ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 2, April - 2023, Page No. : 508 - 517

Glasgow alcoholic hepatitis score (GAHS) a better predictor of one month mortality in alcoholic hepatitis patients

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How to citation this article: Dr. Madhusudhan S, Dr. Swati hegde, Dr. Virender Singh, "Glasgow alcoholic hepatitis score (GAHS) a better predictor of one month mortality in alcoholic hepatitis patients", IJMACR- April - 2023, Volume – 6, Issue - 2, P. No. 508 – 517.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Alcoholic hepatitis (AH) is an acute inflammatory syndrome that occurs in patients after long-term alcohol abuse causing significant morbidity and mortality. Alcoholic hepatitis may deteriorate rapidly in its severe form, which has a high 30-day mortality of up to 50%. Maddrey's discriminant function (DF) has proven helpful in scoring disease severity and guiding specific treatment for Alcoholic hepatitis. MELD score is another important scoring system frequently used but its disadvantage is needing a calculator to calculate and involves logarithms. The Glasgow alcoholic hepatitis score includes age, WBC count, urea level, serum bilirubin level, and prothrombin time ratio also have been shown to predict survival in patients with severe alcoholic hepatitis. In our study, we are comparing the scoring systems of GAHS and mDF to predict the one-month mortality in alcoholic hepatitis patients.

Aims and objectives: To compare Glasgow alcoholic hepatitis score (GAHS) with the modified discriminant function score(mDF) to predict one-month mortality in alcoholic hepatitis patients.

Materials and methods: Prospective observational study was conducted on 80 patients with Alcoholic hepatitis who visited General Medicine OPD/was admitted to General Medicine wards in ESIC MC and PGIMSR between March 2021 to August 2022. The modified discriminant function and Glasgow alcoholic hepatitis scores were calculated and their association with one-month mortality was studied and compared with each other.

Results: Out of 80 patients with Alcoholic hepatitis in our study, 24 patients died within one month suggesting that 30% one-month mortality in our study. The GAHS score (93.8 %) accurately predicted 1-month mortality when compared with mDF (72.5 %). The specificity and the positive predictive value of GAHS (94.6% and 88%) were superior compared to mDF (69.6 % and 52.8%).

In our study, GAHS has higher sensitivity, specificity, Positive predictive value, negative predictive value, and diagnostic accuracy when compared to mDF. Hence the GAHS identifies the severity of alcoholic hepatitis meticulously compared to mDF.

Conclusion: Alcoholic hepatitis is a potentially reversible condition, the high short-term mortality of 40-50 % is unacceptable and it has to be prevented. Both GAHS and mDF predict severity and one-month mortality in alcoholic hepatitis patients. GAHS is easy to calculate. GAHS has higher sensitivity, specificity, Positive predictive value, negative predictive value, and diagnostic accuracy when compared to mDF.

Keywords: alcoholic hepatitis, modified discriminant function (mdf) Score, Glasgow alcoholic hepatitis score (gahs), one month mortality

Introduction

Alcoholic hepatitis is an acute inflammatory syndrome that arises in patients after long-term alcohol abuse causing significant morbidity and mortality[1]. The clinical spectrum of alcoholic hepatitis is varied, ranging from mild to severe disease characterized by rapid onset malaise, tender hepatomegaly, jaundice, and hepatic encephalopathy.

To predict disease severity and mortality risk in patients with alcoholic liver disease, different scoring systems are used such as the Child-Pugh score, ABIC (age, serum bilirubin, INR, creatinine), GAHS (Glasgow alcoholic hepatitis score), MELD (Model for End-stage Liver Disease).

Alcohol Metabolism

The liver is the key organ for alcohol metabolism. Ethanol is processed by three main enzyme systems:

1) Alcohol dehydrogenase (ADH)
2) cytochrome P450 isoenzymes (mainly cytochrome P450 2E1)
3) catalase.

Among these, ADH is the foremost enzyme system involved in alcohol metabolism. It metabolizes 80-85% of ethanol. Ethanol is transformed to acetaldehyde by these three systems[2].

Metabolic Abnormalities

Alcoholic liver disease results in metabolic ab normalities including acetaldehyde - induced protein interference, impaired carbohydrate and lipid metabolism due to a shift in NADH/NAD+ ratio, and oxidative stress from CYP2E1 and superoxide generation.

Immune and Inflammatory Mechanisms

Alcoholic liver disease leads to dysregulated cytokine production and Kupffer cell stimulation, causing increased production of pro-inflammatory cytokines such as TNF-α, which is associated with disease severity and mortality. Inflammatory cytokines like IL-1, IL-6, and TNF-α trigger inflammation and cellular death, while TGF-β promotes collagen synthesis.

Diagnosis of Alcohol abuse

Alcohol abuse can be diagnosed based on an individual's frequent problems in social, legal, occupational, and interpersonal relationships, as well as drinking in unsafe situations. Doctors can use various questionnaires to diagnose alcohol abuse, such as the CAGE, TWEAK, MAST, and AUDIT. The AUDIT is a 10-item

questionnaire proposed by the WHO for screening problem drinking. It quantitates the amount consumed and includes short-term as well as long-term drinking patterns[3]. Laboratory tests are required to confirm the diagnosis of alcohol-related liver disease (ALD).

Risk Factors and Clinical Profile

Alcoholic hepatitis is caused by excessive and prolonged alcohol intake, which overwhelms the liver's ability to process the alcohol, leading to inflammation and injury. Risk factors include age, gender, genetics, and malnutrition. Symptoms include jaundice, abdominal pain and swelling, fatigue, nausea and vomiting, and weight loss[1].

Histology of Alcoholic hepatitis

Alcoholic hepatitis can be diagnosed through histology, which shows ballooning, Mallory bodies, neutrophil infiltration, fibrosis, and cholestasis. Fibrosis is predominantly seen in zone 3, and periportal fibrosis is common in frequent binge drinking[2]. Marked cholestasis is associated with higher mortality.

Diagnosis and Laboratory features of Alcoholic Hepatitis

Alcoholic hepatitis (AH) is clinically diagnosed based on the onset of jaundice within the prior 8 weeks, ongoing consumption of greater than 40 (female) or 60 (males) g alcohol/day for 6 or more months, with less than 60 days of abstinence before the onset of jaundice, AST greater than 50, AST/ALT greater than 1.5, and both values less than 400 IU/L, and serum bilirubin (total) greater than 3.0 mg/dL. Definite AH is clinically diagnosed and biopsy proven. Probable AH is clinically diagnosed in patients with heavy alcohol use and typical liver tests, negative markers for immune and metabolic liver disease, and absence of certain conditions[4].

Laboratory tests are helpful in diagnosis, with liver enzymes showing an increase in AST and ALT, a ratio of AST/ALT greater than 2 being indicative of alcoholic liver disease, and a ratio greater than 3 highly suggestive. Serum bilirubin levels greater than 8 mg/dL signify severe disease, and prothrombin time with INR values greater than 4 seconds above control value can predict poor prognosis.

Prognostication and Management of Alcoholic Hepatitis

Alcoholic hepatitis (AH) has a variable prognosis, with severe disease associated with a high mortality rate. Factors such as HCV infection, alcohol use >120 g/day, infection, and gastrointestinal bleeding are associated with a poor prognosis. The mDF, MELD, Glasgow alcoholic hepatitis score (GAHS), ABIC score, and Lille's score are used to predict short-term prognosis. Nutritional support, corticosteroids, with or without N-acetylcysteine (NAC) in patients with mDF >32, MELD >18, and GAHS >9, and pentoxifylline in patients with contraindications for corticosteroids or with hepatorenal syndrome are among the treatments investigated for AH[5]. Liver transplantation is an option for patients non-responsive to these measures, although it is limited by the restricted availability of liver grafts and patient eligibility. AH patients with mild disease have short-term survival rates of 90-100%, whereas those with a mDF value of 32 or more experience a 28-day mortality rate of 35-45%. A score of ≥9 indicates a poor prognosis for both the GAHS and ABIC score, while a Lille score >0.45 signifies steroid failure.

Aims and objectives

To compare Glasgow alcoholic hepatitis score with the modified discriminant function score to predict one-month mortality in alcoholic hepatitis patients.

Materials and methods

A prospective observational study was conducted on 80 patients with Alcoholic hepatitis who visited General Medicine OPD or who was admitted to General Medicine wards in ESIC MC and PGIMSR between March 2021 to August 2022. These patients were subjected to thorough history, clinical examination, bio chemical investigations, and ultrasonogram of the abdomen. The modified discriminant function and Glasgow alcoholic hepatitis scores were calculated and their association with one-month mortality was studied and compared with each other.

Inclusion criteria

Patient willing to give informed consent, patients with age > 18 years, patients with hepatitis with alcohol consumption of 60g/day in males and 40g/day in females for > 6 months, patients with serum Bilirubin > 3mg/dl, AST >50U/l, AST/ALT >1.5 were included.

Exclusion criteria

Patients not willing to give informed consent, patients with HbsAg positive status, HCV-positive status, GI bleeding, Autoimmune Liver Disease, Liver malignancy, Secondaries in the Liver, Metabolic Liver diseases (Wilson's disease, Haemochromatosis), Drug-induced hepatitis, and patients with chronic kidney disease were excluded.

How the study was conducted

Patients diagnosed with alcoholic hepatitis were taken into the study after applying the inclusion and exclusion criteria. These patients were subjected to thorough history, clinical examination, biochemical investigations, and ultrasonogram of the abdomen. They were followed up for one month after they were diagnosed with Alcoholic hepatitis.

Assessment Panel Includes History with specific focus on alcoholic intake-amount, type and duration and with AUDIT score ≥8 in males and ≥7 in females and elderly males' age. Biochemical Investigations - White cell count, serum urea, serum albumin, PT and INR, SGOT and SGPT, ultrasonogram of abdomen done to exclude cirrhosis and malignancy. The patients were followed up for one month and their mortalities were assessed and the Modified Discriminant Function score and Glasgow Alcoholic Hepatitis score were calculated and analyzed.

Modified Discriminant Function = 4.6 X (Patient's PT – Control PT) + Total Serum Bilirubin(mg/dl)

A Modified Discriminant function score ≥ 32 is associated with high short-term mortality.

Glasgow Alcoholic Hepatitis Score

SCORE	1	2	3
AGE	<50	>50	
TLC (10^9)	<15	>15	
UREA (mmol/L)	<5	>5	
INR	<1.5	1.5-2	>2
Total Bilirubin (micromol / L)	<125	125-250	>250

A Glasgow Alcoholic Hepatitis score ≥ 9 signifies patients to have a high risk of mortality.

In this study, the alcoholic hepatitis patients with mDF ≥ 32 were treated with prednisolone for four weeks and then tapered over the next four weeks. If the patient had contraindications to steroids, pentoxifylline was given.

The patients were followed up for one month and mortality is observed. The sensitivity, specificity, and accuracy of mDF and GAHS in calculating one-month mortality were calculated. The results were analyzed.

A p-value of 0.05 is considered statistically significant.

Results

The one-month mortality prediction by modified discriminant function(mDF) and GAHS score is calculated and compared with observed one-month mortality. The results are tabulated and analyzed as follows:

Age distribution

In our study age of patients ranged from 25 to 64 years with a Mean age of 41.9±9.4 years.

Table 1: Showing Age group Distribution.

Age group distribution [years]	Frequency	Percentage
21-30	10	12.5
31-40	25	31.2
41-50	29	36.2
≥ 51	16	20
Total (N)	80	100

Graph 1: showing Age distribution of Alcoholic hepatitis.

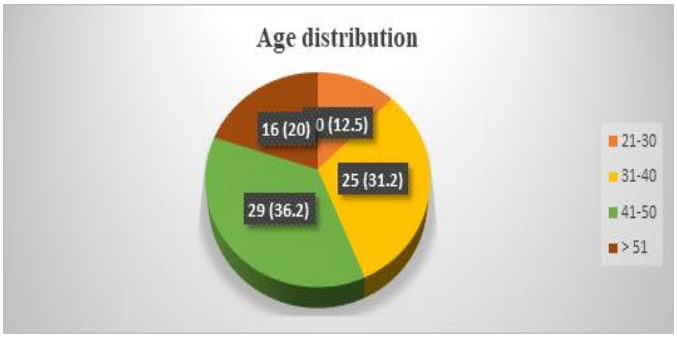
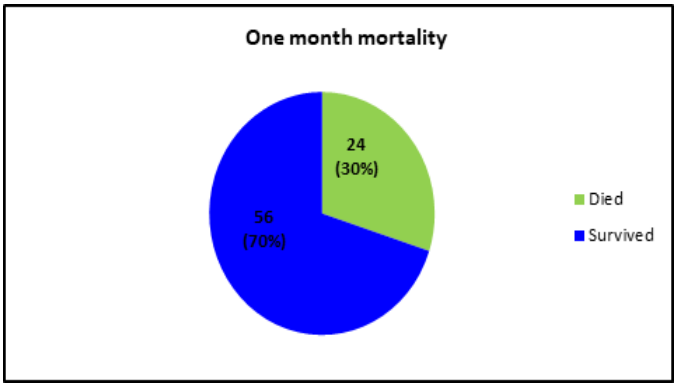


Table 2: showing Incidence of one-month mortality.

		Frequency	Percentage
One month mortality	Died	24	30
	Survived	56	70

Graph 2: showing the incidence of one-month mortality.



In our study, from the above table, we could infer that 30% of the patients accounting for 24 died among 80 patients.

Comparison of scoring systems

Sensitivity Specificity Analysis for mDF

Table 3: showing mDF score and one-month mortality.

		One month mortality		Total
		Death	Survived	
mDF	≥ 32	19	17	36
	< 32	5	39	44
Total		24	56	80

Graph 3: showing Association of mDF scoring with one-month mortality.

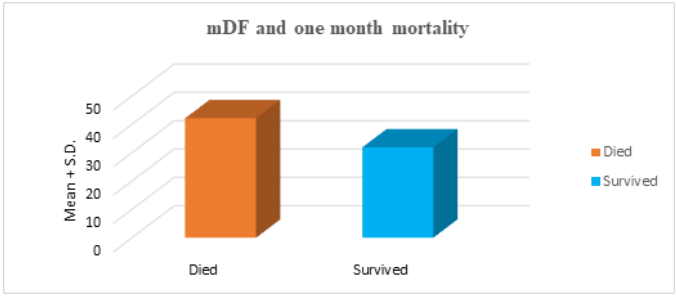


Table 4: showing Sensitivity Specificity Analysis for MDF score.

	Estimate (%)	95% CI
Sensitivity	79.2	70.3 to 88.1
Specificity	69.6	60.0 to 80.0
Positive Predictive Value	52.8	41.9 to 63.7
Negative Predictive Value	88.6	81.6 to 95.6

Diagnostic Accuracy	72.5	62.7 to 82.3

In our study mDF has a diagnostic accuracy of 72.5 % in predicting 1 month mortality. Also, out of 36 patients who had mDF of > 32, 19 patients died and 17 survived with a specificity of 69.6%. Out of 44 patients who had an mDF score < 32, 5 patients died and the positive predictive value is found to be 52.8% which is low.

Sensitivity Specificity Analysis for GAHS

Table 5: showing GAHS score and one-month mortality.

		One month mortality		Total
		Death	Survived	
GAHS	≥ 9	22	3	25
	< 9	2	53	55
Total		24	56	80

Graph 4: showing Association of GAHS with one month mortality.

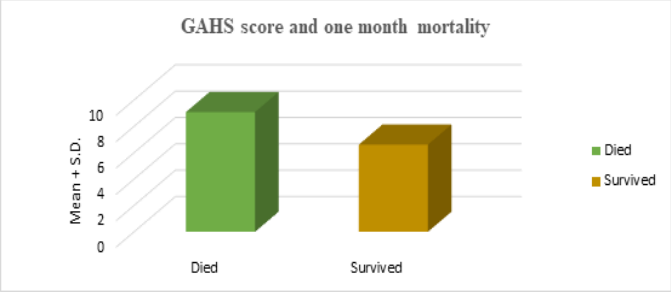


Table 6: showing Sensitivity Specificity Analysis for GAHS score.

	Estimate (%)	95% CI
Sensitivity	91.7	91.7 to 100
Specificity	94.6	90.0 to 99.8
Positive Predictive Value	88.0	80.9 to 95.1
Negative Predictive Value	96.4	91.7 to 100
Diagnostic Accuracy	93.8	88.8 to 99.2

In our study, the GAHS has a diagnostic accuracy of 93.8% in predicting 1 month mortality.

Also, out of 25 patients who had GAHS of > 9, 22 patients died and only 3 survived with a specificity of 94.6%. Out of 55 patients who had GAHS <9, 2 patients died.

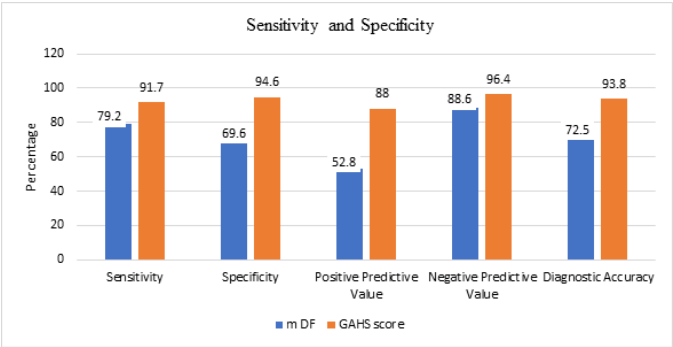
Also, the positive predictive value is 88%. Therefore, in our study, GAHS has higher sensitivity, specificity, Positive predictive value, negative predictive value, and diagnostic accuracy when compared to mDF.

Hence the GAHS identifies the severity of alcoholic hepatitis meticulously compared to mDF and this can be used in deciding upon treatment with steroids or pentoxifylline.

Table 7: showing Comparison of Accuracy of mDF and GAHS in predicting the one-month mortality in Alcoholic hepatitis.

Parameter	mDF	GAHS
Sensitivity	79.2	91.7
Specificity	69.6	94.6
Positive Predictive Value	52.8	88
Negative Predictive Value	88.6	96.4
Diagnostic Accuracy	72.5	93.8

Graph 5: showing Comparison of Sensitivity and specificity of GAHS score and mDF score.



After completing our study with 80 patients with alcoholic hepatitis, it was found to be that the GAHS score (93.8 %) accurately predicted 1-month mortality when compared with mDF (72.5 %). The specificity and the positive predictive value of GAHS (94.6% and 88%) were far superior compared to mDF (69.6 % and 52.8%). Out of the 44 patients with mDF < 32, five patients died.

Of these five patients, three had GAHS ≥ 9 indicating that had GAHS been used to identify the severity, these patients could have benefitted from the treatment of corticosteroids or pentoxifylline. Two patients who died had both GAHS < 9 and mDF <32. In this case, both scores failed to identify the severity.

Discussion

Alcoholic hepatitis is a serious and potentially life-threatening condition resulting from heavy and prolonged alcohol abuse. The severity of alcoholic hepatitis is assessed using various scores like Maddrey's discriminant function(mDF) score, Model for end-stage liver disease (MELD) score, Glasgow alcoholic hepatitis score (GAHS), Alcoholic hepatitis severity index (AHASI), ABIC score, etc. In our study, among 80 patients, 24 died at the end of one month (30%). The mean age of patients who died at the end of one month was 46.8years±9.8, suggesting that as the age increases, the risk of one month mortality increases too.

In a systemic review by Hughes E et al showed that the overall mortality from alcoholic hepatitis was 26% at 28 days, 29% at 90 days, and 44% at 180 days after admission. The mean age of patients in our study who died at the end of one month was 46.8years±9.8, suggesting that as the age increases the risk of one month mortality increases too[6]. A study done by Gautam R et al concluded the same that as age increases mortality risk increases at the end of one month, while another study done by Noas T M et al showed 28-day mortality was seen more in patients < 50 years[7].

In our study, we found that the majority of patients presented with pallor and Icterus along with other symptoms like ascites, signs of liver cell failure, hepatomegaly, hepatorenal syndrome, etc. We found that Icterus (96.2%) was the main presentation than pallor (36.2%). While other studies like Pooja J B et al showed edema and ascites (80-90%) were the main presentations than jaundice. However similar findings were seen in studies done by Chetan N et al and Chavan VB et al where jaundice was the most common presentation than ascites. However, in contrast, the study done by Hemang S et al showed that ascites and melena were the most common presentation in Alcoholic hepatitis cases. Noas TM et al showed in their study that Jaundice was the main symptom in all the patients who died at the end of one month[7]. In our study, the patients who expired at the end of one month had raised White cell count, low hemoglobin, and low platelet count, which was similar to results done by Noas T Met al[7] and Pooja J B et al.

Our study also showed that Liver function tests like serum bilirubin, and enzyme levels SGOT/SGPT were raised in all patients who expired at the end of one month compared to those who survived, also Prothrombin time was increased with INR > 2 in those who expired. These findings were similar to the studies done by Vasumathi G et al[8] and Noas TM et al[7]. Serum urea level was also raised in our study in patients who expired indicating the effect of hepatorenal syndrome, hence predicting the mortality in Alcoholic hepatitis patients, this finding was also similar to the study done by Pooja J B et al.

Comparing the scoring systems to predict the one-month mortality.

The observed mortality was 30% in our study. Of the 24 patients who died, 19 were detected as having the severe disease by both mDF and GAHS. But 3 patients who had mDF < 32 and GAHS ≥9 died. 2 patients who had both mDF < 32 and GAHS < 9 died and both scores failed to identify the severity.

GAHS identifies severity in all patients identified by mDF ≥ 32, apart from identifying severe disease in patients with mDF < 32. The severity predicted by GAHS had an accuracy of 93.8% compared to that calculated by mDF which had 72.5% accuracy. In our study, GAHS had a better sensitivity, specificity, and PPV (91.7%, 94.6% and 88 %respectively) than mDF. Thus it is obvious that GAHS has much better severity prediction compared to mDF and this helps treat patients.

A similar study done by Noas TM et al also showed that GAHS had good diagnostic accuracy (81.5%) than mDF(60.5%) and MELD score(53.4%)[7].

In the study conducted by Forrest E H et al, 241 patients were studied. On the day of admission, the GAHS was more statistically significant than mDF in finding out 28 and 84-day mortality. When compared with MELD, the day 1 GAHS was equally accurate in predicting 28-day mortality and more accurate in predicting day 84 outcome[9].

In a study conducted by Lafferty H et al, 182 patients were studied prospectively and compared with the historical group which was treated as per mDF. At GAHS < 9, the survival rate at day 28 and day 84 were similar. On the day of admission, if GAHS ≥ 9 who were treated had a survival of 71 % at day 28, compared to 41 % of the comparison group with a p-value of 0.0002.

A study was conducted by Sandahl T D et al in Denmark with 274 patients, the predicted 28-, 84- and 180 –day mortality of the patients by MELD, GAHS, and ABIC scores were found to be similar[5].

In the study conducted by Palaniappan N et al at Nottingham, a total of 44 patients with biopsy-proven alcoholic hepatitis were studied. It was concluded that mDF, MELD, GAHS, and ABIC scores were similar in accuracy in predicting short-term mortality. All these scoring systems were found to be poor in predicting long-term mortality.

In a study conducted by Ali S et al, 82 patients were studied in the UK, and found to be mDF, GAHS, and CP were of equal accuracy in predicting 28-day mortality. In addition, a very high PT, raised creatinine, gastrointestinal bleeding, and encephalopathy at the time of admission are associated with increased mortality.

Vasumathi G et al, conducted a prospective observational study of 50 Alcoholic hepatitis patients in Stanley Medical College, Chennai. It was concluded that the GAHS score is found to have higher sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy when compared to the mDF score[8].

In a study conducted by Papa Stergiou V et al on 71 patients with biopsy-proven AH, admitted between November 2007-September 2011. All parameters were analyzed to assess prognostic models with respect to 30- and 90-day mortality, to validate the Maddrey Discriminant Function (DF); Glasgow Alcoholic Hepatitis Score (GAHS); Mayo End-stage Liver Disease (MELD); Age, Bilirubin, INR, Creatinine (ABIC); MELD-Na, UK End-stage Liver Disease (UKELD), and three scores of corticosteroid response at 1 week: an Early Change in Bilirubin Levels (ECBL), a 25% fall in bilirubin, and the Lille score as prognostic scores concluded that MELD, DF, GAHS, ABIC, and scores of corticosteroid response proved to be valid in an independent cohort of biopsy-proven alcoholic hepatitis.[10]

Table 8:

Studies	Population (number)	Results
Altamirano- Gomez	120	GAHS is superior to mDF in predicting in-hospital mortality.
EH Forrest	241	GAHS is more accurate than mDF in predicting 28 and 84-day mortality.
H Lafferty	182	Improvement is seen in outcomes if patients are treated with GAHS grading for severity.
Sandahl	274	MELD, GAHS, and ABIC scores are equal in accuracy.
N Palaniappan	44	mDF, ABIC, MELD, and GAHS are equal in accuracy. CP score is poor in accuracy.
S. Ali	82	GAHS, mDF, and CP are equal in accuracy.
G. Vasumathi et al	50	GAHS score is found to have higher sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy when compared to the mDF score
Papa Stergiou V et al	71	MELD, DF, GAHS, ABIC, and scores of corticosteroid response proved to be valid in an independent cohort of biopsy-proven alcoholic hepatitis.

The above studies show the accuracy of GAHS in comparison with other prognostic scoring systems.

Conclusions

Both GAHS and mDF predict one-month mortality in alcoholic hepatitis patients.

Our study proves that the GAHS score is also an equally effective method to predict 1 month mortality in alcoholic hepatitis patients. GAHS score is easy to calculate at the bedside. GAHS has higher accuracy compared to mDF. Each factor included in GAHS – age, bilirubin, urea, and White cell count, with exception of prothrombin time had a statistically significant rise in those patients who died compared to the survivors, indicating that each factor itself gives a clue to the prognosis of the disease. In our study, GAHS had a higher sensitivity, specificity, Positive predictive value, negative predictive value, and diagnostic accuracy when compared to mDF. Hence the GAHS identified the severity of alcoholic hepatitis meticulously compared to mDF.

Overall, our study emphasizes the importance of using an accurate scoring system to identify disease severity and make timely treatment decisions in patients with alcoholic hepatitis.

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