ORIGINAL ARTICLE

FACTORS ASSOCIATED WITH FIBROSIS IN CHRONIC HEPATITIS C PATIENTS

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ABSTRACT

Objective: To identify the factors associated with fibrosis progression in a Pakistani cohort of Chronic hepatitis C (CHC) patients.

Material & Methods: A retrospective study was conducted at the Asian Institute of Medical Sciences, Hyderabad involving 350 CHC patients diagnosed between 2021 and January 2024. Data on demographics, clinical characteristics, and laboratory findings were collected. Fibrosis severity was assessed using non-invasive markers (FIB-4 index, APRI score), transient elastography, and, where available, liver biopsy reports. Multivariate logistic regression analysis was performed.

Results: The mean age of participants was 45.2 years, with a male predominance (62.3%). Advanced age (>50 years) was significantly associated with severe fibrosis (OR 2.34, $p = 0.001$). Other factors linked to advanced fibrosis included male gender (OR 1.89, $p = 0.017$), HCV genotype 3 (OR 2.61, $p < 0.001$), prolonged infection duration (>10 years, OR 1.75, $p = 0.021$), insulin resistance (HOMA-IR >2.5, OR 2.95, $p < 0.001$), alcohol consumption (OR 3.12, $p < 0.001$), and co-infection with HBV or HIV (OR 2.58, $p = 0.003$).

Conclusion: This study identifies critical factors influencing fibrosis progression in CHC patients in Pakistan. Targeted monitoring and management of high-risk groups, along with early diagnosis and timely intervention, can help mitigate complications and improve patient outcomes. Public health efforts should prioritize these strategies to address the burden of CHC-related fibrosis.

Key Words: Chronic hepatitis C, Fibrosis, Pakistan, Risk factors.

This article may be cited as: Zaki M, Memon S, Jiskani SA, Qadir B, Chaang A. Factors associated with fibrosis in chronic hepatitis C patients. Ann Allied Health Sci. 2024;10(2):49-53.

INTRODUCTION

Hepatitis C virus (HCV) poses a considerable global health burden, infecting approximately 71 million individuals globally. It is a major contributor to chronic liver diseases.[1] Chronic hepatitis C (CHC) is marked by persistent liver inflammation, which triggers the accumulation of extracellular matrix proteins, particularly collagen, leading to fibrosis. The severity of fibrosis is a crucial predictor of clinical outcomes, determining the risk of cirrhosis and liver failure.[2] The progression of fibrosis in CHC patients results from a complex interaction of viral, host, and environmental factors. HCV genotype 3, in particular, is associated with a more aggressive disease trajectory and faster fibrosis progression compared to other genotypes.[3,4]

Host factors, including age and gender, significantly affect fibrosis development. Older patients exhibit faster fibrosis progression, likely due to diminished liver regenerative capacity and prolonged viral exposure.[5] Men are more prone to advanced fibrosis than women, potentially due to the protective effects of estrogen which may inhibit fibrogenesis.[6] Genetic predispositions, such as polymorphisms in genes related to immune response and fibrosis regulation also play a role. Variants in the PNPLA3 gene and those associated with TGF-β signaling pathways have been implicated in increased fibrosis risk.[7]

Metabolic factors are also important contributors to fibrosis acceleration. Insulin resistance promotes fibrosis through mechanisms involving hepatic stellate cell activation and increased production of fibrogenic cytokines.[8] Additionally, environmental factors such as alcohol use and co-infections with HBV or HIV further exacerbate fibrosis progression. Alcohol induces oxidative stress and inflammation [9], while co-infections amplify liver damage through synergistic effects.[10]

This study aims to identify risk factors associated with fibrosis progression in CHC patients in Pakistan. The findings are intended to guide targeted interventions and improve public health strategies.

MATERIAL AND METHODS

This retrospective study was conducted to assess data from patients diagnosed with CHC at the Asian Institute of Medical Sciences in Hyderabad. Data collection covered the period from 2021 to January 2024. The study included adult patients (aged 18 years or older) with a confirmed diagnosis of CHC based on clinical evaluation and the detection of HCV RNA. To ensure the study's focus on CHC-associated fibrosis, patients with significant comorbid liver diseases or co-infections like HIV were excluded.

Relevant demographic, clinical, and laboratory data were extracted from patient medical records. Demographics included information related to age, gender, and socio-economic factors while information related to clinical history included data on HCV infection duration, prior antiviral treatments, and treatment outcomes.

In addition, laboratory findings including baseline and follow-up HCV viral loads, liver function tests (ALT, AST, bilirubin), and other biomarkers were documented. The severity of liver fibrosis was assessed using Fibrosis-4 (FIB-4) index and Aspartate Aminotransferase to Platelet Ratio Index (APRI) scores were calculated. Similary, liver stiffness, an indicator of fibrosis, was evaluated through transient elastography (FibroScan) and ultrasound imaging. Where available, biopsy reports were analyzed using established scoring systems such as METAVIR for histological confirmation of fibrosis.

Retrospective use of anonymized data was consistent with prior informed consent obtained during initial treatment. Patient identifiers were removed. The study complied with the Declaration of Helsinki, emphasizing respect, fairness, and integrity in research involving human participants. The collected data were analyzed using appropriate statistical tools. Summary statistics described the demographic and clinical features of the patients. Logistic regression models were applied to identify independent factors linked to fibrosis progression. The strength of association for fibrosis-related factors was quantified using odds ratios (OR).

RESULTS

The study analysed data from 350 patients diagnosed with CHC, between 2021 and January 2024. The mean age of the participants was 45.2 years (SD ± 12.3), with an age range of 18 to 75 years. The majority of the patients were male, comprising 62.3% (n = 218) of the cohort, while females accounted for 37.7% (n = 132). The average duration of HCV infection among the participants was 9.6 years (SD ± 5.4). **(Table 1)** The FIB-4 index and APRI score were calculated. Transient elastography results were available for 280 patients (80%), and liver biopsy reports were available for 90 patients (25.7%). **(Table 2)** Several factors are significantly associated with advanced fibrosis (F3-F4). **(Table 3)**

Table 1: Demographic and clinical characteristics of the study population

Characteristic	Total (n=350)	Male (n=218)	Female (n=132)
Age, mean (SD), years	45.2 (12.3)	47.1 (11.8)	41.8 (12.7)
Age Range, years	18-75	19-75	18-70
Duration of HCV infection, mean (SD), years	9.6 (5.4)	9.8 (5.2)	9.2 (5.8)
Gender			
- Male	218 (62.3%)	218 (100%)	0 (0%)
- Female	132 (37.7%)	0 (0%)	132 (100%)
HCV Genotype			
- Genotype 1	105 (30.0%)	67 (30.7%)	38 (28.8%)
- Genotype 2	40 (11.4%)	22 (10.1%)	18 (13.6%)
- Genotype 3	190 (54.3%)	118 (54.1%)	72 (54.5%)
- Genotype 4	15 (4.3%)	11 (5.0%)	4 (3.0%)

Table 2: Fibrosis assessment results

Assessment Method	Mean (SD) / n (%)	Mild Fibrosis (n=120)	Moderate Fibrosis (n=150)	Severe Fibrosis (n=80)
FIB-4 Index	2.6 (1.4)	1.5 (0.8)	2.8 (0.9)	4.1 (1.2)
APRI Score	1.2 (0.9)	0.7 (0.3)	1.5 (0.5)	2.3 (0.7)
Transient Elastography	11.5 kPa (3.8) (n=280)	7.8 kPa (1.9)	12.1 kPa (2.5)	17.4 kPa (3.0)
Liver Biopsy (METAVIR)				
- F0-F1 (Mild)	38 (42.2%)	38 (100%)	0	0
- F2-F3 (Moderate)	42 (46.7%)	0	42 (100%)	0
- F4 (Severe)	10 (11.1%)	0	0	10 (100%)

Table 3: Multivariate analysis of factors associated with advanced fibrosis

Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age (>50 years)	2.34	1.45-3.78	0.001
Male Gender	1.89	1.12-3.20	0.017
HCV Genotype 3	2.61	1.62-4.21	<0.001
Duration of Infection (>10 years)	1.75	1.10-2.79	0.021
Insulin Resistance (HOMA-IR >2.5)	2.95	1.85-4.71	<0.001
Alcohol Consumption	3.12	1.78-5.47	<0.001
Co-infection with HBV or HIV	2.58	1.37-4.86	0.003

DISCUSSION

This study provides critical insights into the factors contributing to fibrosis progression in patients with CHC in a Pakistani cohort. Key risk factors identified include advanced age, male gender, HCV genotype 3, prolonged infection duration, insulin resistance, alcohol consumption, and co-infections with HBV or HIV. These findings align with existing research and emphasize the complex interplay of viral, host, and environmental factors in liver fibrosis development. Advanced age emerged as a significant factor, with patients over 50 demonstrating a higher risk of severe fibrosis (F3-F4) compared to younger individuals (OR 2.34, p = 0.001). This observation corroborates prior studies highlighting age-related increases in fibrosis progression due to reduced liver regenerative capacity and prolonged exposure to HCV. [11, 12]

Male gender was significantly associated with advanced fibrosis (OR 1.89, p = 0.017). This aligns with studies suggesting estrogen's protective role in women, which may inhibit hepatic stellate cell activation and collagen deposition.[13, 14] As androgen levels decline with age, the lack of estrogen's protective effects in men may further accelerate fibrosis.[15]The study confirmed HCV genotype 3 as a strong predictor of severe fibrosis (OR 2.61, p < 0.001). This genotype is known to be more fibrogenic due to its unique characteristics promoting steatosis and inflammation.[16] In South Asia, where genotype 3 is prevalent, early intervention is crucial for better outcomes.[17]

Patients with a longer HCV infection duration (>10 years) faced an increased risk of advanced fibrosis (OR 1.75, p = 0.021). Chronic exposure to the virus exacerbates hepatic inflammation and fibrogenesis, underscoring the need for timely diagnosis and treatment.[18] Insulin resistance was another significant factor associated with fibrosis (OR 2.95, p < 0.001). Metabolic factors, particularly insulin resistance, contribute to hepatic steatosis, inflammation, and fibrosis through oxidative stress and cytokine pathways. [19, 20] Addressing metabolic dysfunction in CHC patients is critical for mitigating fibrosis progression.

Alcohol intake was identified as a potent risk factor for severe fibrosis (OR 3.12, p < 0.001). Alcohol exacerbates liver damage by promoting oxidative stress, steatosis, and impaired immune response.[21] Counseling for alcohol cessation is essential to prevent rapid fibrosis progression. Co-infections with HBV or HIV raised the risk of severe fibrosis (OR 2.58, p = 0.003). These co-infections exacerbate liver disease through heightened immune activation and severe hepatic inflammation. [22,23]

Patients with risk factors like older age, male gender, genotype 3, and prolonged infection duration should undergo regular monitoring and early intervention. Addressing metabolic factors through lifestyle modifications and therapeutic measures could slow disease progression. Additionally, public health campaigns promoting alcohol cessation should be a cornerstone of CHC management strategies.

As a retrospective study, inherent biases related to data collection and patient selection cannot be excluded. The reliance on non-invasive markers and imaging for fibrosis assessment, though practical, may not fully capture the nuances of liver fibrosis compared to biopsy. Prospective studies with larger and more diverse populations are needed for validation and deeper understanding.

CONCLUSION

This study highlights critical factors associated with fibrosis progression in CHC patients in Pakistan. A multifaceted approach addressing both viral and host factors is essential to improve outcomes, reduce liver-related complications, and alleviate the burden of CHC in resource-limited settings.

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