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Original Articles

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Etiology, Complications, and Outcomes of Liver Cirrhosis in Patients Referred to or Hospitalized at Imam Khomeini Hospital, Ardabil, Iran (2019–2024): A Cross-Sectional Study

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Abstract

Introduction: Liver cirrhosis is a progressive chronic liver disease characterized by fibrosis and architectural distortion, leading to complications such as portal hypertension, ascites, encephalopathy, and esophageal varices. As the prevalence of viral and metabolic liver diseases changes globally, understanding regional etiological patterns is essential.

Methods: In this retrospective cross-sectional study, 200 patients with confirmed liver cirrhosis were evaluated using hospital records. Demographic characteristics, substance use, etiology, complications, and hospitalization outcomes were analyzed using SPSS v26. Statistical significance was defined as $p<0.05$.

Results: Nonalcoholic steatohepatitis (NASH) was the most common cause of cirrhosis (44.1%), followed by hepatitis B (20.6%), autoimmune hepatitis/PSC (10.8%), alcoholic liver disease (9.3%), and hepatitis C (8.8%). Wilson disease and cardiac cirrhosis were rare. Etiology differed significantly across age groups ($p=0.003$), but not by sex or clinical outcome. Portal hypertension was the most frequent complication (≈94%), followed by ascites (34.8%) and esophageal varices (26.5%). Overall mortality was 19%, while hospitalization duration and frequency did not vary significantly among etiological groups.

Conclusion: NASH has become the leading cause of liver cirrhosis in this population, reflecting the growing impact of metabolic disorders. These findings emphasize the importance of preventive strategies, lifestyle modification, and effective management of metabolic risk factors to reduce the burden of cirrhosis.

Keywords: Liver cirrhosis; Etiology; Non-alcoholic steatohepatitis (NASH); Hepatitis B.

Introduction

Cirrhosis is defined by fibrosis and nodule formation in the liver secondary to chronic injury, leading to disorganization of normal lobular architecture [1]. Various causes can damage the liver, including viral infections, toxins, hereditary conditions, or autoimmune processes [2]. Initially, the liver forms scar tissue (fibrosis) without losing function. After chronic injury, most liver tissue becomes fibrotic, resulting in loss of function and development of cirrhosis [2]. The clinical manifestations of cirrhosis often reflect the severity of liver injury rather than the cause of the liver disease. Fibrosis and vascular remodeling increase portal vein pressure and its complications, such as gastrointestinal varices and splenomegaly. Ascites and hepatic encephalopathy result from hepatocyte insufficiency and high portal pressure [3,4]. Cirrhosis is one of the leading causes of complications and mortality in patients with chronic liver disease worldwide. In 2019, cirrhosis was associated with 2.4% of global deaths. Given the increasing prevalence of obesity and alcohol consumption on one hand, and improved management of HBV and HCV infections on the other, the epidemiology and

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burden of cirrhosis are changing [5]. Many studies have been conducted on the causes of cirrhosis in different parts of the world. In Europe and North America, excessive alcohol consumption is the most common cause of cirrhosis, whereas in many Asian and African countries, HBV and HCV are the most important causes [6]. In Iran, due to the high prevalence of hepatitis B, it has been reported as the most common cause of cirrhosis [7,8]. Although viral hepatitis remains the leading cause of cirrhosis globally, the prevalence of NAFLD and alcohol-related cirrhosis is increasing [9,10]. In the past decade, major changes in the etiology and burden of liver disease have been observed [11–13]. Global deaths from cirrhosis increased between 2012 and 2017, but age-standardized death rates (ASDRs) decreased. However, ASDR for NAFLD- related cirrhosis increased during this period, while ASDR for other causes decreased [14]. Some patients develop cirrhosis following hereditary diseases such as Wilson disease (copper accumulation) and hemochromatosis (iron storage) [15]. Other uncommon causes include severe reactions to certain drugs and congestive heart failure [16]. Since many patients whose disease progresses to cirrhosis have no symptoms, no accurate statistics on this disease are available in Iran [17]. Knowing the cause of cirrhosis is essential for predicting complications, making appropriate treatment decisions, and implementing preventive measures [18]. Due to insufficient information on the etiology of cirrhosis in the Ardabil region, the present study was designed to investigate the etiology, complications, and outcomes of liver cirrhosis over a five-years period (2019–2024).

Materials & Methods

This was a cross-sectional descriptive study. The study population included all patients diagnosed with liver cirrhosis who were referred to or hospitalized at Imam Khomeini Hospital, Ardabil, between 2019 and 2024. Patients were enrolled by consecutive sampling. According to reference [19], with an estimated prevalence of 7% and a margin of error of 0.05, the sample size was determined as 200 patients. A comprehensive checklist was completed for each patient, including demographic information (age, sex, occupation, place of residence), alcohol consumption and drug use, hospitalization history, number of hospitalizations, reason for hospitalization, etiology of cirrhosis (HBV, HCV, drug-induced, autoimmune, NASH, cryptogenic), type of complication (ascites, esophageal varices, portal vein thrombosis, SBP, PTHN), and outcome (survival or death during the last hospitalization). Data were entered into SPSS v26 for statistical analysis. Descriptive statistics (frequency tables, mean, percentage, standard deviation) were used. Normality was assessed using the Kolmogorov-Smirnov test. Chi-square test was used for qualitative variables. ANOVA or Kruskal-Wallis was used for quantitative variables. Statistical significance was set at $p<0.05$. All patient information remained confidential.

Results

A total of 200 patients with confirmed liver cirrhosis were included in this study. The mean age of participants was 62.6 ± 14.9 years, ranging from 22 to 92 years. As shown in Table 1, the majority of patients, 93 individuals (46.5%), were aged 66 years or older, followed by 64 patients (32.0%) in the 51 to 65 years age group, 31 patients (15.5%) in the 37 to 50 years group, and 12 patients (6.0%) in the youngest age group of 22 to 36 years. Regarding sex distribution, 117 patients (58.5%) were male and 83 patients (41.5%) were female, yielding a male-to-female ratio of approximately 1.4:1. Most patients lived in urban areas, with 148 individuals (74.0%) residing in cities compared to 52 patients (26.0%) from rural areas. The most common occupational groups were housewives, accounting for 78 patients (39.0%), and self-employed individuals, comprising 77 patients (38.5%). Employed individuals made up 25 patients (12.5%), unemployed 18 patients (9.0%), and students only 2 patients (1.0%). The mean duration of hospitalization was 11.9 ± 7.1 days, with a range of 4 to 56 days, and the mean number of hospitalizations per patient was 3.0 ± 1.8, ranging from 1 to 14 times.

Regarding the etiology of cirrhosis, Table 2 presents the detailed distribution. Non-alcoholic steatohepatitis (NASH) was the most common cause, identified in 90

patients, which accounted for 45.0% of all cases. Hepatitis B virus infection ranked second, found in 42 patients (21.0%). Alcoholic hepatitis was present in 18 patients (9.0%), hepatitis C virus infection in 17 patients (8.5%), and autoimmune hepatitis in 14 patients (7.0%). Primary sclerosing cholangitis (PSC) was diagnosed in 7 patients (3.5%), drug-induced hepatitis in 9 patients (4.5%), Wilson disease in 2 patients (1.0%), and cardiac cirrhosis in 1 patient (0.5%).

Table 1. Demographic characteristics of patients

Characteristic	Category	No	Percent (%)
Age group (year)	22–36	12	6.0
	37–50	31	15.5
	51–65	64	32.0
	≥66	93	46.5
Sex	Female	83	41.5
	Male	117	58.5
Residence	Rural	52	26.0
	Urban	148	74.0
Occupation	Self-employed	77	38.5
	Unemployed	18	9.0
	Housewife	78	39.0
	Student	2	1.0
	Employed	25	12.5

Table 2. Etiology of liver cirrhosis among patients

Etiology	Frequency (n)	Percent (%)
NASH	90	45.0
Hepatitis B	42	21.0
Alcoholic hepatitis	18	9.0
Hepatitis C	17	8.5
Autoimmune hepatitis	14	7.0
Drug-induced hepatitis	9	4.5
PSC	7	3.5
Wilson disease	2	1.0
Cardiac cirrhosis	1	0.5
Total	200	100

It should be noted that due to incomplete hospital records and the lack of diagnostic biopsies at our center, some NASH diagnoses were based on clinical suspicion, exclusion of other causes, and patient medical history, rather than definitive histologic criteria.

When analyzed by sex, NASH remained the most common cause in both groups, with 44 cases among males (37.6% of all males) and 46 cases among females (55.4% of all females). Alcoholic hepatitis was predominantly seen in males, with 16 cases compared to only 2 cases in females. Similarly, hepatitis B was more common in males, with 31 cases versus 11 cases in females. Autoimmune hepatitis showed a slight female predominance, with 8 cases in females and 6 in males. However, the overall distribution of etiologies across sexes did not reach statistical significance ($p = 0.053$).

Age had a significant impact on the distribution of cirrhosis etiologies ($p = 0.01$). NASH was most prevalent in older age groups: 53 of the 90 NASH cases (58.9%) occurred in patients aged 66 years or older, and another 30 cases (33.3%) were in the 51 to 65 years age group. Alcoholic hepatitis showed a peak in middle-aged groups, with 9 cases (50%) in the 51 to 65 years group and 4 cases (22%) in the 37 to 50 years group. Hepatitis B was also most common in the elderly, with 28 cases in patients aged 66 years or older. Autoimmune hepatitis and PSC were more evenly distributed across age groups. Wilson disease was observed only in the 37 to 50 years age group (2 cases), and the single case of cardiac cirrhosis occurred in a patient aged 66 years or older.

A total of 310 complications were documented among the 200 patients, as many patients presented with more than one complication. Portal hypertension was the most frequently reported complication, observed in 188 patients, representing approximately 94.0% of the study population. Figure 1 displays the frequency of major complications. Ascites was the second most common complication, occurring in 108 patients, which accounted for 34.8% of all complications or 54.0% of all patients. Esophageal varices were documented in 82 patients (26.5% of complications), and hepatic encephalopathy in 43 patients (13.9% of complications). Less common complications included portal vein thrombosis in 21 patients (6.8% of complications), spontaneous bacterial peritonitis (SBP) in 20 patients (6.5%), and hepatorenal syndrome in 11 patients (3.5%). Twelve patients (3.9%) presented with non-specific symptoms such as jaundice, weakness, or abdominal pain without other major complications. When complications were analyzed by etiology, NASH and hepatitis B were associated with the highest burden of most complications, and this association was statistically significant ($p = 0.01$). significant differences were observed in hospitalization duration (p

= 0.9) or number of hospitalizations (p = 0.8) across different etiologies.

Regarding patient outcomes, of the 200 patients, 162 (81.0%) were discharged alive, while 38 (19.0%) died during hospitalization. Table 3 presents mortality rates by etiology. The highest number of deaths occurred in patients with NASH (15 deaths, representing 16.7% of all NASH patients), followed by hepatitis B (9 deaths,

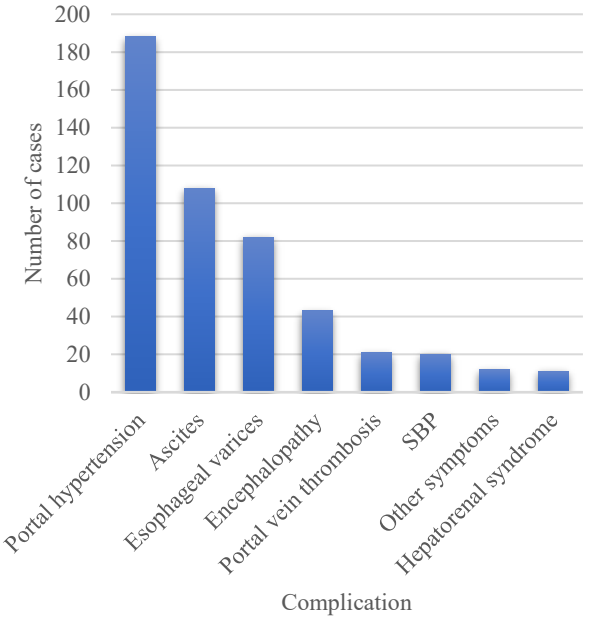


Figure 1. Frequency of clinical complications

hepatitis (5 deaths, 27.8% of alcoholic patients). The highest mortality rate was observed in patients with drug-induced hepatitis (44.4%), though the small sample size (n=9) limits interpretation. The association between etiology and in-hospital mortality was not statistically significant (p = 0.5).

Table 3. In-hospital mortality by etiology

Etiology	patients (n)	Deaths (n)	Mortality rate (%)
NASH	90	15	16.7
Hepatitis B	42	9	21.4
Alcoholic hepatitis	18	5	27.8
Drug-induced hepatitis	9	4	44.4
Autoimmune hepatitis	14	2	14.3
Hepatitis C	17	2	11.8
PSC	7	1	14.3
Cardiac cirrhosis	1	0	0
Wilson disease	2	0	0

Discussion

The present study on 200 patients with liver cirrhosis showed that the most common etiology was non-alcoholic steatohepatitis (NASH) in 45% of cases, followed by hepatitis B (21%) and hepatitis C (8.5%). Alcoholic hepatitis (9%), autoimmune hepatitis (7%), drug-induced hepatitis (4.5%), PSC (3.5%), Wilson disease (1%), and cardiac cirrhosis (0.5%) were less common.

This pattern indicates that in our study population, contrary to some Western countries where alcohol plays a major role, metabolic and viral factors have a larger share. Zhai et al. [20] similarly identified NASH as the most common cause of cirrhosis. However, unlike our findings where hepatitis B ranked second and hepatitis C third, the global study by Alberts et al. [21] reported higher overall proportions of HBV and HCV. In our study, alcoholic causes had a relatively small share, while global results showed a continuous increase in alcohol's share of disease burden [20].

Perz et al. [22] reported that globally, approximately 57% of cirrhosis cases are caused by hepatitis B (30%) or hepatitis C (27%). Jepsen et al. [23] reported that globally the three main causes of cirrhosis have almost equal shares: hepatitis C (26%), alcohol (24%), and hepatitis B (23%), with NAFLD having a smaller share (8%) but increasing. Huang et al. [24] also reported that HBV and HCV are the most important causes of cirrhosis worldwide (HBV ~42% and HCV ~21%), but noted that the share of NAFLD and alcoholic cirrhosis is increasing.

Analysis of age distribution showed that most NASH cases occurred in the ≥66 years group (53 cases) and 51–65 years group (30 cases). Sajja et al. [25] similarly showed that patients with NAFLD/NASH developed cirrhosis at an older average age (60 years). Hester et al. [26] showed that in patients with NASH-related hepatocellular carcinoma, individuals were typically older. Michitaka et al. [27] also reported that patients with NASH-induced cirrhosis had a higher mean age (approximately 66 years).

Regarding sex distribution, NASH was most frequent in both sexes (46 females vs. 44 males). Alcohol-related causes were more prominent in males (16 vs. 2

females). Huang et al. [24] reported that for NASH, cirrhosis incidence in females is higher than males (female-to-male ratio = 1.3). Sagnelli et al. [28] showed that hepatitis B and alcoholic causes were more common in males. Stroffolini et al. [29] also showed that alcohol and hepatitis B are more common in males, while NASH has a higher share in females.

Regarding hospitalization duration, the longest mean duration was for Wilson disease (16 days), followed by hepatitis C (13.88 days) and alcoholic hepatitis (12.22 days). Chowdhury [30] reported that patients with alcohol-induced and hepatitis C cirrhosis had longer stayed. Gala et al. [31] also showed that patients with alcoholic cirrhosis had longer hospital stays.

The most common complications in our study were portal hypertension (≈94%), ascites (34.8%), esophageal varices (26.5%), and encephalopathy (13.9%). Çavuşoğlu et al. [32] similarly reported that ascites and encephalopathy were more common in ALD, hepatitis B, and NASH. Sivanathan et al. [33] reported that esophageal varices (60%) and ascites (49%) had the highest prevalence. Topdagi et al. [34] similarly reported ascites (83%) and varices (56%) as the most common complications.

Overall mortality in our study was 19%. Among deceased patients, the most common causes were NASH (15 cases) and hepatitis B (9 cases). Kim et al. [35] reported that in the United States, mortality from cirrhosis had an upward trend. Huang et al. [24] reported that mortality from NAFLD-related cirrhosis has had an upward trend unlike other causes. Ye et al. [36] reported that global cirrhosis mortality increased by approximately 47.15% between 1990 and 2017, with NASH showing the fastest growth. Hagström et al. [37] reported that NAFLD patients had lower mortality (41.2%) compared to alcoholic cirrhosis.

Conclusion

The findings of this study demonstrate that non-alcoholic steatohepatitis (NASH) is the most common etiology of liver cirrhosis in the studied population from Ardabil, northwest Iran, accounting for 45% of cases, surpassing viral hepatitis. The high prevalence of metabolic factors highlights the urgent need for preventive programs, lifestyle modification, and management of underlying chronic conditions such as obesity, diabetes, and metabolic syndrome. Hepatitis B remains the second most common cause, emphasizing the continued importance of vaccination and antiviral treatment programs.

This study has several limitations: single-center design, which limits generalizability; retrospective design with reliance on medical records, some of which were incomplete; lack of definitive diagnostic criteria for some NASH cases (no biopsy or FibroScan in many patients); portal hypertension was reported "approximately" in 94% without standardized documentation; and small sample size for rare etiologies.

Informed Consent

Written informed consent was obtained from all participants or their legal guardians prior to enrollment.

Ethics Approval

This study was approved by the Ethics Committee of Ardabil University of Medical Sciences (Ethics Code: IR.IAU.ARDEBIL.REC.1402.175).

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Conflicts of Interest (COI)

The authors declare that they have no conflicts of interest.

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