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A Comparative Analysis of Scheuer Scoring System and Ishak Modified Histological Activity Index in Assessing Inflammation and Fibrosis from Liver Biopsies of Patients with Chronic Hepatitis

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KEYWORDS

Liver biopsy, chronic hepatitis, fibrosis, scoring systems, necroinflammation

ABSTRACT:

Introduction: Chronic hepatitis is characterized by any biochemical, serological or clinical evidence of persistent or recurring liver disease lasting over six months. Histological evaluation through liver biopsy remains essential for grading and staging of the disease. Among the established scoring systems, the Ishak modified histological activity index (HAI) and the Scheuer system are widely used; yet, comparative data on their concordance remain limited.

Objectives: To determine the utility of the Ishak modified HAI system in comparison to the Scheuer system in determining the grade and stage in liver biopsies of patients with chronic hepatitis

Methods: A total of 31 liver biopsies were included in the study. Each biopsy was independently scored using the Ishak Modified HAI and Scheuer system. Inter-system agreement was measured using Cohen's kappa. Clinical and biochemical data, including transaminase levels, were also evaluated.

Results: There were 19 females and 12 males. Their mean age was 44.5. Cohen's kappa indicated a slight agreement for necro-inflammatory activity i.e grading (0.08) and moderate agreement for fibrosis i.e staging (0.2). The Ishak system offered more detailed stratification, particularly in intermediate stages.

Conclusions: The study concluded that both the systems are nearly equally effective for grading and staging. The level of agreement was more in terms of staging compared to grading. Ishak graded lower than Scheuer in most of the cases, while staging was seen to be higher than the Scheuer system.

1. Introduction

Chronic hepatitis is characterized by any biochemical, serological, or clinical evidence of persistent or recurring liver disease lasting over six months [1]. Millions of people worldwide are impacted by this serious global health issue, which is typified by chronic liver inflammation that can lead to cirrhosis, fibrosis, and eventually, liver failure if treatment is not received. Usually, biochemical indicators, serological testing, and clinical signs are used to make the diagnosis. Nonetheless, histopathological analysis continues to be the most reliable method for determining the extent of liver injury and directing the development of suitable treatment plans [2–8]. Histological evaluation of chronic hepatitis entails staging the degree of fibrosis and evaluating the degree of necroinflammation. In addition to helping physicians assess disease progression and the efficacy of drug therapy, these parameters offer vital prognostic information [9, 26]. To standardize the assessment of liver biopsies and guarantee uniformity in grading and staging across various investigations and clinical contexts, a number of histological scoring systems have been created. Among these, the Ishak Modified Histological Activity Index (HAI) and the Scheuer scoring system are quite commonly used for evaluating liver fibrosis and inflammation [8,11]. A widely followed and rather easy-to-understand technique in standard clinical practice is the Scheuer grading system. By classifying liver samples according to the degree of fibrosis and inflammation, it is a useful tool for overall evaluation [2, 7]. However, because of its simplicity, it cannot always identify small differences in the course of the disease, which could have important clinical implications. The Ishak Modified HAI, on the other hand, offers a more thorough assessment of liver histology and a more extensive scoring system. This approach provides a detailed evaluation of fibrosis and necro-inflammatory activity by combining several criteria. Despite being widely used in research settings, its intricacy has made it questionable if it can be used in ordinary clinical settings [9, 11, 16]. Considering the significance of thorough histological evaluation in chronic hepatitis, it is essential to ascertain the comparative efficacy of these two scoring systems. A comparative examination of the Scheuer scoring system and the Ishak Modified HAI may yield insights into their utility, reliability, and clinical application. To the best of our knowledge, a limited number of studies have

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assessed the comparative efficacy of the Scheuer and Ishak Modified HAI scoring systems in evaluating the grade and stage of chronic hepatitis [4]. This study aims to ascertain if the Ishak Modified HAI provides enhanced diagnostic accuracy and prognostic significance relative to the Scheuer system by examining biopsies from the liver of patients with chronic hepatitis due to any etiology. The study will also examine the possible benefits and drawbacks of each system, ultimately informing best practices for histopathological assessment in chronic hepatitis.

2. Objectives

To determine the utility of Ishak modified HAI in comparison to the Scheuer system in determining the grade and stage in liver biopsies of patients with chronic hepatitis

3. Methods

The study included liver biopsies from 31 patients with chronic hepatitis. Among these, 5 individuals tested positive for hepatitis B markers, whereas 1 patient tested positive for hepatitis C markers. The remaining 25 patients showed a range of possible etiologies, which were evaluated on the biopsy. All 31 liver biopsies were found adequate for study. Biopsies that were at least 1.5 cm in length and those that had at least three to five portal tracts were included in this study. The slides were stained using routine Hematoxylin and Eosin. Special stains like Masson's trichrome and Gordon and Sweets reticulin stain was used to demonstrate the architectural and fibrotic features. Other special stains were also carried out as required. Biopsies were then assessed for necro-inflammatory changes and fibrosis and scored using the Scheuer system and Ishak index. The scores were compared and correlated with the etiology and clinicopathological features. The utility of the Ishak modified HAI was then compared against the Scheuer scoring system. Following a discussion of the points of difference for comparing different classifications and statistical computations, a consensus score was calculated. Based on the numerical score that was finally assigned, the cases were then grouped into minimal (0-3), mild (4-8), moderate (9-12) and severe (13-18) to enable a comparison of the Ishak modified HAI necroinflammation with the four composite scores of the Scheuer system (41). Similarly, to assess the stage the scores were categorized into 4 categories in Ishak system – mild (1), moderate (2), marked (3 – 4) and pre-cirrhotic (5 – 6) and Scheuer system – minimal (0), mild (1), moderate (2), marked (3) and pre-cirrhotic (4). The level of agreement between the different scoring systems for chronic hepatitis, including the grade and stage, was determined using the weighted kappa test (K). The threshold level of significance was defined as P-values of less than 0.05.

4. Results

This study was conducted over a period of 42 months and included 31 patients. There were 19 females and 12 males (Male: Female ratio = 1:2). Their mean age was 44.5 (range was from 25 – 64). Out of 31 patients, the majority of them (41.94%, 13/31) were being evaluated for episodes of recurrent jaundice. The next most likely cause was observed to be a Hepatitis B virus infection (19.35%, 6/31). These patients tested positive for HBsAg. Hepatitis C was found as the cause in 3.23% of the patients (1/31) **(Figure 1).** The serum transaminases (SGOT and SGPT) levels were normal in 20 patients (64.52%), increased twofold in 8 patients (25.81%) and elevated threefold in 3 patients (9.68%). All of the biopsies' relative comparisons using the two scoring systems are demonstrated in **Table 1.** On histological examination, the biopsies showed varying degrees of portal inflammation, interface hepatitis and fibrosis. **Table 2** shows the comparison of the necro-inflammatory activity (grade) of the two systems. Weighted kappa was calculated to be 0.08 which indicated a slight agreement. However, the p-value was not found to be statistically significant (0.29).

Table 3 demonstrates the comparison between the fibrosis (stage) of the two systems. Weighted kappa was calculated to be 0.21 which indicated a moderate agreement between the two scoring systems in terms of staging. p-value was found to statistically significant (0.03).

5. Discussion

Chronic hepatitis is characterized by histologically confirmed inflammation, necrosis, and fibrosis, as well as biochemical, serological, or clinical indications of ongoing or recurrent liver illness for longer than six months [1, 8].

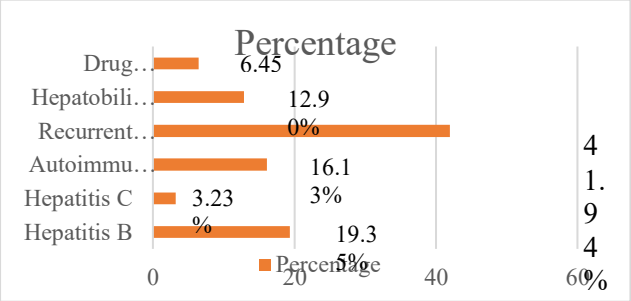

Figure1: Most likely etiologies

	Scheuer system		Ishak modified HAI	
	Necro-inflammation (grade)	Fibrosis (stage)	Necro-inflammation (grade)	Fibrosis (stage)
1	05-Aug	01-Apr	Aug-18	02-Jun
2	03-Aug	01-Apr	Jun-18	02-Jun
3	01-Aug	01-Apr	Feb-18	01-Jun
4	01-Aug	02-Apr	Jan-18	02-Jun

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5	03-Aug	03-Apr	Jun-18	06-Jun
6	0/8	0/4	0/18	0/6
7	06-Aug	03-Apr	Aug-18	03-Jun
8	05-Aug	0/4	Oct-18	0/6
9	02-Aug	0/4	Apr-18	0/6
10	03-Aug	01-Apr	Feb-18	02-Jun
11	04-Aug	02-Apr	Sep-18	03-Jun
12	05-Aug	03-Apr	Oct-18	05-Jun
13	03-Aug	02-Apr	Mar-18	03-Jun
14	03-Aug	02-Apr	May-18	03-Jun
15	06-Aug	01-Apr	Sep-18	02-Jun
16	04-Aug	01-Apr	May-18	02-Jun
17	02-Aug	03-Apr	Mar-18	03-Jun
18	01-Aug	0/4	Mar-18	0/6
19	04-Aug	03-Apr	Aug-18	03-Jun
20	04-Aug	02-Apr	Jul-18	02-Jun
21	02-Aug	01-Apr	Mar-18	01-Jun
22	04-Aug	02-Apr	May-18	02-Jun
23	01-Aug	0/4	Feb-18	0/6
24	04-Aug	02-Apr	Apr-18	02-Jun
25	03-Aug	02-Apr	Apr-18	02-Jun
26	02-Aug	01-Apr	Mar-18	01-Jun
27	02-Aug	0/4	Feb-18	0/6
28	04-Aug	02-Apr	Jul-18	02-Jun
29	03-Aug	02-Apr	Mar-18	01-Jun
30	04-Aug	02-Apr	Apr-18	03-Jun
31	01-Aug	01-Apr	Jan-18	02-Jun

Table 1: Scores of grade and stage of liver biopsies

Table 2: Comparison of necroinflammatory activity (grade)

	Ishak Modified HAI			
Scheuer scoring system	Minimal (0-3)	Mild (4-8)	Moderate (9-12)	Severe (13-18)
Minimal (0-1)	6 (19.35%)	0	0	0
Mild (2)	4 (12.9%)	1 (3.2%)	0	0
Moderate (3)	3 (9.7%)	4 (12.9%)	0	0
Severe (4)	0	8 (25.9%)	4 (12.9%)	1 (3.2%)
Total	13 (42%)	13 (42%)	4(12.9%)	1(3.2%)

Table 3: Comparison of the fibrosis (stage)

	Ishak stage			
Scheuer stage	1 (mild)	2 (moderate)	3 (marked)	4 (cirrhosis)
1 (mild fibrosis)	6 (19.4%)	0	0	0
2 (moderate fibrosis)	3 (9.7%)	5 (16.1%)	0	1 (3.2%)
3 (marked fibrosis)	1 (3.2%)	13 (42%)	0	2 (6.5%)
4 (cirrhosis)	0	0	0	0
Total	10 (32.2%)	18 (58%)	0	3 (9.7%)

Every patient has a different morphological pattern of liver tissue damage, and many researchers in hepatobiliary pathology noted that not all instances of chronic hepatitis exhibited a consistent downward trajectory [21]. **de Grote et al**. [20] used this information in 1968 to distinguish between chronic persistent and chronic aggressive hepatitis. However, it was ultimately decided to categorise it into three main etiological components—grade, stage, and etiology—after the discovery of numerous aetiological agents during the past 20

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years. Chronic hepatitis is now known to have a variety of causes including viral, autoimmune, alcoholic, drug-induced, and cryptogenic causes [1, 8]. The Knodell Index, the inaugural system of its kind, was established in 1981 and widely recognized as the benchmark for objective, partially quantitative, and repeatable descriptions of various morphological abnormalities associated with chronic hepatitis [2]. Ishak's modified HAI, is a more contemporary version of Knodell's HAI that was first developed in 1995. This offers successive scores for distinct lesions in four different categories, which are then combined to determine the activity grade. Scheuer's scoring system was primarily intended for chronic viral hepatitis; however, similar to Knodell, it is also widely used for hepatitis due to different etiologies [7]. The current study sought to determine the level of concordance between the two methods regarding both grading (necro-inflammatory activity) and staging (fibrosis). The study demonstrated that while the assessment of necro-inflammatory change showed a slight concordance only between the two systems, the staging or the fibrosis score showed a moderate level of concordance. These findings are similar to a study conducted **by Rosario et al** [9]. The fact that the two scoring methods do not use the same criteria for evaluation for necro-inflammation is probably the cause of the discordance between them regarding the necro-inflammatory activity. In order to determine a necro-inflammatory score, the Ishak system evaluates interface hepatitis (piecemeal necrosis), confluent necrosis, focal lobular necrosis or apoptosis or inflammation, and portal inflammation.

However, the Scheuer system only evaluates portal inflammation, interface hepatitis and lobular activity when determining an activity score.

One possible reason for the lack of agreement between the two systems could be due to the fact that the Scheuer system does not take into consideration confluent necrosis or apoptosis when assigning an activity score. Other subjective findings that are difficult to quantify were also produced by comparing the two scoring systems. The numerical score for the Ishak system varies greatly. To make comparison with the Scheuer activity score easier, the final score had to be divided into 4 categories: minimal, mild, moderate, and severe. For the purpose of this study, the scores of each individual category of Ishak modified HAI could be compared with those of Scheuer system as follows - In the Ishak system, lobular necrosis scores of one and two corresponded to a

Scheuer system score of one, whereas a Scheuer score of two in the corresponding group was similar to scores of three and four (with or without bridging necrosis). A score of one in Scheuer was equal to an interface hepatitis score of one in the Ishak system, scores two and three to two, and score four to three, respectively, in the Scheuer system. In terms of fibrosis, score one and two of Ishak corresponded to score one of Scheuer, three and four of Ishak corresponded to score two of Scheuer, five and six to three and four of Scheuer, respectively.

There were a few problems encountered in the study. The first one was assigning scores for lobular activity. Lobular activity is evaluated in Ishak's system as spotty necrosis and is assigned a separate grade, whereas in Scheuer lobular activity is included as a part of an overall grade and does not have a separate score. Even with expert-applied scoring systems, the second issue—observer variation—was statistically insignificant in terms of reproducible outcomes. These results were consistent with previous publications, as demonstrated by **Bedossa et al**. [22]. Overall, it was found that fibrosis scoring is more consistent than necro-inflammatory scoring.

Both of these scoring systems have advantages and pitfalls. There is currently none that makes use of all available clinical, etiological, and histological data. An etiological diagnosis that takes into account all available serological and biochemical evidence should be included in the diagnosis statement. The etiological diagnosis should be based on a verbal approximation of the fibrosis stage and necro-inflammatory activity. For research purposes, the detailed system, the Ishak Modified HAI, is more appropriate. This system is more demanding and thus more likely to produce disparities between and within observers for ordinary clinical practice. The more straightforward one, such as Scheuer system, might be utilized for routine reporting while still providing clinicians with valuable information for patient follow-up.

6. Conclusion

It is concluded that both the methods are nearly equally effective for staging and grading however, the level of agreement was more in terms of staging as compared to grading. Ishak modified HAI graded lower than Scheuer in most of the cases, while staging was seen to be higher than in Scheuer system. Liver biopsies continue to be the foundation for determining the outcomes and management of patients, even in the face of advancements in other diagnostic procedures.

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