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Research Paper

# Causes and complications among patients with cirrhosis in Guilan province, Iran

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## ABSTRACT

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**Background:** Cirrhosis presents with various etiologies and complications that may differ between individuals. This study aimed to evaluate causes and complications in patients with cirrhosis.

**Method:** This cross-sectional study was conducted on 308 patients with cirrhosis in Guilan province, Iran. Patient data including demographics, cirrhosis etiology, complications, and laboratory findings were recorded. Statistical analysis was performed using SPSS software version 20 with significance set at $P < 0.05$.

**Results:** Out of 308 liver cirrhosis cases, 68.2% were male, with a mean age of 59.29±15.1 years, predominantly urban residents (81.5%). Non-alcoholic fatty liver disease/ metabolic syndrome (NAFLD/MetS) was the leading cause (47.7%), with a higher prevalence in males (59.6%, P=0.004), while autoimmune liver disease was more frequent in females ($P < 0.001$). Viral hepatitis contributed significantly, with hepatitis B virus (HBV) and C (HCV) in 17.9% and 9.7% of cases, respectively, both showing male predominance. Ascites were the most common complication (82.8%), significantly associated with age ($P = 0.015$). Esophageal varices (54.6%) and variceal bleeding (26%) were linked to age and longer disease duration ($P < 0.001$). Other complications, including hepatic encephalopathy (33.5%), hepatocellular carcinoma (7.2%), and portal vein thrombosis (10%), showed no significant trends with age, gender, or disease duration ($P > 0.05$).

**Conclusion:** Liver cirrhosis demonstrated distinct patterns based on gender and age, highlighting the need for personalized care. The causes and complications related to cirrhosis underscored the importance of demographic-specific approaches in prevention, early detection, and management to optimize outcomes for cirrhosis patients.

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## 1. Introduction

Cirrhosis represents a significant global health burden, accounts for approximately one million deaths globally. The global incidence of liver cirrhosis has increased by 58.21% from 1990 to 2021 [1,2]. This chronic liver condition is characterized by progressive fibrosis and the conversion of normal liver architecture into structurally abnormal nodules, ultimately leading to impaired liver function [3].

The global prevalence of cirrhosis has been steadily increasing, with estimates suggesting that it affects approximately 2% of the world's population, though rates vary significantly across regions and populations [4,5].

The etiology of cirrhosis is diverse and demonstrates notable geographic and demographic variations. In Western countries, alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD) predominate, while viral hepatitis (particularly hepatitis B virus (HBV) and hepatitis C virus (HCV)) remains the leading cause in many Asian and African countries [5–7]. Other significant etiologies that can result in liver dysfunction are include autoimmune conditions such as autoimmune liver disease, primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), and various toxic substances and other viruses [8–10]. The rising global prevalence of obesity and metabolic syndrome (MetS) has led to NAFLD emerging as an increasingly important cause of cirrhosis worldwide [7,11,12].

Cirrhosis typically manifests through a complex array of signs and symptoms reflecting both hepatic dysfunction and portal hypertension [13]. Early symptoms may be nonspecific, including fatigue, weakness, and loss of appetite. As the disease progresses, patients may develop more specific manifestations such as jaundice, ascites, peripheral edema, and hepatic encephalopathy [14]. Portal hypertension can lead to potentially life-threatening complications including variceal bleeding, while the risk of hepatocellular carcinoma (HCC) is significantly increased in cirrhotic patients [15,16].

Gender differences in liver disease have gained increasing attention in recent years [17,18]. Studies suggest that hormonal factors, lipid profiles, and genetic differences may contribute to gender-specific patterns in liver disease progression, potentially leading to severe outcomes and additional comorbidities [7,17,19,20]. Understanding these differences is crucial for optimizing screening, prevention, and treatment strategies.

However, comprehensive data on gender-specific patterns of cirrhosis complications and their relationship with age and disease duration remain limited, particularly in Middle Eastern populations.

The current study addressed this knowledge gap by examining causes and complications among patients with cirrhosis in the Guilan province population, north of Iran.

## 2. Materials and Methods

### 2.1 Study design

This cross-sectional study was conducted on 308 patients with confirmed cirrhosis in Rasht, Iran who complaint of clinical symptoms including fatigue, easy bruising or bleeding, loss of appetite, nausea, lower extremity swelling, weight loss, skin itching, jaundice, ascites, spider angiomas, palmar erythema, confusion, drowsiness, and slurred speech (indicative of hepatic encephalopathy). Laboratory tests and ultrasound evaluations were conducted for these patients, and only those with a confirmed diagnosis of cirrhosis were enrolled in the study.

### 2.2 Data collection

Demographical data and clinical characteristics of the patients including age, gender, habitat (rural, urban), laboratory findings, and underlying diseases including HBV, HCV, ALD, PSC, PBC, NAFLD, MetS, autoimmune liver disease, and Budd-Chiari syndrome (BCS) were recorded. Cirrhosis etiologies were defined as follows: HBV and HCV infections were confirmed using polymerase chain reaction (PCR) method. ALD was diagnosed based on a documented history of significant alcohol consumption (>20 g/day for women or >30 g/day for men for at least 10 years) in the absence of other liver disease etiologies. NAFLD was diagnosed in patients with hepatic steatosis on imaging or histology without significant alcohol consumption (< 20 g/day for women or < 30 g/day for men) and after exclusion of other causes of chronic liver disease.

MetS was defined according to the International Diabetes Federation criteria [21], requiring central obesity plus any two of the following: raised triglycerides (≥ 150 mg/dL), reduced HDL cholesterol (< 40 mg/dL in men, < 50 mg/dL in women), raised blood pressure (systolic ≥ 130 or diastolic ≥ 85 mmHg), or raised fasting plasma glucose (≥ 100 mg/dL). Patients could have overlapping etiologies, particularly NAFLD and MetS, which frequently coexist; these cases were categorized as "NAFLD/MetS" when both conditions were present. Other etiologies (PSC, PBC, autoimmune liver disease, BCS) were diagnosed based on established clinical, biochemical, imaging, and/or histological criteria. The major disease-related complications such as ascites, esophageal or gastric varices, variceal bleeding, hepatic encephalopathy, HCC, history of spontaneous bacterial peritonitis, portal vein thrombosis, cholangitis episodes, itching, etc. were also recorded. was performed to examine liver status by a radiologist.

### 2.3 Laboratory findings

Hematology and biochemistry tests were performed using XP300 (Sysmex, Japan) and BT1500 (Biotecnica, Italy), respectively. Laboratory findings included white

blood cell count (WBC), hemoglobin (Hb), platelet count (PLT), sodium (Na), albumin (Alb), international normalized ratio (INR), fasting blood sugar (FBS), creatinine (Cr), total bilirubin (BillT), and direct bilirubin (BillD). The normal ranges of laboratory items were as follows: WBC: 4000-11000 cells/µL, Hb for men: 13-17 g/dL and for women: 12-15 g/dL, PLT: 150,000-450,000 cells/µL, Na: 135-145 mEq/L, Alb: 3.3-5.4 g/dL, INR: 1-1.5, FBS: normal < 100 mg/dL, Cr for men: < 1.5 mg/dL and for women: < 1.4 mg/dL, Bill T: 1-1.5 mg/dL, and Bill D: < 0.3 mg/dL.

### *2.4 Statistical Analysis*

Data were reported as number, percentage, and mean ± standard deviation (SD). To assess data normality, the Kolmogorov-Smirnov test was employed. The Chi-square and Fisher's exact tests were used to compare frequencies across various factors. Statistical analyses were performed using SPSS software version 20 and the significant level was set at 0.05.

## 3. Results

Out of 308 cases of liver cirrhosis, 210 (68.2%) were male. The mean age of patients was 59.29 ± 15.1 years (15-90 years) and 251 patients (81.5%) were urban residents. Laboratory findings revealed hypoalbuminemia, anemia, and thrombocytopenia across both genders, with males showing higher bilirubin levels than females, indicating more severe liver dysfunction (Table 1). NAFLD/MetS was the leading cause, accounting for 147 (47.7%) of cases, with a higher prevalence in males (59.6%) compared to females (40.4%) ($P = 0.004$). Viral hepatitis was also a significant contributor, with HCV in 55 (17.9%) of cases, predominantly among males, (44 (80.0%); $P = 0.039$) and HBV in 30 cases (9.7%), also showed male predominance, (86.7%; $P = 0.023$). Autoimmune liver disease was observed in 20 patients (6.5%) and was significantly more frequent in females (70.0%; $P < 0.001$). Among all patients, HCV and HBV co-infection was observed in three cases (1.0%), of which all were males. Co-infection of PSC and autoimmune liver disease occurred in four patients (1.3%), equally distributed between genders, while NAFLD and ALD co-infection was the least frequent, affecting one patient (0.3%), and was observed only in males. None of these co-infections showed significant gender differences (Table 2).

Ascites were the most common complication, affecting 255 patients (82.8%), with a higher prevalence among those aged over 60 years (54.2%; $P = 0.015$). The need for paracentesis was observed in 105 cases (36.1%), significantly different according to disease duration ($P = 0.005$). Esophageal or gastric varices were present in 168 patients (54.6%), increasing significantly with age ($P = 0.038$), and associated with disease duration ($P < 0.001$). Variceal bleeding occurred in 80 patients (26.0%) and had an ascending trend with increasing age ($P = 0.002$) and disease duration ($P < 0.001$).

**Table 1.** Laboratory findings of males and females with cirrhosis (N=308).

| Laboratory findings | Mean ± SD | |
|---|---|---|
| | Male | Female |
| WBC (cells/µL) | 7.2.1 ± 7.8 | 7.2.4 ± 4.8 |
| Hb (g/dL) | 10.2 ± 2.4 | 9.6 ± 1.8 |
| PLT (cells/µL) | 114.8 ± 137.1 | 101.5 ± 60.5 |
| Na (mEq/L) | 134.2 ± 5.5 | 136.1 ± 4.8 |
| Alb (g/dL) | 3.2 ± 0.5 | 3.2 ± 0.5 |
| INR | 1.4 ± 0.6 | 1.4 ± 0.5 |
| FBS (mg/dL) | 105.6 ± 31.6 | 117.0 ± 34.9 |
| Cr (mg/dL) | 1.4 ± 1.1 | 1.2 ± 0.9 |
| Bill T (mg/dL) | 4.3 ± 5.8 | 3.0 ± 3.5 |
| Bill D (mg/dL) | 2.0 ± 3.2 | 1.4 ± 2.2 |

The normal ranges of laboratory items were as follows: Standard deviation (SD); White Blood Cell Count (WBC): 4-11 × $10^9$/L, Hemoglobin (Hb) for men: 13-17 g/dL, Hemoglobin (HB) for women: 12-15 g/dL, Platelet Count (PLT): 150 -450 × $10^9$/L, Sodium (Na): 135-145 mEq/L, Albumin (Alb): 3.3-5.4 g/dL, International Normalized Ratio (INR): 1-1.5 (no unit), Fasting Blood Sugar (FBS): Normal < 100 mg/dL, Prediabetes 100-126 mg/dL, Diabetes > 126 mg/dL, Creatinine (Cr) for men: < 1.5 mg/dL, Creatinine (Cr) for women: < 1.4 mg/dL, Total Bilirubin (Bill T): 1-1.5 mg/dL, Direct Bilirubin (Bill D): < 0.3 mg/dL.

**Table 2.** Prevalence of causes of cirrhosis among males and females with liver cirrhosis (308 patients).

| Causes | Frequency n (%) | | | *P value* |
|---|---|---|---|---|
| | Total | Female | Male | |
| NAFLD or MetS | 147 (47.7) | 58 (39.4) | 89 (60.5) | 0.010 |
| HCV | 55 (17.9) | 11 (20.0) | 44 (80.0) | 0.039 |
| HBV | 30 (9.7) | 4 (13.3) | 26 (86.7) | 0.023 |
| Heart failure | 27 (8.9) | 14 (51.8) | 13 (40.2) | 0.942 |
| Autoimmune liver disease | 20 (6.5) | 14 (70.0) | 6 (30.0) | <0.001 |
| PSC | 14 (4.5) | 4 (28.6) | 10 (71.4) | 0.132 |
| ALD | 7 (2.3) | 0 (0.0) | 7 (100.0) | 0.102 |
| Budd–Chiari syndrome | 6 (1.9) | 2 (33.4) | 4 (66.6) | 0.338 |
| PBC | 2 (0.6) | 1 (50.0) | 1 (50.0) | 0.999 |

Non-Alcoholic Fatty Liver Disease (NAFLD); Hepatitis C Virus (HCV); Hepatitis B Virus (HBV); Primary Sclerosing Cholangitis (PSC); Alcoholic Liver Disease (ALD); Primary Biliary Cholangitis (PBC); Number (n); percentage (%); Metabolic syndrome (MetS). Significant level: P < 0.05.

Hepatic encephalopathy affected 33.5% (n = 103) of patients and showed no significant correlations with age, gender, or disease duration ($P > 0.050$). Hepatocellular carcinoma was rare among patients (7.2%) and portal vein thrombosis affected 10% of cases (n = 31), with no significant associations with age, gender, or disease duration ($P > 0.050$). Other complications, such as recurrent cholangitis attacks, pruritus, and hepatorenal syndrome, were less frequent with a prevalence of 5.6%, 11.0%, and 16.3%, respectively, and showed no statistically significant trends with age, gender, and disease duration ($P > 0.050$) (Table 3).

## 4. Discussion

Cirrhosis poses a significant public health burden, as it is associated with high morbidity and mortality rates, often leading to complications [22,23]. Understanding the related risk factors is crucial for prevention and early intervention strategies to reduce the incidence of cirrhosis and improve outcomes for affected individuals, emphasizing the need for comprehensive public health initiatives aimed at awareness, screening, and management of liver disease. The predominance of male patients in our study was consistent with various international studies, including a large-scale study by Tan et al. that reported a high global burden of cirrhosis in males [24].

A study by Wu et al. illustrated that the death rate of liver cirrhosis and other chronic liver diseases among men was significantly higher than among women [3]. The male predominance likely reflects both biological factors and higher exposure to risk factors among men, such as alcohol consumption and viral hepatitis particularly HBV and HCV due to higher rates of unsafe injection practices and specific occupational exposures [23,25]. The emergence of NAFLD, MetS and HCV as the leading causes of cirrhosis among the studied population highlighted the need for targeted preventive and therapeutic strategies.

**Table 3.** Comparison of complication types based on duration of disease, gender, and age groups (N=308).

| Complication type | | Total | Frequency n (%) Gender | | | Age (year) | | | | Duration of disease (year) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Male | Female | *P* value | <40 | 40-60 | 60< | *P* value | <2 | 2-5 | 5< | *P* value |
| Ascites | No | 53 (17.2) | 35 (66.0) | 18 (34.0) | 0.746 | 12 (22.6) | 18 (33.9) | 23 (43.5) | 0.015 | 27 (50.1) | 19 (35.8) | 7 (14.1) | 0.220 |
| | Yes | 255 (82.8) | 175 (68.6) | 80(31.4) | | 21 (8.2) | 96 (37.6) | 138 (54.2) | | 130 (51.0) | 67 (26.2) | 58 (22.8) | |
| Need for Paracentesis | No | 203 (65.9) | 138 (44.8) | 64 (55.2) | 0.893 | 28 (13.8) | 74 (36.4) | 101 (49.8) | 0.201 | 111 (54.6) | 60 (29.5) | 32 (15.9) | 0.005 |
| | Yes | 105 (36.1) | 74 (24.0) | 32 (76.0) | | 8 (15.7) | 36 (34.2) | 61 (50.1) | | 43 (40.9) | 27 (25.7) | 35 (33.4) | |
| Esophageal or Gastric Varices | No | 140 (45.4) | 93 (66.4) | 47 (33.6) | 0.623 | 10 (7.2) | 49 (35.0) | 81 (57.8) | 0.038 | 90 (64.2) | 30 (21.4) | 20 (14.4) | <0.001 |
| | Yes | 168 (54.6) | 117 (69.6) | 51 (30.4) | | 26 (15.5) | 63 (37.5) | 79 (47.0) | | 67 (39.9) | 56 (33.3) | 45 (26.8) | |
| Gastric or Esophageal Variceal Bleeding | No | 228 (74.0) | 150 (65.7) | 76 (34.3) | 0.402 | 18 (8.0) | 84 (36.8) | 126 (55.2) | 0.002 | 132 (57.9) | 60 (26.3) | 36 (15.8) | <0.001 |
| | Yes | 80 (26.0) | 57 (34.3) | 22 (65.7) | | 18 (22.6) | 27 (33.7) | 35 (43.7) | | 25 (31.2) | 24 (30.0) | 31 (38.8) | |
| Hepatic Encephalopathy | No | 205 (66.5) | 134 (63.3) | 71 (36.7) | 0.154 | 28 (13.7) | 77 (37.5) | 100 (48.8) | 0.214 | 108 (52.6) | 55 (26.8) | 42 (20.6) | 0.596 |
| | Yes | 103 (33.5) | 76 (73.8) | 27 (26.2) | | 8 (7.9) | 36 (34.9) | 59 (57.2) | | 49 (47.5) | 31 (30.1) | 23 (22.4) | |
| Hepatocellular Carcinoma | No | 286 (92.8) | 193 (67.5) | 93 (32.5) | 0.234 | 35 (12.3) | 107 (37.4) | 144 (50.3) | 0.247 | 143 (50.0) | 80 (28.0) | 63 (22.0) | 0.727 |
| | Yes | 22 (7.2) | 18 (81.8) | 4 (8.2) | | 1 (4.6) | 6 (27.2) | 15 (68.2) | | 12 (54.5) | 7 (31.8) | 3 (13.7) | |
| Portal Vein Thrombosis | No | 277 (90.0) | 193 (70.0) | 83 (30.0) | 0.103 | 33 (12.0) | 101 (36.4) | 143 (51.6) | 0.931 | 139 (50.2) | 78 (28.2) | 60 (21.6) | 0.655 |
| | Yes | 31 (10.0) | 17 (54.8) | 14 (45.2) | | 3 (9.7) | 12 (38.7) | 16 (51.6) | | 18 (58.0) | 8 (25.8) | 5 (16.2) | |
| Recurrent Cholangitis Attacks | No | 291 (94.4) | 199 (68.3) | 92 (31.7) | 0.990 | 36 (12.5) | 107 (36.7) | 148 (50.8) | 0.310 | 148 (50.9) | 79 (27.1) | 64 (22.0) | 0.320 |
| | Yes | 17 (5.6) | 12 (70.5) | 5 (29.5) | | 0 (0.0) | 6 (35.3) | 11 (64.7) | | 9 (52.9) | 7 (41.1) | 1 (6.0) | |
| Pruritus | No | 274 (89.0) | 188 (68.6) | 86 (31.4) | 0.920 | 31 (11.4) | 101 (36.8) | 142 (51.8) | 0.901 | 138 (50.3) | 75 (27.3) | 61 (22.4) | 0.238 |
| | Yes | 34 (11.0) | 23 (67.6) | 11 (32.4) | | 5 (14.7) | 12 (35.3) | 17 (50.0) | | 21 (61.8) | 10 (29.4) | 3 (8.8) | |
| Hepatorenal Syndrome | No | 258 (83.7) | 168 (65.1) | 90 (34.8) | 0.272 | 43 (16.7) | 80 (31.0) | 135 (52.3) | 0.070 | 144 (55.8) | 60 (23.2) | 54 (21.0) | 0.590 |
| | Yes | 50 (16.3) | 38 (76.0) | 10 (24.0) | | 3 (6.0) | 15 (30.0) | 32 (64.0) | | 32 (64.0) | 10 (20.0) | 8 (16.0) | |

Number (n); percentage (%), Significant level: $P < 0.05$

Huang et al. reported that HCV infection is the leading cause of global mortality associated with cirrhosis, followed by ALD [5]. On the other hand, a study by Choudhary and Duseja found NAFLD as a prominent contributor to cirrhosis in several countries [26]. NAFLD begins with the accumulation of excess fat in liver cells, which can lead to non-alcoholic steatohepatitis (NASH) in some individuals [6]. Over time, persistent inflammation and ongoing liver cell damage can result in the formation of scar tissue, ultimately leading to cirrhosis [2]. Additionally, the increasing prevalence of NAFLD in the context of rising obesity rates, insulin resistance, and MetS further exacerbates this issue, making it one of the leading causes of cirrhosis globally [28].

The strong male predominance in viral hepatitis-related cirrhosis observed in our study was more pronounced than in many Western studies but aligns with epidemiological patterns reported in other Middle Eastern and Asian studies [29,30]. This pattern may reflect regional differences in transmission routes, screening practices, and access to antiviral therapy. Differences in transmission routes, such as higher rates of unsafe injection practices, sexual transmission, or mother-to-child transmission in certain populations, can contribute to increased infection rates among men [31]. Additionally, variations in healthcare access, including the availability and affordability of screening programs and antiviral treatments, may result in delayed diagnosis and treatment in men, exacerbating disease progression [32]. Furthermore, cultural and social factors, such as stigma or gender roles that affect healthcare-seeking behavior, could also play a significant role in this observed predominance [33,34]. In the current study, we observed a higher prevalence of autoimmune liver disease among females. Evidence reported a higher prevalence of autoimmune liver disease in female patients [35]. Women are generally more susceptible to autoimmune conditions due to the influence of sex hormones, particularly estrogen, which is believed to play a role in modulating immune responses [36]. While many autoimmune liver diseases predominantly affect females, PSC's higher occurrence in males highlights the complexity of autoimmune conditions and the need to consider both biological and environmental factors in their epidemiology [35]. The laboratory findings in our study revealed similar patterns of liver dysfunction between genders, though with subtle differences. The observed thrombocytopenia and hypoalbuminemia in both genders align with established markers of advanced liver disease. Sohail et al. demonstrated a possible association between leukopenia and thrombocytopenia, which may affect chronic liver disease treatment and prognosis [37]. Thrombocytopenia is frequently observed in patients with cirrhosis due to a combination of mechanisms that affect PLT production, sequestration, and destruction [38]. One major factor contributing to this condition is hypersplenism, which leads to an increased pooling of PLT in an enlarged spleen caused by portal hypertension. Additionally, the production of PLT is compromised in chronic liver disease due to depressed levels of thrombopoietin, a hormone crucial for regulating PLT production and maturation [38,39]. A particularly notable finding was the association between age, disease duration, and complications. The significant associations between age and specific complications (ascites, varices, and variceal bleeding) suggest age as an independent risk factor for cirrhosis progression. However, our findings showed that gender did not significantly influence complication rates. Haukeland et al. found a reduced mortality rate due to variceal bleeding that may contribute to improved survival without liver transplantation in females with cirrhotic and gastroesophageal varices compared to males [40,41]. Zhang et al. found that in patients with NAFLD and type 2 diabetes (T2D), age was a more significant predictor of liver-related events than the duration of T2D [42], highlighting the importance of screening for advanced liver disease in individuals with NAFLD and T2D at the age over 50 [43].

However, the current study provided valuable knowledge on the importance of screening for chronic liver diseases, some limitations should be noted including the cross-sectional design of the study which prevents causal inference, the single-center nature of the study may limit generalizability, and the lack of follow-up data prevents assessment of long-term outcomes. Additionally, the study's regional focused in one province may not fully represent the cirrhosis patterns in Iran due to potential differences in environmental and genetic factors across populations.

Our findings revealed a significant shift in cirrhosis epidemiology, with NAFLD/metabolic syndrome emerging as the predominant cause, suggesting a transition from traditional liver disease etiologies to lifestyle-related factors. Notable gender-specific patterns were identified, with viral hepatitis predominantly affecting males and autoimmune liver disease showing female predominance. The correlation between complications and disease duration emphasized the critical importance of early detection and gender-specific management approaches, ultimately highlighting the need for personalized treatment strategies focused on both metabolic health and gender-specific risk factors in modern cirrhosis care.

## Ethical declarations

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1396.502). All subjects gave their informed consent to participate in the study. All methods were carried out in accordance with relevant guidelines and regulations that is Declaration of Helsinki.

## Conflict of interest

No potential conflict of interest was reported by the authors.

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## Authors' contributions

M.A and F.J participated in the research design. F.J, M.A, Z.S, N.A, M.A, and F.M participated in writing the first draft. F.J, M.A, Z.S, N.A, M.A, and F.M participated in the performance of the research and data collection. F.J and F.M participated in data analysis. All authors reviewed and confirmed the final manuscript.

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## Declaration of using generative AI and AI-assisted technologies

We used ChatGPT to improve the grammar and language of the manuscript, and all authors reviewed and evaluated the final version.

## References

1. Battle A, Mudd J, Ahlenstiel G, Kalo E. Liver Cirrhosis: Evolving Definitions, and Recent Advances in Diagnosis, Prevention and Management. Livers. 2025;5(3):28. DOI: 10.3390/livers5030028
2. Luo X, He Y, Jiang Z, Liao J. Global burden of liver cirrhosis: trends from 1990-2021 and projections to 2060. J Health Popul Nutr. 2025;44(1):370. DOI: 10.1186/s41043-025-01109-5 PMID: 41126322
3. Wu XN, Xue F, Zhang N, Zhang W, Hou JJ, Lv Y, et al. Global burden of liver cirrhosis and other chronic liver diseases caused by specific etiologies from 1990 to 2019. BMC Public Health. 2024;24(1):363. DOI: 10.1186/s12889-024-17948-6 PMID: 38310221
4. Younossi ZM, Wong G, Anstee QM, Henry L. The Global Burden of Liver Disease. Clin Gastroenterol Hepatol. 2023;21(8):1978-1991. DOI: 10.1016/j.cgh.2023.04.015 PMID: 37121527
5. Huang DQ, Terrault NA, Tacke F, Gluud LL, Arrese M, Bugianesi E, et al. Global epidemiology of cirrhosis - aetiology, trends and predictions. Nat Rev Gastroenterol Hepatol. 2023;20(6):388-398. DOI: 10.1038/s41575-023-00759-2 PMID: 36977794
6. Amponsah-Dacosta E. Hepatitis B virus infection and hepatocellular carcinoma in sub-Saharan Africa: Implications for elimination of viral hepatitis by 2030? World J Gastroenterol. 2021;27(36):6025-6038. DOI: 10.3748/wjg.v27.i36.6025 PMID: 34629817
7. Amini-Salehi E, Letafatkar N, Norouzi N, Joukar F, Habibi A, Javid M, et al. Global Prevalence of Nonalcoholic Fatty Liver Disease: An Updated Review Meta-Analysis comprising a Population of 78 million from 38 Countries. Arch Med Res. 2024;55(6):103043. DOI: 10.1016/j.arcmed.2024.103043 PMID: 39094335
8. Sarcognato S, Sacchi D, Grillo F, Cazzagon N, Fabris L, Cadamuro M, et al. Autoimmune biliary diseases: primary biliary cholangitis and primary sclerosing cholangitis. Pathologica. 2021;113(3):170-184. DOI: 10.32074/1591-951X-245 PMID: 34294935
9. Kalurazi TY, Shakoori V, Nasiri S, Foumani AA, Hesni E, Mahfoozi L, et al. Clinical characteristics and laboratory findings of patients with COVID-19 in Rasht, Iran. J Curr Biomed Rep. 2022;3:91-7. DOI: 10.52547/JCBioR.3.2.91
10. Haghighi M, Khoshrang H, Rimaz S, Kalurazi TY, Atrkar Z, Roushan SG, et al. Evaluation of sequential organ failure assessment (SOFA) score efficiency in predicting the mortality of intensive care unit admitted COVID-19 patients. J Curr Biomed Rep. 2021;2(4):168-75. DOI: 10.52547/JCBioR.2.4.168
11. Ashoobi MT, Joukar F, Mojtahedi K, Maroufizadeh S, Javid M, Parvaneh A, et al. Elevated liver enzymes and diabetes in the PERSIAN Guilan cohort study. Caspian J Intern Med. 2024;16(1):73-82. DOI: 10.22088/cjim.16.1.73 PMID: 39619755
12. Alizadeh A, Joukar F, Ghorani N, Mansour Ghanaei A, Tabatabaii MJ, Faraji N, et al. Prevalence of Hepatic Space-Occupying Lesions Based on Sonographic Findings in Patients Referred to Guilan Cohort Center, Iran. Hepatitis Mon. 2022;22(1):e124888. URL: https://sid.ir/paper/987323/en
13. Baumert LS, Shih A, Chung RT. Management of liver disease and portal hypertension in common variable immunodeficiency (CVID). JHEP Rep. 2023;5(11):100882. DOI: 10.1016/j.jhepr.2023.100882 PMID: 37869072
14. Sharma B, John S. Hepatic Cirrhosis. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025. PMID: 29494026
15. De Gaetano V, Pallozzi M, Cerrito L, Santopaolo F, Stella L, Gasbarrini A, et al. Management of Portal Hypertension in Patients with Hepatocellular Carcinoma on Systemic Treatment: Current Evidence and Future Perspectives. Cancers (Basel). 2024;16(7):1388. DOI: 10.3390/cancers16071388 PMID: 38611066
16. Allaire M, Rudler M, Thabut D. Portal hypertension and hepatocellular carcinoma: Des liaisons dangereuses…. Liver Int. 2021;41(8):1734-1743. DOI: 10.1111/liv.14977 PMID: 34051060
17. Floreani A, Gabbia D, De Martin S. Are Gender Differences Important for Autoimmune Liver Diseases? Life (Basel). 2024;14(4):500. DOI: 10.3390/life14040500 PMID: 38672770
18. Matz-Soja M, Berg T, Kietzmann T. Sex-related variations in liver homeostasis and disease: From zonation dynamics to clinical implications. J Hepatol. 2025;S0168-8278(25)02442-0. DOI: 10.1016/j.jhep.2025.08.007 PMID: 40846185
19. Nevola R, Tortorella G, Rosato V, Rinaldi L, Imbriani S, Perillo P, et al. Gender Differences in the Pathogenesis and Risk Factors of Hepatocellular Carcinoma. Biology (Basel). 2023;12(7):984. DOI: 10.3390/biology12070984 PMID: 37508414
20. Shahdkar M, Goorabzarmakhi MO, Shafizadeh M, Joukar F, Maroufizadeh S, Faraji N, et al. Association between dyslipidemia and elevated liver enzymes: A cross-sectional study from the PERSIAN Guilan cohort study. Endocr Metab Sci. 2025:100272. DOI: 10.1016/j.endmts.2025.100272
21. Zhu L, Spence C, Yang JW, Ma GX. The IDF Definition Is Better Suited for Screening Metabolic Syndrome and Estimating Risks of Diabetes in Asian American Adults: Evidence from NHANES 2011-2016. J Clin Med. 2020;9(12):3871. DOI: 10.3390/jcm9123871 PMID: 33260754
22. Liu YB, Chen MK. Epidemiology of liver cirrhosis and associated complications: Current knowledge and future directions. World J Gastroenterol. 2022;28(41):5910-5930. DOI: 10.3748/wjg.v28.i41.5910 PMID: 36405106
23. Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. J Hepatol. 2023;79(2):516-537. DOI: 10.1016/j.jhep.2023.03.017 PMID: 36990226

24. Tan D, Chan KE, Wong ZY, Ng CH, Xiao J, Lim WH, et al. Global Epidemiology of Cirrhosis: Changing Etiological Basis and Comparable Burden of Nonalcoholic Steatohepatitis between Males and Females. Dig Dis. 2023;41(6):900-912. DOI: 10.1159/000533946 PMID: 37703863
25. Kasarinaite A, Sinton M, Saunders PTK, Hay DC. The Influence of Sex Hormones in Liver Function and Disease. Cells. 2023;12(12):1604. DOI: 10.3390/cells12121604 PMID: 37371074
26. Choudhary NS, Duseja A. Screening of Cardiovascular Disease in Nonalcoholic Fatty Liver Disease: Whom and How? J Clin Exp Hepatol. 2019;9(4):506-514. DOI: 10.1016/j.jceh.2019.02.005 PMID: 31516267
27. Bashir A, Duseja A, De A, Mehta M, Tiwari P. Non-alcoholic fatty liver disease development: A multifactorial pathogenic phenomena. Liver Res. 2022;6(2):72-83. DOI: 10.1016/j.livres.2022.05.002 PMID: 39958625
28. Grander C, Grabherr F, Moschen AR, Tilg H. Non-Alcoholic Fatty Liver Disease: Cause or Effect of Metabolic Syndrome. Visc Med. 2016;32(5):329-334. DOI: 10.1159/000448940 PMID: 27921044
29. Pisaturo M, Onorato L, Russo A, Coppola N. Prevalence of occult HBV infection in Western countries. J Med Virol. 2020;92(12):2917-2929. DOI: 10.1002/jmv.25867 PMID: 32275083
30. Poovorawan K, Soonthornworasiri N, Sa-Angchai P, Mansanguan C, Piyaphanee W. Hepatitis B vaccination for international travelers to Asia. Trop Dis Travel Med Vaccines. 2016;2:14. DOI: 10.1186/s40794-016-0031-z PMID: 28883958
31. Lloyd AR, Franco RA. Sexual Transmission of Viral Hepatitis. Infect Dis Clin North Am. 2023;37(2):335-349. DOI: 10.1016/j.idc.2023.02.010 PMID: 37105646
32. Li C, Thapa D, Mi Q, Gao Y, Fu X. Disparities in hepatitis B virus healthcare service access among marginalised poor populations: a mixed-method systematic review. Infect Dis Poverty. 2024;13(1):58. DOI: 10.1186/s40249-024-01225-0 PMID: 39123232
33. Brown R, Goulder P, Matthews PC. Sexual Dimorphism in Chronic Hepatitis B Virus (HBV) Infection: Evidence to Inform Elimination Efforts. Wellcome Open Res. 2022;7:32. DOI: 10.12688/wellcomeopenres.17601.3 PMID: 36212217
34. Le TV, Vu TTM, Mai HT, Nguyen LH, Truong NT, Hoang CL, et al. Social Determinants of Stigma and Discrimination in Vietnamese Patients with Chronic Hepatitis B. Int J Environ Res Public Health. 2019;16(3):398. DOI: 10.3390/ijerph16030398 PMID: 30708943
35. Invernizzi F, Cilla M, Trapani S, Guarino M, Cossiga V, Gambato M, et al. Gender and Autoimmune Liver Diseases: Relevant Aspects in Clinical Practice. J Pers Med. 2022;12(6):925. DOI: 10.3390/jpm12060925 PMID: 35743710
36. Yang Q, Kennicott K, Zhu R, Kim J, Wakefield H, Studener K, et al. Sex hormone influence on female-biased autoimmune diseases hints at puberty as an important factor in pathogenesis. Front Pediatr. 2023;11:1051624. DOI: 10.3389/fped.2023.1051624 PMID: 36793337
37. Sohail R, Hassan IH, Rukh M, Saqib M, Iftikhar M, Mumtaz H. Assessing Thrombocytopenia and Chronic Liver Disease in Southeast Asia: A Multicentric Cross-Sectional Study. Cureus. 2023;15(8):e43356. DOI: 10.7759/cureus.43356 PMID: 37700968
38. Peck-Radosavljevic M. Thrombocytopenia in chronic liver disease. Liver Int. 2017;37(6):778-793. DOI: 10.1111/liv.13317 PMID: 27860293
39. Mitchell O, Feldman DM, Diakow M, Sigal SH. The pathophysiology of thrombocytopenia in chronic liver disease. Hepat Med. 2016;8:39-50. DOI: 10.2147/HMER.S74612 PMID: 27186144
40. Haukeland JW, Småstuen MC, Pålsdatter PP, Ismail M, Konopski Z, Jørgensen KK, et al. Effect of gender on mortality and causes of death in cirrhotic patients with gastroesophageal varices. A retrospective study in Norway. PLoS One. 2020;15(3):e0230263. DOI: 10.1371/journal.pone.0230263 PMID: 32163489
41. Hosseini-Ghaziani SK, Shafaghi A, Joukar F, Letafatkar N, Habibi A, Maroufizadeh S, et al. Platelet count/spleen diameter ratio for the non-invasive diagnosis of esophageal varices in Iranian patients with cirrhosis: Platelet count/spleen diameter ratio and esophageal varices. J Curr Oncol Med Sci. 2024;4(3):883-90. URL:http://submission.journalofcoms.com/index.php/JCOMS/article/view/237
42. Zhang X, Wong GL, Yip TC, Cheung JTK, Tse YK, Hui VW, et al. Risk of liver-related events by age and diabetes duration in patients with diabetes and nonalcoholic fatty liver disease. Hepatology. 2022;76(5):1409-1422. DOI: 10.1002/hep.32476 PMID: 35334125
43. Georgieva M, Xenodochidis C, Krasteva N. Old age as a risk factor for liver diseases: Modern therapeutic approaches. Exp Gerontol. 2023;184:112334. DOI: 10.1016/j.exger.2023.112334 PMID: 37977514