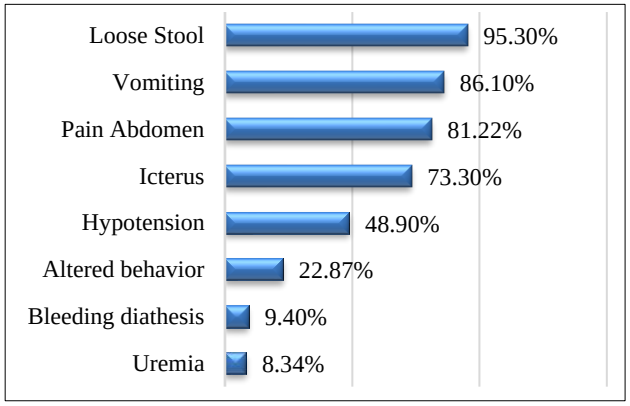

Figure 1: Clinical features of patients with mushroom toxicity.

Disease outcome was predicted using the MELD score, which was 20.09+6.29. The mean serum albumin was 3.54+0.76 mg/dl, total bilirubin 2.76+1.84 mg/dl, mean direct bilirubin 4.25+5.05 mg/dl, aspartate transaminase 247.63+60.43 IU/l, 309.14+76.33 IU/l, prothrombin time 17.03+7.75 sec, INR 2.35+1.24, serum creatinine 1.16+0.63 mg/dl and a mean C-reactive protein (CRP) 0.85+0.312 mg/dl (Table 1).

The mean MELD score in discharged patients was significantly lower than in patients who succumbed to the illness (17.48 versus 26.60, p<0.05) (Figure 2).

The mortality was 28.6%. A statistically significant positive correlation was observed between MELD score and death as the outcome among our patients (r=0.664, p<0.001) (Table 2).

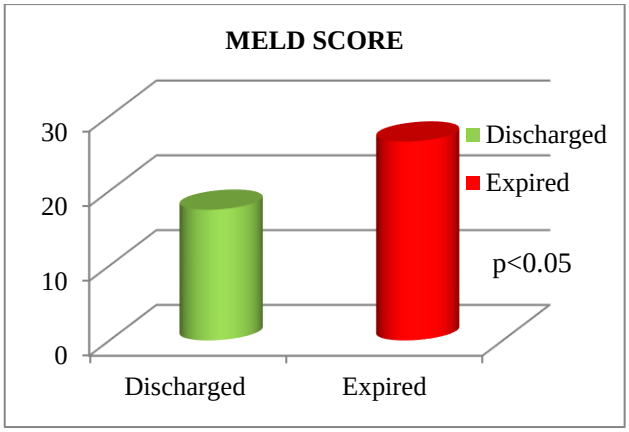

Figure 2: Comparing MELD score in different disease outcomes.

Table 1: Demographic-clinical profile and laboratory parameters of patients.

Parameters	Mean	Standard deviation
Sex ratio (M: F)	4:5	-
Age (years)	32.54	13.8
Day of presentation	3.86	1.004
S. albumin (mg/dl)	3.5486	0.76118
Total bilirubin (mg/dl)	2.7691	1.84956
Direct bilirubin (mg/dl)	4.2528	5.05523
AST IU/l	247.63	60.4359
ALT IU/l	309.14	76.3314
PT (seconds)	17.0396	7.75943
INR	2.3571	1.24812
S. creatinine (mg/dl)	1.1660	0.63211
CRP (mg/dl)	0.8528	0.31262
MELD score	20.09	6.294

We also found a positive correlation between a latter-day of presentation with death and the MELD score, although it was not statistically significant (r=0.227, p=0.189, r=0.266, p=0.123, respectively) (Figure 3 and Table 2).

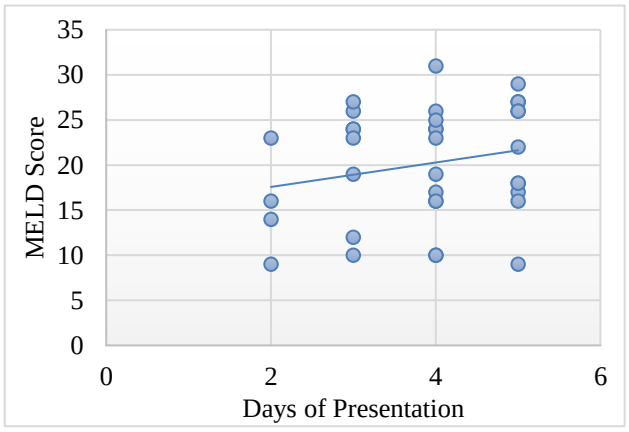

Figure 3: Correlation between MELD score and day of presentation.

Table 2: Correlation between meld score, day of presentation and disease outcome (death).

Variable	r	P
Death		
MELD score	0.664	<0.001
Day of presentation	0.227	0.189
	Day of presentation	
MELD score	0.266	0.123

DISCUSSION

Ingestion of wild mushrooms is common among the tea tribe workers of Upper Assam, India; this population comprises a significant chunk of the footfall at the Assam Medical College and Hospital.[17]

In our study, gastrointestinal symptoms such as loose stool, vomiting, pain abdomen, diarrhoea, and jaundice were the most common symptoms, and the other features were coagulopathy, hypotension and renal failure, which is similar to those reported in other studies done in India and abroad.[18-21]

The mortality of patients with mushroom toxicity varies with geographical distribution. In our study, the mortality was 28.6%. In a couple of studies done in Assam, the mortality was 13.82% and 14.7%, respectively.[18,22] In a study conducted in Turkey, the mortality was 1.02% and, in another study, done in Iran, the mortality was 12%.[19,23]

Among the laboratory parameters, liver function was affected in most patients, with the average AST, ALT, and INR being 247.63 IU/l, 309.14 IU/l, and 2.35, respectively. A similar trend was noticed in another two studies in which the median ALT was much higher (2185 IU/l and 1596.5 IU/l, respectively).[24,25]

In the present study, the average MELD score in patients discharged in good health was 17.48, whereas it was significantly higher (26.6) in patients who died. A positive correlation between increasing MELD scores and mortality was also found. There are only a couple of studies in the world that have studied MELD score as a predictor of outcomes in patients with mushroom toxicity. The results of our study were corroborated with those in a Chinese study where the MELD score was significantly higher in the death group, and the MELD score positively correlated with mortality.[26] Another study from Turkey showed an association of a higher MELD score with mortality, and a MELD score of <15 was associated with a favourable outcome.[25]

Late presentation after ingestion of wild mushrooms was found to be associated with increased mortality. Early medical intervention in any disease is associated with better outcomes; however, in the case of mushroom toxicity, the mortality rate in their patients was found comparatively lower due to early treatment.[19] This finding was supported by our results when we established a positive correlation between a latter-day presentation and increasing MELD scores, although it was statistically insignificant.

There was a relatively smaller sample size, and it was limited to a small geographic area. Hence, further studies are warranted in a larger population in the future, The MELD score was calculated on the first day. It changes over time and is dynamic, so should be determined regularly during the study duration. Hence in the present study, the MELD score may not reflect the correlation with mortality over time.

CONCLUSION

Overall, in this hospital-based prospective observational study carried out in Assam Medical College and Hospital, Dibrugarh, Assam, India with a total of 35 participants, a significant positive correlation between MELD score and mortality and a positive correlation between latter-day presentation and a worse outcome were established. Therefore, we can conclude that in patients with mushroom toxicity presenting with predominant features of acute liver failure, the MELD score calculated on the day of the presentation can serve as a useful prognostic marker.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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