Original Article

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Pathology Section

Hepatitis Activity Index and its Clinical and Biochemical Parameters in Liver Diseases- A Retrospective Study

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ABSTRACT

Introduction: Hepatitis Activity Index (HAI) is a scoring system devised by Ishak K et al., for grading and staging chronic hepatitis. The HAI provides a numerical score that is both objective and reproducible, it may be useful as either an alternative or supplement to the use of conventional pathological terminology in the study and management of chronic hepatitis patients.

Aim: To assess the efficiency of HAI scoring in the non neoplastic liver diseases by relating it with the clinical and biochemical parameters.

Materials and Methods: This retrospective study was conducted in the Department of Pathology at Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India, from 2010 to 2015. A total of 57 neoplastic cases and 41 non neoplastic cases were retrieved. The data was reassessed, HAI score and grade was noted and compared with the clinical and biochemical parameters. Chronic liver disease was classified as chronic viral hepatitis {Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV)} or cirrhosis. Alkaline phosphatase levels, Serum Glutamic Oxaloacetic Transaminase (SGOT) levels, Serum Glutamic Pyruvic Transaminase (SGPT) levels were analysed. Descriptive analysis was done and the data was represented as frequency and percentage in Microsoft Excel.

Results: Among the non neoplastic cases, 21 (51.2%) belonged to hepatitis and cirrhosis and 20 (48.8%) belonged to others. In patients with high alkaline phosphatase levels, the predominant HAI score was 4. In cases with high SGOT levels, the predominant HAI score was 5 and 6. In cases with high SGPT levels, the HAI score was 5,6, and 7.

Conclusion: The HAI is useful in assessing the extent of active inflammation. It gives an objective guideline to the treating physician. The HAI score in combination with clinical and biochemical parameters offers a better insight into disease severity.

Keywords: Cirrhosis, Fibrosis, Ishak scoring, Inflammation, Management, Neoplastic

INTRODUCTION

It is reported that around 400 million people are suffering from chronic Hepatitis B Virus (HBV) infection worldwide and in upto 40% of these cases cirrhosis has set in and the patients have progressed to end stage liver disease [1,2].

Chronic Active Hepatitis (CAH) is a "necro-inflammatory lesion of the liver diagnosed by characteristic pathologic changes in the liver biopsy specimen." In the early reports of these patients the clinical and biochemical alterations often accompanying this disease were emphasised; they described the poor prognosis associated with severe CAH, and also provided an outline of the treatment regimens; however, they were associated with significantly decreased mortality and morbidity [3-6]. Recent reports suggest that severe CAH patients represent only a small percentage of the total population whose liver biopsy specimens are interpreted as having CAH [7,8]. Many of these patients are completely free of any clinical symptoms and are reported to have only mild alterations in serum aminotransferases, y-globulin, and bilirubin. The natural history of asymptomatic CAH is yet to be understood totally and any guidelines for treatment have yet to be established.

Chronic hepatitis needs to be graded, based on the degree of inflammation and hepatocellular injury; this condition may lead to the fibrosis stage. The end stage of chronic hepatitis is cirrhosis with clinical decompensation [9,10].

Hepatitis Activity Index (HAI) grading and staging are two vital scores that determine the mild, moderate or the severe nature of the disease [11]. Though several scoring systems have been developed and are in use Ishak scoring system is more popular [12]. Conventional clinical and pathological descriptions of histology of serial liver biopsy specimens do not readily provide definitive endpoints for statistical analysis. The HAI provides a numerical score that is both objective and reproducible, it may be useful as either an alternative or supplement to the use of conventional pathological terminology in the study and management of chronic hepatitis patients in whom histological changes in serial liver biopsy specimens may be the only prognostic indicator available for evaluation.

Hence, this study was performed to assess the efficiency of HAI scoring in the non neoplastic liver diseases by relating it with the clinical and biochemical parameters.

MATERIALS AND METHODS

A retrospective study was performed with the liver biopsy data reported in the Department of Pathology over a period of 5 years from 2010 to 2015. This study was conducted at Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India. The Institutional Ethical Committee approved the conduct of the study (Ref: CSP-MED/13/JUN/07/35).

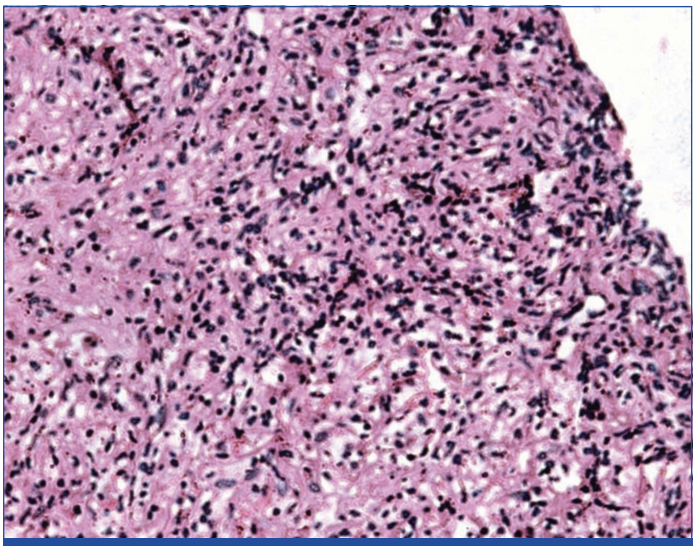
Inclusion and Exclusion criteria: The non neoplastic cases of hepatitis and cirrhosis were identified, reassessed, HAI score and grade noted as per Ishak scoring system [12], and compared with the clinical and biochemical parameters. All non neoplastic cases were identified and included in the study. All neoplastic cases were excluded from the study.

Procedure

Liver biopsy samples were embedded in paraffin. Sections were stained with Haematoxylin and Eosin (H&E), Perls, and Reticulin stain. As half of the liver sample is frozen for virologic studies, the mean sizes of the initial and final biopsy specimens were 15.6±7.5 mm and 17±6.5 mm. Chronic liver disease was classified as chronic viral hepatitis {Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV)} or

cirrhosis. The cirrhosis cases were further confirmed using the special stain- Massons Trichome [Table/Fig-1]. Necro inflammatory activity and fibrosis were semi-quantitatively assessed according to the HAI score. Histologic analyses were performed by the same pathologist using current technical conditions.

- Clinical parameters such as age, gender, aetiology of hepatitis were recorded.
- Biochemical parameters such as alkaline phosphatase levels, Serum Glutamic Oxaloacetic Transaminase (SGOT) levels, Serum Glutamic Pyruvic Transaminase (SGPT) levels were recorded.
- Hepatitis Activity Index (HAI) grading and staging are two vital scores that determine the mild, moderate or severe nature of the disease [11]. Though several scoring systems have been developed and are in use but Ishak K et al., scoring system is more popular [12].



[Table/Fig-1]: Special stain- Massons Trichrome showing cirrhosis in liver biopsy (H&E stains, X100).

STATISTICAL ANALYSIS

Hepatitis activity index score was considered as outcome variable of interest. The descriptive analysis was done and the data was represented as frequency and percentage. Microsoft Excel was used for statistical analysis.

RESULTS

The mean age of the study population was 42.1 years. Among the 98 evaluated cases of liver biopsy, 57 cases were neoplastic (58.16%) and 41 cases were non neoplastic (41.84%). Among the non neoplastic cases, chronic liver diseases like hepatitis and cirrhosis in which HAI scoring was done were 21 cases (51.2%) and cases with infectious aetiology, vascular lesions, and storage disorders constituted the other 20 (48.7%) cases [Table/Fig-2]. In the chronic liver diseases, majority of the cases (n=6) were due to alcohol intake, followed by three cases of Hepatitis B, two cases of biliary cirrhosis, and one case of Hepatitis C.

Liver biopsy cases evaluated	Number of cases (n)	Percentage (%)
Neoplastic	57	58.16%
Non neoplastic	41	41.84%
• Hepatic and cirrhosis	21	51.21%
• Other infectious aetiology	20	48.78%

[Table/Fig-2]: Summary of total liver biopsy.

Biochemical markers: Alkaline phosphatase levels were less than 200 in 14 cases and more than 300 in four cases. Serum Glutamic Oxaloacetic Transaminase (SGOT) levels were below 100 in 14 cases and ≥100 in seven cases. Serum Glutamic Pyruvic Transaminase (SGPT) levels were less than 100 in 17 cases and ≥100 in four cases [Table/Fig-3]. In cases with high alkaline phosphatase levels (n=6) the predominant HAI score was 4. In cases with high SGOT levels (n=6) the predominant HAI score was 5 and 6. In cases with high SGPT levels (n=3) the HAI score was 5,6, and 7. The predominant HAI scores were score 2 and 3 and the predominant HAI stage was stage 4. The total HAI score was 2 and 3 among 19.05% respectively. Based on HAI staging, 47.6% of the participants had stage 4 i.e. cirrhosis [Table/Fig-4]. The management of the patients based on the HAI scoring has been mentioned in [Table/Fig-5].

Variables	Number of cases (n)	Percentage (%)
Age distribution		
<20 years	2	9.52
20 to 30 years	1	4.76
31 to 40 years	5	23.81
41 to 50 years	9	42.86
51 to 60 years	3	14.29
>60 years	1	4.76
Gender		
Male	15	71.43
Female	6	28.57
Aetiology		
Hepatitis B	3	14.29
Hepatitis C	1	4.76
Alcohol	6	28.57
Biliary cirrhosis	2	9.52
Cause not identified	9	42.86
Alkaline phosphatase levels (IU/L)		
<200	14	66.67
200-300	3	14.29
>300	4	19.05
SGOT levels (units/litre)		
<100	14	66.67
≥100	7	33.33
SGPT levels (units/litre)		
<100	17	80.95
≥100	4	19.05

[Table/Fig-3]: Summary of baseline parameters in hepatic cirrhosis group (n=21).

HAI score	Number of cases (n)	Percentage (%)
Periportal/periseptal interface hepatitis (piecemeal necrosis)		
Score 0	2	9.52
Score 1	9	42.86
Score 2	7	33.33
Score 3	2	9.52
Score 4	1	4.76
Confluent necrosis		
Score 0	17	80.95
Score 1	4	19.05
Focal (spotty) lytic necrosis, apoptosis, and focal inflammation		
Score 0	13	61.90
Score 1	6	28.57
Score 2	1	4.76
Score 3	1	4.76
Score 4	0	0
Portal inflammation		
Score 0	4	19.05
Score 1	8	38.10

Score 2	6	28.57
Score 3	2	9.52
Score 4	1	4.76
Total score		
Score 0	1	4.76
Score 1	2	9.52
Score 2	4	19.05
Score 3	4	19.05
Score 4	3	14.29
Score 5	1	4.76
Score 6	3	14.29
Score 7	2	9.52
Score 8	0	0
Score 9	1	4.76
Score≥10	0	0
HAI stage		
Stage 0 (No Fibrosis)	4	19
Stage 1 (Portal Fibrosis with or without short fibrous septa)	5	23.8
Stage 2 (Fibrous septa)	1	4.8
Stage 3 (Transition to cirrhosis)	1	4.8
Stage 4 (Cirrhosis, probable or definite)	10	47.6

[Table/Fig-4]: Summary of HAI score (N=21).

Hepatitis activity index score	Management
Stage 0	Follow-up
Stage 1	Medical intervention
Stage 2	Medical intervention
Stage 3	Medical and surgical intervention
Stage 4	Surgical intervention

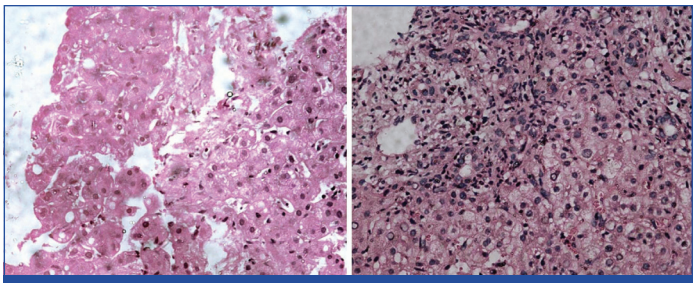
[Table/Fig-5]: The patients further referred for management based on the HAI scoring.

DISCUSSION

This study evaluated liver biopsy specimens using HAI scoring system. The study's findings proved that HAI scoring system can aid in assessing the severity of the disease and in the diagnosis and management. In this current study, 21 out of the total 98 liver biopsy showed hepatic cirrhosis. Among the 21 samples, 42.86% aetiology was not identified, followed by 28.57% alcoholic aetiology and 14.29% had hepatitis B viral aetiology. Among them, 66.67% had alkaline phosphatase levels less that 200 and SGOT less than 100 respectively. The SGPT was less than 100 in 80.95% of the specimens.

In most forms of chronic liver diseases, the pathologists are expected to assign a grade and stage as part of the evaluation of the liver biopsy as it will help in predicting the patient outcome [13]. There are many simple grading systems like International Association for the Study of the Liver (IASL), metavir activity score,and Batts-Ludwig score but the information conveyed to the clinician from these systems are limited and hence in the present study authors have used the Ishak hepatitis activity index (HAI) score as it provides more information than the other scoring systems [14-16].

The HAI scoring is done based on four major histopathological parameters. First, periportal of interface hepatitis graded as absent, mild (focal, few), moderate and severe with scores ranging from 0 to 4. Second, confluent necrosis [Table/Fig-6] graded as absent, focal, zone 3 necrosis in some area, necrosis in most area, necrosis with occasional portal central bridging, necrosis with multiple bridging and panacinar necrosis with scores from 0 to 4. Third, Focal lytic necrosis graded as one focus, two foci, five to ten and more than ten foci in 10 power objectives with score range 0 to 4. Lastly, portal inflammation as mild, moderate, sever and marked with scores 0 to 4. Based on this scoring and grading in this current study, periportal or periseptal interface hepatitis [Table/Fig-7] was seen in majority of cases (42.86%) with score 1, the confluent necrosis in majority of the cases (80.96%) was score 0, the focal lytic necrosis, apoptosis and focal inflammation in majority of cases (61.90%) was score 0 and portal inflammation in majority of cases (38.10%) was score 1. The predominant HAI score in the present study was score 2 and 3 and the predominant stage in this study was stage 4 (10 cases).



[Table/Fig-6]: Section of liver biopsy showing confluent necrosis (H&E stain, X100).
[Table/Fig-7]: Section of liver biopsy showing Interface hepatitis (H&E stain, X100). (Images from left to right)

This current study related the HAI score with the biochemical markers. In cases with high alkaline phosphatase levels six cases the predominant HAI score was 4. In cases with high SGOT levels (six cases) the predominant HAI score was 5 and 6. In cases with high SGPT levels (three cases) the HAI score was 5,6 and 7. Highest HAI score in patients with elevated liver enzymes was 7. Highest HAI score in patients with cirrhosis was 9.5. Cirrhosis cases had low serum enzyme levels. Eleven patients with low serum enzymes had HAI score ≥2.

The management in the current study was done based on the HAI scoring system. Patients in stage 0 was advised for follow-up, stage 1 and 2 patients were managed with medical intervention, stage 3 patients with both medical and surgical intervention and stage 4 with surgical intervention. Hence, the management of the condition can be done based on this scoring.

Previous studies in literature have insisted on the need for using a histopathological scoring system in diagnosing chronic hepatitis and cirrhosis [12-14]. The scoring can also aid in determining the prognosis of the patients. Patients with initial high scores were observed to have guarded prognosis [17]. The HAI score should be related with the aetiology of the disease and the biochemical parameters.

Limitation(s)

The limitation of the current study is its retrospective nature, hence clinical follow-up of the patients was not possible. Large prospective studies with clinical and biochemical correlation is recommended in further.

CONCLUSION(S)

Based on this study findings, HAI score in combination with the clinical and biochemical parameters can give more information for the therapeutic intervention and management of patients. Hence, utilisation of HAI score in routine reporting of liver biopsy is recommended.

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