PROGNOSTIC UTILITY OF GLASGOW ALCOHOLIC HEPATITIS SCORE (GAHS) IN ALCOHOLIC HEPATITIS

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ABSTRACT

BACKGROUND

Severe alcoholic hepatitis is associated with high mortality, 40-50% mortality at one month has been reported. Many scoring systems have been applied to predict survival in alcoholic hepatitis. Patients with high risk need aggressive treatment. So, an accurate scoring system is essential to predict the patients who are at high risk.

The aim of this study was to assess the short term (28 day) prognostic utility of Glasgow Alcoholic Hepatitis Score (GAHS) in alcoholic hepatitis by comparing with mDF and MELD scores.

MATERIALS AND METHODS

76 patients with alcoholic hepatitis admitted to medical wards in our hospital, meeting the inclusion and exclusion criteria were assessed within 24 hours. Scoring was done on day one with each scoring system, GAHS score taking parameters of age, total WBC count, serum bilirubin, blood urea and Prothrombin Time; mDF score with Prothrombin Time and serum bilirubin; MELD score with serum bilirubin, PT/INR, and creatinine level. Patients were followed up for 28 days with day-to-day in-hospital analysis of status and by telephonic conversation after discharge.
Study Design**-** Cross-sectional analytical study.

RESULTS

At 28th day, 40 patients survived, and 36 patients died. The median scores for survivors and non-survivors at 28 days were: for GAHS 7 (range 5-10) and 9 (range 7-11), for mDF 58 (range 2.6-214.8) and 85 (range 28.8-510.8), for MELD 21.8 (range 10-38.8) and 31 (range 11-55) respectively. For the prediction of survival at 28th day, the GAHS score >9 has sensitivity 83.3%, specificity 80%, accuracy 81.57%, p <0.001; mDF score >32 has sensitivity 88.88%, specificity 35%, accuracy 60.52%, p<0.044; mDF >77 has sensitivity 55.55%, specificity 60%, accuracy 57.89%, p>0.05; MELD score >11 has sensitivity 100%, specificity 12.5%, accuracy 53.94%, p>0.05; MELD score >27 has sensitivity 77.77%, specificity 70%, accuracy 73.68%, p <0.001. Other independent factors for high mortality were ascites, encephalopathy, high bilirubin level.

CONCLUSION

GAHS, easy to calculate at bed side, has high sensitivity, specificity and accuracy in short term (28 days) prediction of mortality in alcoholic hepatitis, superior to mDF and MELD scoring systems.

KEYWORDS

Alcoholic Hepatitis, GAHS, mDF, MELD.

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BACKGROUND

Alcoholic liver disease encompasses a spectrum of liver injuries including fatty infiltration (steatosis), alcoholic hepatitis, fibrosis (cirrhosis) and hepatocellular carcinoma. Alcoholic hepatitis is necroinflammation with or without fatty infiltration and fibrosis (Macsween R. N. et al).[1] Alcoholic hepatitis may be asymptomatic with only hepatomegaly and dull ache over the liver, or symptomatic with full blown features like nausea, vomiting, fever, jaundice, anaemia, weight loss, malnutrition, ascites or encephalopathy. Stigmata of chronic alcoholic liver disease such as spider naevi, palmar erythema, Dupuytren's contracture, parotid enlargement may be present. Laboratory data shows elevated AST and ALT levels with values less than 300 IU/ml, and AST/ALT ratio greater than 2 (Cohen J. A. et al).[2] Elevation of gamma glutamyl transferase (GGT) has sensitivity 70% and specificity 60-80%. Bilirubin level >5 mg/dl with a prolonged prothrombin time >4 seconds correlate with severe disease (Fletcher L.M. et al[3]).

Severe alcoholic hepatitis is associated with high mortality rate, 30-40% at one month. At present, understanding of pathophysiology has improved, but

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outcome has not improved much. Steroid is only moderately effective in the treatment (Carither L. Jr. et al,[4] O'Shea R.s. et al[5]). Further improvement in treatment is needed for better outcome, which needs an accurate identification of patients with high risk of mortality. There are many scoring systems applied to predict survival in alcoholic hepatitis. The patient risk stratification and allocation of treatment is entirely dependent on scoring system that predicts survival versus mortality.

Maddrey and colleagues[6] devised and introduced in 1978, the Discriminant Function (DF) scoring system taking serum bilirubin and prothrombin time, to predict the risk of mortality in alcoholic hepatitis and identify the patients who may benefit from steroid. The disease severity is well correlated with serum bilirubin and prothrombin time after vitamin K administration. A DF score >93 indicated a poor prognosis. In 1989 modified DF was introduced to use for placebo-controlled corticosteroid trial. An mDF score >32 with encephalopathy highly correlated with a short-term mortality rate of >50%. The mDF scoring was approved by the American college of gastroenterology.

MELD score was devised to predict outcome in patients undergoing transjugular intrahepatic portosystemic shunts but later on, it was used to predict mortality in patient awaiting liver transplant, taking the variables serum bilirubin, PT-INR and serum creatinine level. The 30-day survival was 30% with MELD score> 11, and 96% with MELD score <11. Both MELD and mDF scores had similar sensitivity but MELD had higher specificity (Kamath P.S. et al,[7] Dunn W et al[8]).

Glasgow Alcoholic Hepatitis Score (GAHS) was devised by logistic regression analysis and introduced by a group of investigators in UK (Forrest & colleagues[9]), taking the variables age, total WBC count, blood urea level, prothrombin time-INR and total bilirubin level. A GAHS score >9 had poor prognosis. Forrest et al[10] showed that the day 1 GAHS had an accuracy of 81% when predicting the 28-day outcome which was much superior to mDF. Further GAHS was proved to be more accurate than MELD in predicting short and long-term survival.

MATERIALS AND METHODS

Inclusion Criteria

The study was done between June 2014 to January 2018 in our college. A total of 76 male patients above 18 years with a history of excess consumption of alcohol (more than 30g of alcohol per day) for at least three weeks prior admission were studied. The diagnosis of alcoholic hepatitis was confirmed by clinical and laboratory parameters within 24 hours.

Exclusion Criteria

Early death or discharge from hospital within 48 hours, GI bleeding, viral hepatitis, biliary obstruction, hepatocellular carcinoma, treatment with steroid or Pentoxyphylline were excluded from the study.

A detail history, including alcohol intake was taken.

On examination the features noted were-jaundice, anaemia, hepatic facies, parotid swelling, gynaecomastia, palmar erythema, loss of axillary and pubic hair, malnutrition, abdominal venous prominences, testicular atrophy, hepatomegaly, splenomegaly and ascites. Laboratory investigations done included- CBC, blood urea, creatinine, total and direct bilirubin, AST, ALT, ALP, GGT, Prothrombin time with INR, serum albumin, lipid profile, HBsAg, antibody for HCV, X-ray chest, USG of abdomen and ascitic fluid analysis. The diagnosis was confirmed within 24 hours, by clinical features and laboratory investigations with elevated bilirubin level, elevated AST & ALT level below 300 IU/ml and AST/ALT ratio greater than 2, with or without elevated GGT. The patients were monitored for 28 days with day-to-day analysis of status during hospital stay, and by telephonic conversation after discharge. The day one prognostic scores were calculated using the formula.

1. mDF= 4.6 x (Prothrombin $Time_{patient}$- $PT_{control}$) + total serum bilirubin (mg/dl);
2. MELD= 3.8 x $\log_e$bilirubin (mg/dl) + 11.2 x $\log_e$INR + 9.6 x $\log_e$ creatinine (mg/dl);
3. GAHS is calculated my summing up all the scores of the variables given in the table 1 below:

Score	1 point	2 points	3 points
Age (years)	< 50	> 50	--
Total WBC count (10^9/L)	< 15	>15	--
urea (mmol/L)	< 5	> 5	--
Prothrombin Time/INR	< 1.5	1.5-2.0	> 2.0
Total bilirubin (mg/dl)	< 7.4	7.4-14.8	> 14.8

Table 1. GAHS Calculation

Statistical analysis was done at day 28 by dividing the patients into two groups: survivors and non-survivors. Mean + SD for all the factors with poor prognosis and Median with range for each factor used for GAHS, MELD and mDF were calculated. Student's t-test done for age, bilirubin, urea, creatinine, total count and prothrombin time to see if any significant difference exists; p value <0.05 considered significant. Chi-square test and p value calculated for each prognostic score. The sensitivity (TPR) and specificity (TNR) were calculated by taking the median value as cut off point. The prognostic utility of GAHS to assess short term mortality (28 day) was determined by comparing its sensitivity and specificity to those of mDF and MELD; also compared with the finding of other investigators.

RESULTS

The important features the patients presented with were as follows in the tables-

Symptom or Sign	Patients Affected (%) (with Number)		
	Survivor (n=40)	Non-Survivor (n=36)	Overall (n=76)
Fever	17.5 (7)	22.2 (8)	19.7 (15)
Jaundice	45.1 (18)	100 (36)	71 (54)
Hepatic encephalopathy	27.5 (11)	61.1 (19)	39.4 (30)
Hepatomegaly	83.33 (30)	86.1 (31)	80.2 (61)
Splenomegaly	20 (8)	41.6 (15)	30.2 (23)
Ascites	12.5 (5)	66.6 (24)	38.1 (29)

Table 2(a). Signs and Symptoms of Patients in the Study

Laboratory Test	Mean value with ± SD		
	Survivor (n=40)	Non-survivor (n=36)	P value
tWBC (per mm3)	8516(± 5715)	14507(± 10484)	<0.01
Sr. bilirubin(mg/dl)	5.7(± 4.8)	11.6(± 8.6)	< 0.001
PT (seconds)	25.8(± 12.5)	37.7(± 26.9)	< 0.01
Urea (mmol/L)	5.4(± 2.7)	11.2 (± 6.6)	< 0.001
Creatinine(mg/dl)	1.1(± 0.6)	1.8(± 1.2)	< 0.01

Table 2(b). Laboratory Values of Patients in the Study

28 day Mortality									
Parameters	Median with Range	Cut off Value	Expired (36)	Survived (40)	Total (76)	CI (%)	TPR (%)	TNR (%)	p Value
Age	42 (22-58)	positive test > 50	11	13	24	95	30.5	67.5	> 0.1
		negative test< 50	25	27	52				
tWBC x10^3/cmm	7.5 (3-24)	Positive test>15	17	6	23	95	47	85	<0.025
		Negative test<15	19	34	53				
bilirubin(mg/dl)	5 (1.8-20)	positive test>5.5	27	18	39	95	75	70	<0.001
		negative test< 5.5	9	28	37				
		positive test > 7.5	19	7	26	95	52.7	82.5	<0.005
		negative test<7.5	17	33	50				
Urea (mmol/L)	5.62(3.6-17.9)	positive test> 5	29	18	47	95	80.5	55	<0.005
		negative test<5	7	22	29				
creatinine(mg/dl)	1.1(0.6-3.9)	positive test>1.5	19	7	26	95	52.7	82.5	<0.01
		negative test< 1.5	17	33	50				
PT/ INR	26.4 (11.87)/ 2.4 (1- 5.2)	positive test>2	29	20	49	95	80.5	50	<0.025
		negative test<2	7	20	27				
Encephalopathy		present	22	11	33	95	61.1	72.5	<0.01
		absent	14	29	43				
Ascites		present	24	5	29	95	66.6	87.5	<0.001
		absent	12	35	47				

Table 3. 28-day Mortality with Different Variables

28-day Mortality										
	Cut off value	Expired (36)	Survived (40)	Total (76)	TPR (%)	TNR (%)	PPV (%)	NPV (%)	ACC (%)	p value
GAHS	positive test >9	30	8	38	83.33	80	78.94	84.21	81.57	<0.001
	negative test <9	6	32	38						
mDF	positive test >32	32	26	58	88.88	35	55.17	77.77	60.52	<0.044
	negative test <32	4	14	18						
	positive test >77.8	20	16	36	55.55	60	55.55	60	57.89	>0.05
	negative test <77.8	16	24	40						
MELD	positive test >11	36	35	71	100	12.5	50.7	100	53.94	>0.05
	negative test <11	0	5	5						
	positive test >27	28	12	40	77.77	70	70	77.77	73.68	<0.001
	negative test <27	8	28	36						

Table 4. Comparison of Different Scores (GAHS, mDF and MELD)

The median length of hospital stay was six days (range 4-24 days). The 28 day mortality rate was 47.5% (36 out of 76 patients). This shows alcoholic hepatitis has a high mortality rate.

Table 2(a) shows the clinical features jaundice, hepatic encephalopathy and ascites have high mortality.

Table 2(b) shows the mean ± SD values of the laboratory features tWBC, bilirubin level, prothrombin time, blood urea and creatinine level which has influence on mortality in alcoholic hepatitis.

Table 3 shows the 28-day mortality for age, tWBC, bilirubin, urea, creatinine and PT/INR at their respective cut off value, and encephalopathy and ascites with their CI, TPR (sensitivity), TNR (specificity) and p values. All parameters have high mortality except the age (above 50).

Table 4 shows the GAHS, mDF and MELD scores with the median with range at their respective cut off values and the predictive utility of each score by sensitivity, specificity, accuracy and p values. GAHS at score >9 has high sensitivity, specificity and accuracy with p<0.001. The mDF at score>32 has high sensitivity but low specificity, at score >77 specificity increased but sensitivity decreased. The MELD at score > 11 has very high sensitivity and accuracy but very low specificity, at score >27 the specificity increased.

The GAHS score at >9 identified the patients with alcoholic hepatitis at high risk of short term mortality more accurately (accuracy 81.57) than mDF and MELD.

DISCUSSION

Alcoholic hepatitis has high mortality rate (30-40% at one month). Accurate identification of patients at high risk is essential to guide the physicians for aggressive treatment, and for further research.

Forrest et al in their study noted that the age, PT, urea and tWBC above their cut off values were associated with poor outcome and devised GAHS and validated as a prognostic score. Similar to their observation, in the present study, the day one bilirubin > 5.5 ($p<0.001$), blood urea >5 mmol/L ($p<0.005$), INR > 2 ($p<0.025$), and tWBC > 15000 ($p<0.0025$) were highly significant in predicting mortality but the age > 50 was not significant ($p > 0.05$). Lafferty H. et al11 in their study concluded that GAHS > 9 identified the patients who may benefit from treatment of alcoholic hepatitis.

The mDF has high sensitivity (88.8%) but low specificity (35%) at score >32, at score >77 the specificity increased (55.55%) but sensitivity decreased (55.55%). Kulkarni et al[12] have also noted high mortality with score <32. Further mDF relies on absolute value of prothrombin time which varies significantly with different assays. Hence prediction of outcome is inaccurate.

The MELD score showed high sensitivity (100%) but very low specificity (12.5%) at score >11, and at score >27 the specificity increased (70%) due to increase in true negative value as noted by Dun et al. Further, it includes creatinine which limits its usefulness.

GAHS uses easily available biochemical and haematological parameters at bed side whereas mDF and MELD are difficult to calculate at bed side. Biopsy is not required for confirmation, which does not affect the accuracy as shown by Forrest et al. They also showed GAHS to be superior to mDF and MELD in predicting the outcome with higher specificity. The present study also showed that GAHS is more accurate than mDF and MELD in predicting the outcome. Further, the total WBC count, an inflammatory marker is not included in other scores, which with count > 15000/cmm is associated with more mortality as noted by Mathurin et al.[13]

Other parameters which predicted independently were bilirubin >5.5/dl ($p<0.001$), ascites ($p<0.001$), encephalopathy ($p<0.01$) as noted by Orrego H. et al[14] and Sheth M. et al.[15]

CONCLUSION

Glasgow Alcoholic Hepatitis Score (GAHS) is superior to mDF and MELD in sensitivity, specificity and accuracy in predicting mortality in alcoholic hepatitis and can be used to assess the prognosis.

REFERENCES

[1] MacSween RN, Burt AD. Histologic spectrum of alcoholic liver disease. Semin Liver Dis 1986;6(3):221-232.

[2] Cohen JA, Kaplan MM. The SGOT/SGPT ratio--an indicator of alcoholic liver disease. Diag Dis Sci 1979;24(11):835-838.

[3] Fletcher LM, Kwoh-Gain I, Powell EE, et al. Markers of chronic alcohol ingestion in patient with nonalcoholic steatohepatitis: an aid to diagnosis. Hepatology 1991;13(3):455-459.

[4] Carithers RL, Herlong HF, Diehl AM, et al. Methylprednisolone therapy in patients with severe alcoholic hepatitis. A randomized multicenter trial. Ann Intern Med 1989;110(9):685-690.

[5] O'Shea RS, McCullough AJ. Treatment of alcoholic hepatitis. Clin Liver dis 2005;9(1):130-134.

[6] Maddrey WC, Boitnott JK, Bedine MS, et al. Corticosteroid therapy of alcoholic hepatitis. Gastroenterology 1978;75(2):193-199.

[7] Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. Hepatology 2001;33(2):464-470.

[8] Dunn W, Jamil LH, Brown LS, et al. MELD accurately predicts mortality in patients with alcoholic hepatitis. Hepatology 2005;41(2):353-358.

[9] Forrest EH. Prognostic evaluation of alcoholic hepatitis. J Hepatol 2005;43(4):738-739.

[10] Forrest EH, Evans CD, Stewart S, et al. Analysis of factors predictive of mortality in alcoholic hepatitis and derivation and validation of the Glasgow alcoholic hepatitis score. Gut 2005;54(8):1174-1179.

[11] Lafferty H, Stanley AJ, Forrest EH. The management of alcoholic hepatitis: a prospective comparison of scoring systems. Aliment Pharmacol Therapy 2013;38(6):603-610.

[12] Kulkarni K, Tran T, Medrano M, et al. The role of the discriminant factor in the assessment and treatment of alcoholic hepatitis. J Clin Gastroenterol 2004;38(5):453-459.

[13] Mathurin P, Duchatelle V, Raymond MJ, et al. Survival and prognostic factors in patients with severe alcoholic hepatitis treated with prednisolone. Gastroenterology 1996;110(6):1847-1853.

[14] Orrego H, Israel Y, Blake JE, et al. Assessment of prognostic factors in alcoholic liver disease: toward a global quantitative expression of severity. Hepatology 1993;3(6):896-905.

[15] Sheth M, Riggs M, Patel T. Utility of the Mayo End-stage Liver Disease (MELD) scores in assessing prognosis of patients with alcoholic hepatitis. BMC Gastroenterol 2002;2:2.