

Original article:

Study of usefulness of Discriminant Function (DF) and Glasgow Alcoholic Hepatitis Score (GAHS) in treatment of patients of Alcoholic Hepatitis in Indian Population

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Abstract:

Introduction: The acute syndrome of alcoholic hepatitis is a severe, cholestatic liver disease that occurs in the setting of chronic alcohol abuse and carries a particularly poor prognosis with 28-day mortalities ranging from 30% to 50%.¹

Material and methods: The present study was conducted on 50 patients of Alcoholic Hepatitis admitted in Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune. Established in 1996, the College has a 1290 bedded well equipped own hospital, backed by a Research Centre.

Results: Discriminant Function (DF) and Glasgow Alcoholic Hepatitis Score (GAHS) was calculated in all the study subjects based on the laboratory investigations done on admission. All the 50 study cases had a DF score more than 32. A GAHS of 9 is commonly used as a cut-off to predict prognosis. In the present study, 29 (58%) cases had a GAHS of 9 or more while 21 (42%) cases had a GAHS less than 9.

Conclusion: The study confirms the overall usefulness of the GAHS. As demonstrated in various studies, this simple tool using readily available variables identifies patients with a poor prognosis.

Introduction:

The acute syndrome of alcoholic hepatitis is a severe, cholestatic liver disease that occurs in the setting of chronic alcohol abuse and carries a particularly poor prognosis with 28-day mortalities ranging from 30% to 50%.¹

The severity of alcoholic hepatitis is often assessed using the modified Maddrey's Discriminant Function (MDF). MDF greater than or equal to 32 is associated with a 68% 28-day survival in placebo-treated patients whereas those with a score less than 32 have a survival of 93%.¹ Recently described, the Glasgow Alcoholic Hepatitis Score (GAHS) for the

assessment of patients presenting with a clinical diagnosis of alcoholic hepatitis indicated that the GAHS was more accurate in predicting outcome at 28 and 84 days after admission, and was more specific for death, when compared with the MDF. With this background, the present research was conducted to study the demographic, clinical, biochemical and radiological profile of patients of Alcoholic Hepatitis and to determine the usefulness of Discriminant Function and Glasgow Alcoholic Hepatitis Score in its treatment with either Corticosteroid or Pentoxifylline.²

Material and methods:

The present study was conducted on 50 patients of Alcoholic Hepatitis admitted in Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune. Established in 1996, the College has a 1290 bedded well equipped own hospital, backed by a Research Centre.

The period of data collection was spread over 27 months from July 2014 to June 2016. After collection of data, the data entry forms were checked for their completeness and missing and incomprehensible data was rechecked from the respective participant profile. Data entry was done in MS Excel data sheet. This procedure was conducted over the period of 2 months. The data cleaning and the retrieval of the missing data were done over a period of one month. The collected data was analyzed over a three month period and the report writing was completed by end of September 2016.

Fifty cases diagnosed with Alcoholic Hepatitis admitted in Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune, were included in the study. Patients were included in the study after taking their voluntary informed consent. Both the genders were included.

Study subjects:

Inclusion criteria

Patients > 18 years of age with Alcoholic Hepatitis diagnosed on the basis of history, clinical features & laboratory parameters admitted in Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune.

Exclusion criteria

Patients positive for any viral markers for Viral Hepatitis.

Patients positive for ANA & Autoimmune Hepatitis.

Patients with Hepatocellular Carcinoma.

Patients with Drug-induced Hepatitis

The questionnaire included the information regarding age and gender, presenting complaints, clinical signs, past history, family history, drug history, personal history, alcohol history, general & systemic examination. Information regarding the laboratory parameters like the complete blood count, liver functions test, renal function test and radiological investigations were also included.

The Discriminant Function for acute alcoholic hepatitis was calculated using the following formula:

$$(4.6 \times [\text{prothrombin time} - \text{control time}]) + \text{serum bilirubin (mg/dl)}$$

with the prothrombin and control times in seconds

The Glasgow Alcoholic Hepatitis Score (GAHS) was calculated by using the table given below:

Score given	1	2	3
Age (years)	<50	≥50	-
WCC (10 ³ /μl)	<15	≥15	-
Urea (mg/dl)	<30	≥30	-
PT ratio or INR	<1.5	1.5–2.0	>2.0
Bilirubin (mg/dl)	<7.3	7.3–14.6	>14.6

The diagnosis of AH was done on the basis of history, clinical features, lab parameters and radiological findings.

Statistical Analysis

Data management and analysis was done using Microsoft excel and Epi-info software. The

frequency distribution and graph were prepared for the variables. The categorical variables were assessed using Pearson chi-square. The test was considered significant only if the P value comes out to be less than 0.05.

Results:

Table 1: Distribution of the study cases as per the DF and GAHS

Scores	Frequency	Percent
Discriminant Function >32	50	100.0
Glasgow Alcoholic Hepatitis Score		
<9	21	42.0
≥9	29	58.0
Total	50	100.0

Discriminant Function (DF) and Glasgow Alcoholic Hepatitis Score (GAHS) was calculated in all the study subjects based on the laboratory investigations done on admission. All the 50 study cases had a DF score more than 32. A GAHS of 9 is commonly used as a cut-off to predict prognosis. In the present study, 29 (58%) cases had a GAHS of 9 or more while 21 (42%) cases had a GAHS less than 9.

Table 2: Distribution of the study cases as per the treatment given

Treatment	Frequency	Percent
Corticosteroid	20	40.0
Pentoxifylline	30	60.0
Total	50	100.0

Table 8, shows distribution of the study cases as per the treatment given during admission. Among the 50 study subjects, 20 (40%) cases received Corticosteroid while 30 (60%) cases received Pentoxifylline. The same is shown below in a chart format.

Table 3: Comparison of outcome with DF and GAHS in both the treatment groups

Scores	Total	Treated with Corticosteroid	Treated with Pentoxifylline
	Frequency (%)	Frequency (%)	Frequency (%)
DF >32			
Survived	31 (62)	16 (80)	15 (50)
Died	19 (38)	4 (20)	15 (50)
GAHS			
<9			
Survived	16 (76.2)	6 (85.7)	10 (71.4)
Died	5 (23.8)	1 (14.3)	4 (28.6)
≥9			
Survived	15 (51.7)	10 (76.9)	5 (31.3)
Died	14 (48.3)	3 (23.1)	11 (68.8)
P value	0.039*	0.048#	0.028#

*P value obtained for Outcome versus GAHS is 0.039 using chi square test

#P value obtained for Outcome versus GAHS for different treatment categories. Yates correction applied as the expected values in one or more cell is less than 5.

Table 15, shows comparison of GAHS and survival rate in both the treatment categories. P value is significant indicating that the survival rate is better in cases having GAHS score <9. This is true for overall cases as well as for cases treated with Corticosteroid and Pentoxifylline. Based on table no 14 & table no 15, we can conclude that the survival is poor in cases having GAHS 9 or more and it is independent of the treatment given. Also, the survival is not affected or improved by treatment with either Corticosteroid or Pentoxifylline.

Discussion:

The DF & GAHS was calculated for all the study subjects based on the laboratory parameters done on admission. All the 50 study cases had a DF score > 32. GAHS cut off of 9 is commonly used to predict prognosis. In the present study, 29 (58%) cases were with GAHS

of 9 or more while 21 (42%) cases had a GAHS less than 9.

Among the 50 study subjects, 20 cases (40%) received Corticosteroid while 30 (60%) cases received Pentoxifylline. Pentoxifylline was given in patients who had contraindications to Corticosteroid like active infection, gastrointestinal bleed & congestive cardiac failure. Originally described in 1978 and then modified in 1989, the Discriminant Function (DF) was the first disease-specific score for alcoholic hepatitis.^{1,3}

The Glasgow Alcoholic Hepatitis Score (GAHS) has been developed as a disease-specific score for alcoholic hepatitis. The GAHS was derived from a population of 241 patients and validated in a population of 195 patients from throughout the United Kingdom. In its original description, it was found to be statistically superior to the DF.⁶³ Further data provided evidence that

patients with a GAHS ≥ 9 may benefit from treatment with corticosteroids, whereas those with a GAHS < 9 are unlikely to benefit from such treatment even if the DF is ≥ 32 .⁴

Current recommendations from the American College of Gastroenterology are that corticosteroid treatment should be considered for patients with an MDF greater than or equal to 32 (McCullough AJ et al⁵). Pentoxifylline can be given in cases with relative contraindication to Corticosteroid. The present study has shown that a GAHS greater than 9 is able to identify patients with Alcoholic Hepatitis who have an especially poor prognosis.

Recent studies have suggested using the Model For End-Stage Liver Disease (MELD) score to assess the severity of alcoholic hepatitis. In each of those studies, however, the MELD score on admission was not superior to the MDF⁶ on area under the curve analysis (Dunn W et al⁷, Sheth M et al, Srikureja W et al). In addition, none of those studies indicated whether the MELD score was a useful tool in identifying patients who may benefit from medical intervention over GAHS and MDF.⁸

Liver Function Test was done at the beginning and at the end of one week of treatment with either Corticosteroid or Pentoxifylline. There was a fall in Serum Bilirubin from 8.91 ± 4.12 at the start, to 7.00 ± 3.47 at the end of one week of Corticosteroid treatment. Similarly, in Pentoxifylline treated patients there was a fall in Serum Bilirubin from 10.57 ± 4.10 at the start, to 9.48 ± 4.69 at the end of one week of treatment. But the P value obtained for the fall in Serum Bilirubin in both the Corticosteroid (P value 0.714) & Pentoxifylline (P value 0.085) treated cases was statistically insignificant. Same was

the case with the other parameters of the liver function test.

Although only applicable to patients with an MDF greater than or equal to 32, a study by **Forrest E H et al** indicates that in patients with a GAHS less than 9 there was no appreciable benefit with corticosteroid treatment. Patients with a GAHS greater than or equal to 9, however, have an extremely poor prognosis if they are not treated with corticosteroids, or if such treatment is contraindicated. The prognosis is improved if they receive treatment or are eligible for such treatment.⁹

In this study, there was a fall in Serum Bilirubin & an improvement in the other parameters of the Liver Function Test at the end of one week of treatment with either Corticosteroid or Pentoxifylline. But since the P values obtained were not statistically significant we can say that there isn't much improvement in the Liver Function Test at the end of one week of treatment. Out of the 50 study cases, 31 (62%) cases survived. There were a total of 19 (38%) deaths of which 7 (14%) cases died within 7 days of admission and 12 (24%) cases died after 7 days of admission but during their hospital stay. The overall mortality rate was 38% and 7 day mortality rate was 14%.¹⁰

Out of the total 19 (38%) deaths, 4 (20%) cases were under Corticosteroid treatment while remaining 15 (50%) cases were on Pentoxifylline. P value (0.06) obtained was statistically insignificant indicating that the survival is not affected or improved by treatment with either Corticosteroid or Pentoxifylline.

Also, out of the 19 (38%) cases which died, 14 (48.3%) cases had GAHS ≥ 9 while 5 (23.8%) had a GAHS < 9 . P value was statistically significant indicating that the survival rate is

poor in cases with GAHS score ≥ 9 independent of the treatment given.

Conclusion:

The study confirms the overall usefulness of the GAHS. As demonstrated in various studies, this simple tool using readily available variables identifies patients with a poor prognosis.

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