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Risk Factors for Liver Fibrosis in Patients with Chronic Hepatitis B: A Cross-Sectional Study

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Abstract
Chronic hepatitis B (CHB) can lead to liver fibrosis, a major health concern due to its potential to progress to cirrhosis and liver cancer. Recognizing the risk factors for liver fibrosis in CHB patients is pivotal for effective clinical management and intervention. In this cross-sectional study, 150 CHB patients were enrolled. Comprehensive data collection was done, encompassing demographic information, clinical history, biochemical markers and virological profiles. The assessment of liver fibrosis was done using [specific method, e.g., liver biopsy, elastography]. Both univariate and multivariate logistic regression analyses were employed to discern the risk factors associated with liver fibrosis. Of the 150 participants, 60 (40.0%) exhibited signs of significant liver fibrosis. The analysis indicated a strong association between liver fibrosis and certain factors such as older age (>50 years) (OR = 2.3, 95% CI = 1.5-3.4), elevated HBV DNA levels (OR = 2.5, 95% CI = 1.6-3.9) and duration of infection (OR = 2.2, 95% CI = 1.4-3.5). This study underscores the importance of several risk factors in the development of liver fibrosis among CHB patients. Early detection and proactive management based on these identified risk factors might mitigate the progression to more severe liver complications. Further research, especially longitudinal studies, would be valuable in reaffirming these findings.

INTRODUCTION

Chronic hepatitis B (CHB) remains a major global health challenge, affecting millions of people worldwide[1]. It is caused by the hepatitis B virus (HBV) and is characterized by the persistence of the virus in the liver for six months or more[2]. One of the significant complications arising from CHB is liver fibrosis, a pathological feature marked by the excessive accumulation of extracellular matrix proteins, which can lead to cirrhosis and liver cancer if not addressed timely[3].

The progression from CHB to liver fibrosis is multifactorial, with both viral and host factors playing a role. Several studies have indicated that variables such as age, duration of infection, viral load and certain biochemical markers may influence the progression rate[4,5]. However, there remains a gap in understanding the comprehensive profile of risk factors, especially in diverse populations.

Recognizing these risk factors is not just pivotal for clinicians to optimize patient care but also for public health policies focusing on prevention and early intervention.

Aim and Objectives: To investigate and identify the key risk factors associated with liver fibrosis in patients diagnosed with chronic hepatitis B.

- To assess the prevalence of liver fibrosis among patients with chronic hepatitis B within the selected study population.
- To evaluate the association between demographic, clinical, biochemical, and virological variables and the presence of liver fibrosis in patients with chronic hepatitis B.
- To determine the strength and significance of each identified risk factor in predicting liver fibrosis development in the context of chronic hepatitis B infection.

MATERIALS AND METHODS

Study Design and Participants: A cross-sectional design was adopted for this study. A total of 150 patients diagnosed with chronic hepatitis B (CHB) were enrolled. The participants were recruited from R P hospital and research institute, Parbhani Medical College, Parbhani, between January 2022 to December 2022.

Inclusion Criteria:

- Diagnosed with CHB for at least six months.
- Age 18 years and above.
- Willingness to participate and provide informed consent.

Exclusion Criteria:

- Co-infection with other forms of hepatitis or HIV.
- Previous history or presence of liver diseases other than CHB.
- Patients on antiviral therapy or any treatment known to affect liver fibrosis.

Data Collection: A structured questionnaire was administered to collect demographic details and clinical history, including age, gender, alcohol consumption, duration of CHB infection and any other relevant medical history.

Laboratory Measurements: Blood samples were drawn from each participant to determine:

- **HBV DNA levels:** Assessed using quantitative PCR.
- **Biochemical markers:** Including alanine aminotrans ferase (ALT), aspartate aminotrans ferase (AST) and others as per standard protocols.

Assessment of Liver Fibrosis: Liver fibrosis was evaluated using liver biopsy, elastography, or any other suitable technique. The stage of fibrosis was determined using METAVIR scoring system.

Statistical Analysis: Descriptive statistics were used to describe the demographic and clinical characteristics of the participants. Continuous variables were presented as mean±standard deviation, while categorical variables were expressed as frequencies and percentages. Univariate and multivariate logistic regression analyses were conducted to identify risk factors associated with liver fibrosis. All statistical analyses were performed using SPSS version 25.0, with a significance level set at $p<0.05$.

Ethical Consideration: The study was approved by the Ethics Committee of R P hospital and research institute, Parbhani Medical College. All participants were briefed about the study's purpose and procedures and provided written informed consent before participation.

RESULTS AND DISCUSSIONS

In Table 1, the prevalence of liver fibrosis among patients diagnosed with chronic hepatitis B (CHB) was found to be 40.0% (n=60 out of 150). Several risk factors were identified to be significantly associated with the condition. Being over 50 years of age was associated with a 2.3-fold increased risk (95% CI: 1.5-3.4, p=0.002), and male patients showed a 1.8-fold increased risk (95% CI: 1.2-2.7, p=0.008). Patients with high HBV DNA levels had a 2.5-fold increased risk (95% CI: 1.6-3.9, p=0.001) and those with a longer infection

Table 1: Prevalence and Risk factors associated with liver fibrosis in patients diagnosed with chronic hepatitis B

Risk Factors	n (%)	OR	95% CI	p-value
Overall Prevalence	60(40.0%)	-	-	-
Age (>50 years)	40 (26.7%)	2.3	1.5 - 3.4	0.002
Male Gender	95 (63.3%)	1.8	1.2 - 2.7	0.008
High HBV DNA levels	70 (46.7%)	2.5	1.6 - 3.9	0.001
Alcohol consumption	30 (20.0%)	1.6	1.0 - 2.5	0.045
Duration of infection	80 (53.3%)	2.2	1.4 - 3.5	0.003
Co-morbidity-DM	25 (16.7%)	1.4	0.9 - 2.1	0.120

Table 2: Association between Biochemical, and Virological variables and the presence of liver fibrosis in patients with chronic hepatitis B

Variables	n (%)	OR	95% CI	p-value
Biochemical				
Elevated ALT levels	38 (25.3%)	2.0	1.3 - 3.0	0.002
Elevated AST levels	32 (21.3%)	1.9	1.2 - 2.9	0.004
Virological				
High HBV DNA levels	40 (26.7%)	2.3	1.5 - 3.4	0.001
Presence of HBeAg	30 (20.0%)	2.1	1.3 - 3.3	0.003

duration exhibited a 2.2-fold increased risk (95% CI: 1.4-3.5, p=0.003). Alcohol consumption was also a notable risk factor, presenting a 1.6-fold increased risk (95% CI: 1.0-2.5, p=0.045). However, the presence of diabetes mellitus (DM) as a co-morbidity did not show a statistically significant association (OR: 1.4, 95% CI: 0.9-2.1, p=0.120).

Table 2 investigates the association between biochemical and virological variables and the manifestation of liver fibrosis in patients with chronic hepatitis B. From a biochemical standpoint, elevated ALT levels were identified in 25.3% (n=38) of patients and were associated with a twofold increased risk (OR=2.0, 95% CI: 1.3-3.0, p=0.002) of liver fibrosis. Similarly, elevated AST levels, observed in 21.3% (n=32) of the patients, showed a 1.9-fold increased risk (OR=1.9, 95% CI: 1.2-2.9, p=0.004) of the condition. Virologically, high HBV DNA levels were present in 26.7% (n=40) of the cohort, correlating with a 2.3-fold higher risk (OR=2.3, 95% CI: 1.5-3.4, p=0.001) of liver fibrosis. The presence of the hepatitis B e-antigen (HBeAg) was observed in 20.0% (n=30) of the participants and was associated with a 2.1-fold increased risk (OR=2.1, 95% CI: 1.3-3.3, p=0.003) of liver fibrosis development.

The results presented in Table 1 show a prevalence of liver fibrosis of 40.0% among patients with chronic hepatitis B (CHB). This prevalence is somewhat in line with findings by Jiang[4] who reported a 38% prevalence in their cohort. The association between age (>50 years) and liver fibrosis observed in our study, with an odds ratio (OR) of 2.3, corresponds with findings from Chen Qet[5] suggesting age as a significant risk factor for liver fibrosis development.

The study also identified male gender as a notable risk factor (OR=1.8). This result corroborates the research by Zhang[6] which indicated males are at a higher predisposition for liver complications, including fibrosis, in CHB infections. High HBV DNA levels demonstrated a substantial association with liver fibrosis (OR=2.5), a result consistent with the meta-analysis by Lv[7] emphasizing the role of viral replication in fibrosis progression.

Interestingly, our study shows a significant association between alcohol consumption and liver fibrosis (OR=1.6). Previous studies, such as that by Kouroumalis[8] also highlight alcohol as a potential accelerator for fibrotic changes in CHB patients.

Duration of infection was another significant predictor (OR=2.2) for liver fibrosis, which aligns with findings by Lv [7] They proposed that the longer the CHB infection persists, the higher the risk for fibrotic developments.

Lastly, while co-morbidity with diabetes mellitus (DM) showed an increased odds ratio (OR=1.4), this association wasn't statistically significant in our cohort. This is a point of divergence from the study by Kouroumalis[8] which emphasized DM as a prominent factor exacerbating liver fibrosis.

Table 2 underscores the importance of biochemical and virological variables in relation to liver fibrosis among patients with chronic hepatitis B (CHB). Elevated alanine aminotransferase (ALT) levels were observed in 25.3% of the patients, presenting a twofold risk (OR=2.0) of liver fibrosis. This finding aligns with the work of Xiao[9] who identified that ALT, being an enzyme indicative of liver damage, can be a reliable predictor of fibrotic changes in CHB patients.

The study also found elevated aspartate aminotransferase (AST) levels in 21.3% of patients, indicating a close-to-twofold risk (OR=1.9) of fibrosis. This observation corroborates with the meta-analysis by Rinaldi[10] emphasizing the parallel significance of AST, akin to ALT, in fibrosis prediction.

From a virological standpoint, high HBV DNA levels displayed a significant association with liver fibrosis, presenting a 2.3-fold risk. This is consistent with the research conducted by Xu[11] which highlighted that active viral replication can instigate inflammatory responses, culminating in fibrotic alterations.

Moreover, the presence of the hepatitis B e-antigen (HBeAg) in 20% of the patients was

significantly associated with liver fibrosis (OR=2.1). This resonates with the findings of Niu[12] suggesting HBeAg as a marker indicative of active viral replication, leading to heightened inflammatory activity and subsequent fibrosis.

CONCLUSION

In this cross-sectional study focused on identifying risk factors for liver fibrosis in patients with chronic hepatitis B, several significant determinants emerged. Age, particularly being over 50 years, male gender, elevated ALT and AST levels, high HBV DNA concentrations and the presence of HBeAg were strongly associated with increased risk. Additionally, factors like alcohol consumption and the duration of the infection showed considerable relevance. While some co-morbidities, like diabetes mellitus, provided suggestive associations, they were not statistically significant in this cohort. These findings underscore the multifactorial nature of liver fibrosis in the context of chronic hepatitis B and emphasize the importance of early identification and monitoring of these risk factors. By understanding and acting on these associations, clinicians can better manage and potentially mitigate the progression of liver fibrosis in affected patients, offering them improved prognostic outcomes.

Limitations of Study:

Cross-sectional Design: Being a cross-sectional study, it only provides a snapshot of the association between risk factors and liver fibrosis at a specific point in time. This design inherently lacks the ability to infer causality or track the progression and dynamics of liver fibrosis over time.

Sample Size: With a sample size of 150 patients, there might be limitations in the power of the study to detect less common risk factors or subtle associations.

Selection Bias: Participants were recruited from a specific location or hospital, which may not represent the broader population of CHB patients. This could influence the generalizability of the findings.

Reliance on Self-reported Data: Some data, especially related to lifestyle factors like alcohol consumption, were based on self-reports, which might introduce recall bias or under-reporting.

Exclusion Criteria: The exclusion of patients with co-infections or other liver diseases might omit a segment of the CHB population with potentially different risk profiles for liver fibrosis.

Measurement Limitations: The study used specific methods and scoring systems to assess liver fibrosis. There's potential variability and limitations inherent to any diagnostic method, which might affect the accuracy of fibrosis detection.

Unmeasured Confounders: While the study considered several potential risk factors, there might be unmeasured or unknown confounders that influence the development of liver fibrosis in CHB patients, which were not accounted for in the study.

Single Geographic Area: The study's findings may be influenced by regional variations in genetics, diet, healthcare access and other factors. Therefore, the results may not be directly extrapolatable to other geographic or demographic populations.

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