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COMMON ETIOLOGIES OF LIVER CIRRHOSIS AMONG PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: The objective is to determine the frequency of various etiological factors responsible for liver cirrhosis in patients presenting to a tertiary care hospital in Gujranwala, Pakistan.

Materials and Methods: This cross-sectional study was conducted at the Medical Ward, Gujranwala Teaching Hospital /GMC Gujranwala, Pakistan, from Oct 2025 to May 2026. A total of 150 adult patients diagnosed with liver cirrhosis based on clinical, biochemical, and radiological criteria were enrolled using consecutive sampling. All patients underwent testing for hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (anti-HCV) antibodies, and detailed history was obtained for alcohol use, metabolic syndrome, and drug exposure. Descriptive statistics were used to calculate the frequency of each etiology.

Results: The mean age of participants was 52.4 ± 11.2 years, with a male predominance (62.7%). Chronic hepatitis C virus (HCV) infection was the leading cause of cirrhosis, found in 88 patients (58.7%). Hepatitis B virus (HBV) infection accounted for 32 cases (21.3%). Notably, 16 patients (10.7%) had cryptogenic cirrhosis with no identifiable cause. Non-alcoholic fatty liver disease (NAFLD)-related cirrhosis was diagnosed in 8 patients (5.3%), while alcoholic liver disease was observed in only 4 patients (2.7%). Mixed etiology (HBV + HCV) was seen in 2 patients (1.3%). The remaining causes included autoimmune hepatitis (n=1, 0.7%) and Wilson's disease (n=1, 0.7%).

Conclusion: Chronic hepatitis C remains the predominant cause of liver cirrhosis in this Pakistani cohort, followed by hepatitis B. Cryptogenic cirrhosis and NAFLD are emerging as significant contributors. Alcoholic cirrhosis is relatively uncommon, reflecting local epidemiological patterns. These findings underscore the need for continued viral hepatitis screening, early antiviral therapy, and growing awareness of metabolic risk factors.

Keywords: Etiology; hepatitis C; hepatitis B; Liver cirrhosis; NAFLD; Pakistan.

INTRODUCTION

Chronic liver disease can lead to liver cirrhosis characterized by progressive fibrosis and regenerative nodule formation. Various complications like portal hypertension, spontaneous bacterial peritonitis, and hepato-cellular carcinoma arising in this condition, have resulted in substantial morbidity and mortality, making it a global health issue.[1] The prevalence and etiology of cirrhosis vary significantly across different geographical regions and is influenced by genetic, environmental, and socioeconomic factors.

In West, alcoholic liver disease and non-alcoholic fatty liver disease (NAFLD) have emerged as common causes of cirrhosis.[2] However, in the Asia-Pacific region, including Pakistan, chronic viral hepatitis remains the dominant etiological factor. The World Health Organization estimates that Pakistan has one of the highest hepatitis C prevalence rates globally, with approximately 7 to 8 million individuals chronically infected.[3] Similarly, hepatitis B continues to contribute significantly to liver-related morbidity in the region.

To plan healthcare resource allocation and treatment protocols for its prevention, considering the local etiological spectrum of cirrhosis is important. Earlier study from Pakistan has consistently pointed out chronic hepatitis C as the primary cause of cirrhosis.[4] More recent studies suggest an increasing role of NAFLD, driven by rising rates of obesity and type 2 diabetes.[5] Still, many patients remain cryptogenic, requiring further investigation into occult viral infections, autoimmune processes, or less common metabolic disorders.

The present study was therefore designed to find out the existing frequency of various causes of liver cirrhosis among the patients visiting tertiary care hospital in Lahore, Pakistan, over a defined period from October 2025 to May 2026.

MATERIALS AND METHODS

This descriptive, cross-sectional study was conducted in the Department of Medicine at Gujranwala Teaching Hospital /GMC Gujranwala Pakistan, from Oct. 2025 to May 2026. A total of 150 adult patients (age ≥ 18 years) with a confirmed diagnosis of liver cirrhosis were enrolled. Consecutive sampling was employed.

Data Collection

Each patient underwent a comprehensive evaluation:

1. Demographic and clinical data: Age, sex, presenting symptoms (fever, abdominal pain, jaundice, ascites).
2. Laboratory tests: Complete blood count, liver function tests (bilirubin, ALT, AST, alkaline phosphatase), serum albumin, prothrombin time, serum creatinine, and blood urea nitrogen.
3. Viral markers: Hepatitis B surface antigen (HBsAg) by ELISA, and anti-HCV antibodies by third-generation ELISA. Positive anti-HCV samples were confirmed by HCV RNA PCR when available.
4. Alcohol history: A detailed history of alcohol consumption was obtained using a standardized questionnaire. Significant alcohol use was defined as >40 g/day for men and >20 g/day for women for more than 10 years.
5. Metabolic assessment: Fasting blood glucose and lipid profile were obtained. NAFLD-related cirrhosis was diagnosed in the absence of viral hepatitis, significant alcohol intake, or other liver diseases, with presence of at least two components of metabolic syndrome (obesity, diabetes, dyslipidemia, hypertension).[6]
6. Other etiologies: For patients with negative viral markers and no alcohol/metabolic risk factors, additional testing included serum ceruloplasmin (for Wilson's disease), antinuclear antibody (ANA), anti-smooth muscle antibody (SMA), and serum alpha-1 antitrypsin levels when clinically indicated.

Inclusion Criteria

- Clinical features of chronic liver disease (e.g., ascites, splenomegaly, jaundice, palmar erythema)
- Radiological evidence of cirrhosis on abdominal ultrasound (nodular liver surface, coarse echo texture, or signs of portal hypertension)
- Willing to provide informed consent

Exclusion Criteria

- Patients with acute liver failure without evidence of chronic disease
- Known hepatocellular carcinoma at diagnosis (to avoid confounding by cancer-related mortality bias)
- Refusal to participate

Statistical Analysis: Data were entered into SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages. Continuous variables were presented as mean ± standard deviation or median with interquartile range as appropriate. No inferential statistical tests were applied as this was primarily a descriptive epidemiological study.

Ethical Considerations: The study was approved by the Institutional Review Board of Frontier Medical and Dental College, Abbottabad (Ref No. FMDC/ IRB/ 2025/53). Written informed consent was obtained from all participants or their legal guardians. The study was conducted in accordance with the Declaration of Helsinki.

Funding: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

RESULTS

A total of 150 patients [Male=94 (62.7%) and female =56 (37.3%)] with confirmed cirrhosis were enrolled. The baseline characteristics are summarized in Table 1. The mean age was 52.4 ± 11.2 years (range 22–78 years). The male-to-female ratio was approximately 1.7:1. The majority of patients (65.3%) presented with ascites as the predominant feature, followed by jaundice (54.0%) and fever (44.0%).

Etiological Distribution of Cirrhosis; The frequencies of various causes of cirrhosis are presented in Figure 1 and [Table 2].

Table 1: Baseline Clinical Characteristics of Cirrhosis Patients (N=150)

Characteristic	Number (n)	Percentage (%)
Sex		
Male	94	62.7
Female	56	37.3
Presenting Features		
Ascites	98	65.3
Jaundice	81	54.0
Fever	66	44.0
Abdominal pain	74	49.3
Palpable spleen	86	57.3
Child-Pugh Class		
Class A	28	18.7
Class B	72	48.0
Class C	50	33.3

Chronic Hepatitis C (HCV) was the single most common cause, identified in 88 patients (58.7%). Among these, the majority had detectable HCV RNA (93.2%), indicating active viral replication.

Chronic Hepatitis B (HBV) was the second leading cause, found in 32 patients (21.3%). HBeAg positivity was present in 13 (40.6%) of HBV patients, suggesting active disease.

Cryptogenic Cirrhosis accounted for 16 cases (10.7%). These patients had negative viral markers, no significant alcohol history, and no metabolic features. Further workup for autoimmune or metabolic causes remained negative.

NAFLD-related cirrhosis was diagnosed in 8 patients (5.3%). All these patients had at least two components of metabolic syndrome (most commonly type 2 diabetes and obesity).

Alcoholic cirrhosis was observed in only 4 patients (2.7%). All were males with a daily intake exceeding 60 g for more than 15 years.

Mixed infection (HBV + HCV) was seen in 2 patients (1.3%). Autoimmune hepatitis was confirmed in 1 patient (0.7%) based on elevated IgG and positive ANA/SMA. Wilson's disease was diagnosed in 1 young patient (age 22 years) with low serum ceruloplasmin and Kayser-Fleischer rings.

No cases of primary billiary cirrhosis, alpha-1 antitrypsin deficiency, or drug-induced cirrhosis were identified in this cohort.

Table 2: Distribution of Etiological Factors of Cirrhosis (N=150)

Etiology	Number (n)	Percentage (%)
Chronic Hepatitis C	88	58.7
Chronic Hepatitis B	32	21.3
Cryptogenic	16	10.7
NAFLD-related	8	5.3
Alcoholic liver disease	4	2.7
HBV + HCV co-infection	2	1.3
Autoimmune hepatitis	1	0.7
Wilson's disease	1	0.7

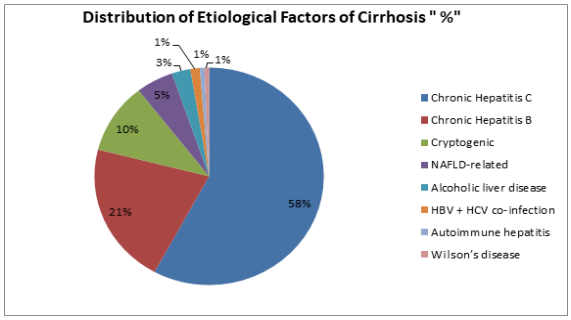

Figure 1: Conceptual description; Pie chart showing percentage Distribution of various Etiological Factors of Cirrhosis.

DISCUSSION

This study provides updated, hospital-based data on the etiological spectrum of liver cirrhosis in Gujranwala, Pakistan, covering a recent eight-month period from Oct 2025 to May 2026. The key findings are threefold: first, chronic hepatitis C remains the dominant cause, accounting for nearly three out of every five cases. Second, hepatitis B continues to be a major contributor. Third, cryptogenic cirrhosis and NAFLD-related cirrhosis together account for approximately 16% of cases, signaling an epidemiological shift toward metabolic liver diseases.

Hepatitis C as the Leading Cause; The finding that HCV is responsible for 58.7% of cirrhosis cases is consistent with previous national estimates. A meta-analysis by Alavi et al. (2019) reported a national HCV antibody prevalence of 5.9% in Pakistan, with higher rates in Punjab province.[3] More recent community-based surveys from 2023 to 2024 have confirmed ongoing transmission, particularly related to unsafe healthcare injections and poor infection control.[7] The high proportion of HCV-related cirrhosis underscores the need for continued scaling up of direct-acting antiviral (DAA) therapy, which has been shown to reverse fibrosis and reduce cirrhosis complications even in advanced disease.[8]

Hepatitis B Burden; HBV was responsible for 21.3% of cirrhosis cases, a figure similar to earlier Pakistani

studies but higher than current Western rates (typically <10%).[2,4] This highlights incomplete vaccination coverage in older adults (current vaccination programs for infants began in the early 2000s) and the need for screening and antiviral treatment for eligible chronic HBV carriers. Recent guidelines from the American Association for the Study of Liver Diseases (AASLD 2023) and European Association for the Study of the Liver (EASL 2024) recommend treatment for all patients with cirrhosis regardless of HBV DNA level.[9,10]

Emerging Role of NAFLD and Cryptogenic Disease; Notably, 5.3% of cirrhosis was attributed to NAFLD, and an additional 10.7% remained cryptogenic. Some experts believe that a proportion of cryptogenic cirrhosis represents "burnt-out" NAFLD where steatosis is no longer evident histologically.[11] A recent longitudinal study from South Asia reported that NAFLD prevalence in the general population has increased to 32% in urban areas, driven by dietary changes and sedentary lifestyles.[12] The relatively low proportion of NAFLD-cirrhosis in our study (5.3%) likely reflects under-diagnosis because:

1. Liver biopsy was not performed for all patients, and non-invasive fibrosis markers may miss early cirrhosis in NAFLD.
2. Many patients with metabolic risk factors also had viral hepatitis, and attribution to NAFLD was only made in purely cryptogenic cases. Therefore, the true burden of NAFLD-cirrhosis may be higher than reported.

Alcoholic Cirrhosis–A Rare cause ; Only 2.7% of cases were attributed to alcohol. This aligns with long-standing observations that alcoholic cirrhosis is relatively uncommon in Pakistan compared to Western nations. Cultural and religious norms limit alcohol consumption in the majority population. However, among non-Muslim minorities and in certain urban subpopulations, alcohol use may be underreported due to social stigma.[13]

A study from Mayo Hospital by Qureshi et al. (2001) reported HCV in 63% and HBV in 27% of cirrhosis patients, very close to our figures.[14] Similarly, a 2020 multicenter study from Karachi found HCV in 55% and HBV in 20%.[15] The consistency of these data over two decades indicates that viral hepatitis remains the major driver of cirrhosis, and efforts to control it have not yet translated into a reduction in end-stage liver disease at the hospital level.

Comparison with Global Data; In contrast, the leading cause of cirrhosis in Europe and the United States is now NAFLD (approximately 35-40%), followed by alcoholic liver disease (25-30%), with HCV declining to less than 15% due to effective DAA treatment.[2,16] This difference reflects both Pakistan's higher viral hepatitis prevalence and the earlier stage of the NAFLD epidemic.

Strengths and Limitations: Strengths of this study include a robust sample size (n=150) from a major referral center, systematic etiological workup, and a recent study period. Limitations include: (1) single-center design, which may not represent rural or community populations; (2) lack of liver biopsy for confirmation in all patients; (3) potential selection bias as only hospitalized patients (often with decompensated disease) were included; (4) possible underdiagnosis of autoimmune and genetic causes due to limited testing availability.

Implications for Clinical Practice and Public Health

Our findings support several actionable recommendations:

- Continued viral hepatitis screening for all adults, especially those over 40 years of age.
- Universal access to DAAs for HCV, and tenofovir/entecavir for HBV, as recommended by the National Hepatitis Control Program.
- Rising awareness of NAFLD among physicians, with routine assessment of metabolic parameters in all liver disease patients.
- Further research using non-invasive fibrosis scores (e.g., FIB-4, FibroScan) to detect NAFLD-cirrhosis in the general population.

CONCLUSION

Chronic hepatitis C virus infection remains the predominant cause of liver cirrhosis among patients presenting to Mayo Hospital, Lahore, followed by hepatitis B. Alcoholic cirrhosis is uncommon, while NAFLD-related cirrhosis and cryptogenic disease are emerging as significant etiologies. These findings emphasize the need for aggressive viral hepatitis control measures and growing attention to the metabolic syndrome as a driver of chronic liver disease in Pakistan.

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