
Global epidemiology of cirrhosis – aetiology, trends and predictions

In the format provided by the
authors and unedited

Supplementary Table 1 | Selected studies^a that provided data for the aetiology of cirrhosis

Study	Study period	Location	Diagnosis of cirrhosis	Study population	Proportion of cirrhosis cases by aetiology
The Americas					
Flemming et al. ¹	2000–2017	Canada	OHIP or ICD codes	Population-based study of 159,549 individuals with an incident diagnosis of cirrhosis in Ontario, Canada	NASH: 52.7%; Alcohol: 24.4%; HCV: 12.3%; HBV: 5.6%
Orman et al. ²	2004–2014	USA	ICD codes	9,261 patients with newly diagnosed cirrhosis in the Indiana Network for Patient Care	Alcohol: 33.5%; viral: 39.0%; NAFLD/other: 24.9%; autoimmune/cholestatic: 2.6% <u>Trends</u> Alcohol: 0.8% increase per year NAFLD: 0.6% increase per year Viral hepatitis: 1.4% decrease per year
Ioannou et al. ³	2001–2014	USA	ICD codes	116,404 patients with cirrhosis in the Veterans Health Administration	HCV: 45%; Alcohol: 31%; NAFLD: 15%; Other aetiologies: 9%
Goldberg et al. ⁴	2006–2014	USA	ICD codes	24,258 patients with compensated cirrhosis and 14,971 with decompensated cirrhosis from the HealthCore Integrated Research Database	<u>Compensated cirrhosis</u> HCV: 23.9%; Alcohol: 23.5%; Possible NASH: 14.5% <u>Decompensated cirrhosis</u> HCV: 26.8%; Alcohol: 43.2%; Presumed NASH: 16.5%
El-Serag et al. ⁵	2016–2019	USA	Histology, radiographic features, elastography, or serum biomarkers	1,717 patients from 5 institutions in Texas, USA, with compensated cirrhosis	Cured HCV: 33.1%; Alcohol: 30.6%; NAFLD: 23.3%; Active HCV: 16.1%; Active HBV: 2.5%
Gonzalez-Chagolla et al. ⁶	2000–2019	Mexico	Clinical, laboratory, radiographic, and endoscopic features	4,584 patients with cirrhosis, 77% with previous decompensations from 6 tertiary hospitals in central Mexico	<u>2000</u> HCV: 45%; Alcohol: 28%; MAFLD ^b : 14% <u>2019</u> HCV: 11%; Alcohol: 33%; MAFLD: 36%
Appel-da-Silva et al. ⁷	2005–2014	Brazil	Clinical, laboratory, radiographic, and endoscopic features	453 patients with cirrhosis that attended a specialist referral clinic	Among patients without HCC at baseline: HCV: 34.9%; Alcohol: 24.6%; HCV and alcohol: 19.6%; HBV: 0.8%; HBV and alcohol: 1.3%; NAFLD: 1.8%; Cryptogenic: 3.2%
Europe					
West et al. ⁸	1987–2006	UK	ICD codes	3,107 people with cirrhosis from the General Practice Research Database, a primary care database	Alcohol: 56.1%; Cryptogenic: 20.8%; Viral hepatitis: 12.0%; Autoimmune/metabolic: 11.0%

Ratib et al. ⁹	1998–2009	England	ICD and OPCS4 codes	5,118 patients with cirrhosis from the Clinical Practice Research Datalink, a primary care database	<u>Males</u> Alcohol: 61.9%; Viral hepatitis: 11.3%; Autoimmune/metabolic: 6.2%; Cryptogenic: 20.7% <u>Females</u> Alcohol: 42.8%; Viral hepatitis: 11.1%; Autoimmune/metabolic: 15.0%; Cryptogenic: 31.1%
Gu et al. ¹⁰	2005–2018	Germany	ICD codes	All hospital admissions in Germany with a diagnosis code for cirrhosis	<u>2005</u> Alcohol: 51.0%; HCV: 7.0%; HBV: 2.5%; NAFLD: 0.80%; NASH: 0.13% <u>2018</u> Alcohol: 52.3%; HCV: 2.7%; HBV: 1.6%; NAFLD: 2.8%; NASH: 0.8%
Javaud et al. ¹¹	2014–2015	France	Histology, portal hypertension, ascites, or oesophageal varices	224 patients with cirrhosis who presented to the emergency department of 3 university hospitals	Alcohol: 51%; HCV: 19%; Mixed viral and alcohol: 13%; HBV: 8%
Hagstrom et al. ¹²	2004–2017	Sweden	Identified using ICD codes and validated by histology, elastography, radiography, or clinical findings	2,609 patients with cirrhosis who were evaluated at a tertiary hospital	<u>2004–2008</u> Viral hepatitis: 43.4%; NAFLD 5.7% <u>2014–2017</u> Viral hepatitis: 31.0%; NAFLD 14.5%
Olafsson et al. ¹³	2010–2015	Iceland	Histology, serum biomarkers, radiological or endoscopic findings	A prospective, population-based study that included all newly diagnosed patients with cirrhosis (<i>n</i> = 157) diagnosed in Iceland	Alcohol: 31%; NAFLD: 22%; Alcohol and HCV: 15%; HCV: 6%; Primary biliary cholangitis: 5%; Autoimmune hepatitis: 4%; Other: 12%; Unknown: 6%
Popescu et al. ¹⁴	2000–2017	Romania	Not specified	852 patients who received liver transplantation in Romania, as part of the national liver transplant program	HBV: 28.2%; HCV: 16.8%; Alcohol: 8.8% (of total patients that received liver transplant)
Stroffolini et al. ¹⁵	2014	Italy	Histology, clinical, biochemical, and ultrasound findings	832 patients with cirrhosis from 16 hospitals in Italy; this study provided a comparison of trends in aetiology with a historical cohort ¹⁶	<u>2001</u> HBV: 13.0%; HCV: 69.9%; Alcohol: 31.9%; NAFLD: 0.2% <u>2014</u> HBV: 17.6%; HCV: 58.6%; Alcohol: 16.0%; NAFLD: 7.3%
Eastern Mediterranean					
Elzouki et al. ¹⁷	2007–2012	Qatar	Not specified	109 patients were admitted to the intensive care unit in a tertiary hospital	HCV: 33.9%; HBV: 21.1%; Alcohol: 25.7%; Cryptogenic: 23.9%
Pourafkari et al. ¹⁸	2011–2013	Iran	Clinical, biochemical, and histology	69 patients with cirrhosis admitted to a university hospital	HBV: 40.6%; alcohol: 21.7%; unknown: 24.6%; HCV 7.2%

Tailakh et al. ¹⁹	2002–2019	Israel	Histology, portal hypertension, ascites, or oesophageal varices	953 Jewish patients and 95 Bedouin patients who attended a tertiary hospital	<u>Jewish patients</u> HCV: 39.2%; NAFLD: 17.2%; HBV: 8.9%; Alcohol: 14.4%; Cryptogenic: 8.8% <u>Bedouin patients</u> HCV: 14.7%; NAFLD: 21.1%; HBV: 17.9%; Alcohol: 2.1%; Cryptogenic: 20.0%
Africa					
Duah et al. ²⁰	2018–2020	Ghana	Histology, clinical, biochemical, and ultrasound findings	186 patients with cirrhosis admitted to a district hospital	HBV: 38.7%; Alcohol: 38.3%; HCV: 3.2%; NAFLD: 2.7%
Apica et al. ²¹	2010–2011	Uganda	Clinical, biochemical, and ultrasound findings	85 patients with decompensated cirrhosis were admitted to a referral hospital	Alcohol: 55.3%; HBV: 27.1%; HCV: 3.5%
South-East Asia					
Mukherjee et al. ²²	2010–2013	India	Histology, serum biomarkers, radiological or endoscopic findings	4,413 patients with cirrhosis from 11 hospitals across India	Alcohol: 34.3%; HBV: 18.1%; HCV: 17.3%; NAFLD: 1.7%
Alvi et al. ²³	2018–2019	Pakistan	Not specified	192 patients with cirrhosis that underwent endoscopic band ligation	HCV 63.4%; HBV: 18.8%; Alcohol: 13.9%
Niriella et al. ²⁴	2013–2014	Sri Lanka	Not specified	135 patients with cirrhosis presenting to a tertiary referral centre	Cryptogenic: 62.6; alcohol: 29.9%; HBV: 1.9%
Nawalerspanya et al. ²⁵	2014–2018	Thailand	Not specified	128 patients who underwent endoscopic variceal surveillance at a tertiary hospital	HBV: 32.8%; HCV: 37.5%; NAFLD: 5.5%; alcohol: 4.7%; others: 7.8%
Western Pacific					
Tan et al. ²⁶	2015–2017	Malaysia	Not specified	105 patients with cirrhosis that underwent endoscopy for variceal surveillance	HCV: 31.0%; HBV: 20.0%; cryptogenic: 23.6%; alcohol: 16.4%; NASH: 3.6%
Tan et al. ²⁷	2016–2020	Singapore	Histology, serum biomarkers, radiological or endoscopic findings	251 patients with cirrhosis listed for liver transplantation at a tertiary hospital	HBV: 28.8%; NAFLD: 18.8%; HCV 10.8%; Alcohol: 9.6%; Others: 32.0%
Huu et al. ²⁸	2014–2015	Vietnam	Elastography and features of portal hypertension	47 patients with cirrhosis who were admitted to a university hospital	HBV: 48.9%; HCV: 36.2%; alcohol: 10.6%
Xiong et al. ²⁹	2003–2013	China	Clinical and imaging features, and/or histology	1,582 patients with a new diagnosis of cirrhosis at a hospital	<u>2003-2013</u> HBV: 59.3%; Alcohol: 9.9%; HCV: 1.0%; primary biliary cholangitis: 4.4%; NASH: 1.9% <u>2012-2013</u> NASH: 3.2%

Enomoto et al. ³⁰	2007–2016	Japan	Clinical, laboratory, and imaging features, and/or histology	48,621 patients with cirrhosis from 79 hospitals in Japan	<u>2007</u> HCV: 58.6%; alcohol 13.7%; HBV: 13.6%; cryptogenic 5.6%; NASH 2.0% <u>2014-2016</u> HCV: 40.2%; alcohol 24.9%; HBV: 9.0%; cryptogenic 7.5%; NASH: 9.1%
Tan et al. ²⁷	2016–2020	Hong Kong	Histology, serum biomarkers, radiological or endoscopic findings	320 patients with cirrhosis listed for liver transplantation at a tertiary hospital	HBV: 53.1%; NAFLD: 1.6%; HCV 7.5%; Alcohol: 7.2%; Others: 30.6%
Jang et al. ³¹	2000–2014	South Korea	KCD-6 codes	15,716 patients with cirrhosis diagnosed at 5 university hospitals	<u>2000-2004</u> HBV: 55.3%; HCV 6.3%; Alcohol 30.6%; NAFLD 1.8% <u>2010-2014</u> HBV: 41.2%; HCV: 8.5%; Alcohol 35.6%; NAFLD: 6.4%

^aStudies were selected to present data from diverse geographical locations; when multiple studies from the same country were available, studies that provided data for temporal trends in the aetiologies of cirrhosis were prioritized for selection. ^bDefinition for MAFLD as described by Eslam et al.³² HBV, hepatitis B virus; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; MAFLD, metabolic associated fatty liver disease.

- 1 Flemming, J. A., Djerboua, M., Groome, P. A., Booth, C. M. & Terrault, N. A. NAFLD and Alcohol-Associated Liver Disease Will Be Responsible for Almost All New Diagnoses of Cirrhosis in Canada by 2040. *Hepatology* **74**, 3330-3344 (2021).
- 2 Orman, E. S. *et al.* Trends in Characteristics, Mortality, and Other Outcomes of Patients With Newly Diagnosed Cirrhosis. *JAMA network open* **2**, e196412 (2019).
- 3 Ioannou, G. N., Green, P., Lowy, E., Mun, E. J. & Berry, K. Differences in hepatocellular carcinoma risk, predictors and trends over time according to etiology of cirrhosis. *PLoS ONE [Electronic Resource]* **13**, e0204412 (2018).
- 4 Goldberg, D. *et al.* Changes in the Prevalence of Hepatitis C Virus Infection, Nonalcoholic Steatohepatitis, and Alcoholic Liver Disease Among Patients With Cirrhosis or Liver Failure on the Waitlist for Liver Transplantation. *Gastroenterology* **152**, 1090-1099.e1091 (2017).
- 5 El-Serag, H. B. *et al.* Risk Factors for Cirrhosis in Contemporary Hepatology Practices-Findings From the Texas Hepatocellular Carcinoma Consortium Cohort. *Gastroenterology* **159**, 376-377 (2020).
- 6 Gonzalez-Chagolla, A. *et al.* Cirrhosis etiology trends in developing countries: Transition from infectious to metabolic conditions. Report from a multicentric cohort in central Mexico. *The Lancet Regional Health – Americas* **7**, 100151 (2022).
- 7 Appel-da-Silva, M. C. *et al.* Incidence of hepatocellular carcinoma in outpatients with cirrhosis in Brazil: A 10-year retrospective cohort study. *World J. Gastroenterol.* **22**, 10219-10225 (2016).

- 8 West, J., Card, T. R., Aithal, G. P. & Fleming, K. M. Risk of hepatocellular carcinoma among individuals with different aetiologies of cirrhosis: a population-based cohort study. *Aliment. Pharmacol. Ther.* **45**, 983-990 (2017).
- 9 Ratib, S., Fleming, K. M., Crooks, C. J., Aithal, G. P. & West, J. 1 and 5 year survival estimates for people with cirrhosis of the liver in England, 1998-2009: a large population study. *J. Hepatol.* **60**, 282-289 (2014).
- 10 Gu, W. *et al.* Trends and the course of liver cirrhosis and its complications in Germany: Nationwide population-based study (2005 to 2018). *Lancet Reg Health Eur* **12**, 100240 (2022).
- 11 Javaud, N. *et al.* Prognosis of cirrhotic patients admitted to Emergency Departments: A multicenter study. *Am. J. Emerg. Med.* **37**, 1317-1321 (2019).
- 12 Hagström, H. *et al.* Etiologies and outcomes of cirrhosis in a large contemporary cohort. *Scand. J. Gastroenterol.* **56**, 727-732 (2021).
- 13 Olafsson, S. *et al.* A nationwide population-based prospective study of cirrhosis in Iceland. *JHEP Rep* **3**, 100282 (2021).
- 14 Popescu, I. *et al.* The Romanian National Program for Liver Transplantation - 852 Procedures in 815 Patients over 17 Years (2000-2017): A Continuous Evolution to Success. *Chirurgia (Bucur.)* **112**, 229-243 (2017).
- 15 Stroffolini, T. *et al.* Characteristics of liver cirrhosis in Italy: Evidence for a decreasing role of HCV aetiology. *Eur. J. Intern. Med.* **38**, 68-72 (2017).
- 16 Stroffolini, T. *et al.* Characteristics of liver cirrhosis in Italy: results from a multicenter national study. *Dig. Liver Dis.* **36**, 56-60 (2004).
- 17 Elzouki, A. N. *et al.* Predicting mortality of patients with cirrhosis admitted to medical intensive care unit: An experience of a single tertiary center. *Arab J. Gastroenterol.* **17**, 159-163 (2016).
- 18 Pourafkari, L. *et al.* Electrocardiographic findings in hepatic cirrhosis and their association with the severity of disease. *Cor Vasa* **59**, e105-e113 (2017).
- 19 Tailakh, M. A. *et al.* Liver Cirrhosis, Etiology and Clinical Characteristics Disparities Among Minority Population. *J Immigr Minor Health* **24**, 1122-1128 (2022).
- 20 Duah, A., Agyei-Nkansah, A., Osei-Poku, F., Duah, F. & Addo, B. P. Sociodemographic characteristics, complications requiring hospital admission and causes of in-hospital death in patients with liver cirrhosis admitted at a district hospital in Ghana. *PLoS One* **16**, e0253759 (2021).
- 21 Apica, B. S., Ocama, P., Seremba, E., Opio, K. C. & Kagimu, M. M. Decompensated cirrhosis-related admissions in a large urban hospital in Uganda: prevalence, clinical and laboratory features and implications for planning patient management. *Afr. Health Sci.* **13**, 927-932 (2013).
- 22 Mukherjee, P. S. *et al.* Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. *PLoS One* **12**, e0187033 (2017).
- 23 Alvi, H., Zuberi, B. F., Rasheed, T. & Ibrahim, M. A. Evaluation of endoscopic variceal band ligation sessions in obliteration of esophageal varices. *Pak J Med Sci* **36**, 37-41 (2020).
- 24 Niriella, M. A. *et al.* Sero-prevalence and vaccination status of hepatitis A and hepatitis B among adults with cirrhosis in Sri Lanka: a hospital based cohort study. *BMC Res. Notes* **10**, 303 (2017).
- 25 Nawalerspanya, S., Sripongpun, P., Chamroonkul, N., Kongkamol, C. & Piratvisuth, T. Validation of original, expanded Baveno VI, and stepwise & platelet-MELD criteria to rule out varices needing treatment in compensated cirrhosis from various etiologies. *Ann. Hepatol.* **19**, 209-213 (2020).
- 26 Wendy Tan, A. Y. & Chieng, J. Y. Endoscopic variceal ligation as primary prophylaxis for oesophageal variceal bleeding at a Malaysian tertiary hospital. *Med. J. Malaysia* **73**, 361-364 (2018).

- 27 Tan, E. X.-X. *et al.* Impact of COVID-19 on Liver Transplantation in Hong Kong and Singapore: A Modelling Study. *The Lancet Regional Health – Western Pacific* **16**, 100262 (2021).
- 28 Bui Huu, H. *et al.* Characterization of SCCA-IgM as a biomarker of liver disease in an Asian cohort of patients. *Scand. J. Clin. Lab. Invest.* **78**, 204-210 (2018).
- 29 Xiong, J., Huang, J., Sun, W., Wang, J. & Chen, D. Non-alcoholic steatohepatitis-related liver cirrhosis is increasing in China: a ten-year retrospective study. *Clinics (Sao Paulo, Brazil)* **70**, 563-568.
- 30 Enomoto, H. *et al.* Transition in the etiology of liver cirrhosis in Japan: a nationwide survey. *J. Gastroenterol.* **55**, 353-362 (2020).
- 31 Jang, W. Y. *et al.* Changes in Characteristics of Patients with Liver Cirrhosis Visiting a Tertiary Hospital over 15 Years: a Retrospective Multi-Center Study in Korea. *J. Korean Med. Sci.* **35**, e233 (2020).
- 32 Eslam, M. *et al.* MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease. *Gastroenterology* **158**, 1999-2014.e1991 (2020).