Paradigm Academic Press
Journal of Innovations in Medical Research
ISSN 2788-7022
DEC. 2024 VOL.3, NO.4

# Alcoholic Liver Disease: Diagnosis and Treatment Strategies

Haradhan Kumar Mohajan[1]

[1] Associate Professor, Department of Mathematics, Premier University, Chittagong, Bangladesh

Correspondence: Haradhan Kumar Mohajan, Associate Professor, Department of Mathematics, Premier University, Chittagong, Bangladesh.

doi:10.56397/JIMR/2024.12.06

**Abstract**

Alcoholic liver disease (ALD) occurs from initial alcoholic fatty liver (steatosis) to more advanced type inflammation, such as alcoholic hepatitis, and liver cirrhosis for chronic excessive continual alcohol consumption. It is considered as the continuous damage to the liver and its functions. Steatosis is the primary stage of the accumulation of macrovesicular fat in the cytosol of hepatocytes. Alcoholic hepatitis (AH) is the second stage of ALD that is a more severe, and inflammatory type of liver injury. Alcoholic cirrhosis is the final stage of ALD that is characterized by excessive liver scarring and liver failure. After years of regularly excessive alcohol consumption is one of the leading causes of ALD worldwide and the most prevalence of it is seen in high-income countries, especially in the western world, such as in Europe and North America. Women are more vulnerable to ALD pathogenesis than men, and after a shorter period of habitual drinking at a lower amount of alcohol they have a high probability of developing ALD. Lifelong stopping of drinking alcohol is an active therapy of ALD. Liver transplantation is the life-saving strategy for cirrhosis patients. This review paper tries to discuss the aspects of ALD, and its diagnosis and management strategy.

**Keywords:** alcohol, hepatitis, cirrhosis, obesity, therapy, liver transplantation

## 1. Introduction

The liver breaks down alcohol that produces harmful chemicals and also removes these from our body. It is the primary but major site of ethanol metabolism, where ethanol is oxidized by three enzymatic pathways: i) the cytosolic alcohol dehydrogenase pathway, ii) the microsomal ethanol oxidizing system, and iii) the peroxisomal catalase pathway (Lieber & Leo, 1998). The liver may be injured through the destruction of its cells if an individual drinks more alcohol than it can process. Chronic consumption of alcohol damages the normal defense mechanism of the liver through the disturbance of the gut barrier system that leads to decrease nutrient absorption (Stickel et al., 2017).

Alcoholic liver disease (ALD) is one of the commonest causes of liver disease that is associated with liver inflammation and injury or progressive fibrosis. It is the second most common cause of chronic liver disease after viral liver disease. Most of the ALD patients are asymptomatic and diagnosed to have fatty liver while undergoing routine health checkup. The worldwide prevalence of ALD has increased and is expected to increase further (Subramaniyan et al., 2021).

If a man takes up to two drinks per day and a woman takes one drink per day considered them as moderate drinkers and daily consumption above those limits can lead to health, personal, and social problems (Askgaard et al., 2015). In men, 40–80g per day of ethanol produces fatty liver; and 160g per day intake for 10–20 years causes hepatitis or cirrhosis. Women tend to develop the advanced liver disease with less alcohol intake (20–40g per day) substantially than men (Bradley et al., 1998). The majority of heavy drinkers do not ultimately develop advanced liver disease; only 35% of excessive drinkers eventually develop steatohepatitis and AH, and only 10% ultimately develop cirrhosis (Friedman, 2018). Fatty liver develops in the earliest in more than 90% of drinkers

who consume 4–5 standard drinks per day (binge drinkers). Alcohol consumption increases the risk of liver disease-related mortality by 260-fold, cardiovascular mortality by 3.2-fold, and cancer mortality by 5.1-fold (Hagstrom et al., 2021).

About 4% (2.5 million) of global deaths are due to liver disease complications of cirrhosis, viral hepatitis, and liver cancer. At present about 43% of the world population drinks alcohol and per capita alcohol consumption is about 6.4 liter per year, and the highest prevalence is seen in high-income countries especially in Europe, and North America where 50% of cirrhosis related deaths occur due to alcohol use. Recently alcohol use increases in Latin America, Africa and Asia (Rossow & Makela, 2021). The lowest rates of alcohol use are observed in Muslim dominated countries (Rehm et al., 2013). Excessive alcohol intake kills 3.3 million people worldwide annually that accounts for 5.9% of all deaths (WHO, 2014).

The disease ALD requires early recognition and specialized medical care. It has higher probability to liver cancer in those who are overweight or obese with comorbidity (Mohajan & Mohajan, 2023a, e). Various other factors heavily influence the progression of ALD are gender, ethnicity, genetic variants, viral hepatitis, and environmental factors (Osna et al., 2017). Sometimes cirrhosis is developed among heavy drinkers without having alcoholic hepatitis (AH) at first. If AH is undiagnosed and untreated, and the patient continues to consume alcohol for a long time, can progress to more advanced type, such as liver fibrosis, or liver cirrhosis over time (Puri et al., 2018). Liver transplantation is an option for an alcoholic liver cirrhosis patient that is widely employed for the survival of the patients (Veldt et al., 2002). Recently the alcohol consumption is slightly decreased in several European countries; but it is rising in some other countries of the world (Stickel et al., 2017). Alcohol consumption is responsible for 3.8% of global mortality and 4.6% of disability-adjusted life-years (DALYs) lost due to premature death (Rehm et al., 2009).

## 2. Literature Review

In any research, literature review is an introductory section, where seminal works of previous researchers are emphasized (Polit & Hungler, 2013). It helps the new researchers to understand the subject area to perform their research efficiently (Creswell, 2007). Vetriselvan Subramaniyan and his coauthors have focused on the mechanism of alcohol-induced metabolic dysfunction, contribution to liver pathogenesis, the effect of pregnancy, and targeted therapy of ALD (Subramaniyan et al., 2021). Praveen Sharma and Anil Arora have observed that recently the ALD has increased due to widespread easy availability of alcohol and sedentary life style of people (Sharma & Arora, 2020).

Michelle Keating and her coauthors have realized that diagnoses of alcoholic hepatitis are chest radiography and cultures of peritoneal fluid, blood, and urine; and treatment is primarily consists of supportive care, such as alcohol cessation and nutritional supports (Keating et al., 2022). Mohannad Dugum and his coauthors have discussed the alcoholic hepatitis of severe form that is a devastating acute condition, which requires early recognition and specialized tertiary medical care (Dugum et al., 2015).

Hiromasa Ishii and his coworkers have realized that factors exert adverse effects on the progression of ALD are gender difference, presence of hepatitis virus, immunologic abnormality, genetic polymorphism of alcohol-metabolizing enzymes, and complication of obesity or overweight (Ishii et al., 2010). Syifa Mustika and Nina Nur Arifah want to explore the diagnostic and therapeutic challenge of ALD among young aged women (Mustika & Arifah, 2017).

Felix Stickel and his coauthors have highlighted on pathophysiology and management of ALD. They have realized that the pathophysiology of ALD is still incompletely understood but relates largely to the direct toxic effects of alcohol and its main intermediate, acetaldehyde. The diagnosis of ALD is relatively easy with a panel of well-evaluated tests, but the treatment of ALD is difficult and grounded in abstinence as the pivotal therapeutic goal (Stickel et al., 2017). Ashwani K. Singal and his coworkers have shown that general measures of ALD are management of liver disease complications, management of alcohol withdrawal syndrome, surveillance for infections and early effective antibiotic therapy, nutritional supplementation, and treatment of the underlying alcohol use disorder (Singal et al., 2018).

## 3. Research Methodology of the Study

All academicians take the research as an essential and influential work of their academic life to lead in academic world (Pandey & Pandey, 2015). Researchers often write a methodology section with details of the research analysis. Methodology is a clear guideline to do a good research that follows scientific methods properly (Kothari, 2008). It provides the research design and analysis procedures to perform a good research (Hallberg, 2006). Therefore, research methodology is a way to the researchers for organizing, planning, designing, and conducting a good research (Legesse, 2014). This study is a qualitative research method that aims to discover meaning and understanding of the study (Parahoo, 2014; Mohajan, 2017, 2018, 2020).

We have used both published and unpublished secondary data sources of ALD to prepare this research paper

(Mohajan, 2024a-e). We have taken help from the journal articles, conference papers, published books and handbooks of famous authors, internet, websites, etc. for performing the job efficiently (Mohajan & Mohajan, 2023a-v, 2024a-j).

## 4. Objective of the Study

Main objective of this article is to discuss the basic concept of ALD for the awareness of the disease. At present ALD is one of the commonest causes of liver disease that is associated with liver inflammation and injury. Consecutive excessive alcohol consumption for a long time is one of the main causes of ALD. Other minor objectives of the study are as follows:

- to provide an overview on alcohol,
- to highlight on various types of ALD, and
- to show the present treatment procedures of ALD.

## 5. An Overview on Alcohol

Alcoholic beverages are popular as a lifestyle habit globally, especially more popular in Europe and North America, and have been established as a part of everyday life. One gram of alcohol can provide about seven calories. Alcohol is a psychoactive substance that has been widely used in many cultures for centuries. It is also thought to be an important component in business and various other social interactions (WHO, 2011). It is also a direct hepatotoxin, and its ingestion causes the initiation of numerous metabolic responses in the body (Russmann et al., 2009). It is oxidized in the liver by alcohol dehydrogenase to acetaldehyde, which is then metabolized to acetate; after further oxidization through the citric acid cycle synthesized in fatty acids and fat. P450 2E1 isoenzyme is the major P450 enzyme involved that can metabolize 10-15% of alcohol consumed (Keating et al., 2022). Alcohol consumption is related to intestinal bacterial overgrowth with reduced alpha diversity, disruption of the intestinal tight junctions with bacterial translocation to the portal circulation, and impaired Kupffer cell clearance of lipopolysaccharide (Purohit et al., 2008).

Alcohol directly acts on the liver parenchymal cells to initiate the abnormalities of intestinal barrier functions, alteration of microbiota, and increased toll-like receptors activation in liver cells (Subramaniyan et al., 2021). The excess use of it can develop liver disease, some cancers, cardiovascular diseases, and more than 200 fatal diseases. Alcohol not only damages liver but also damages many other vital organs of the body, such as gastrointestinal tract, pancreas, blood, circulatory organs (heart, blood and blood vessels), brain, cranial nerves, oropharynx, esophagus, colon, rectum, female breast, and also immune system (Ishii et al., 2010). Alcohol consumption is also a major cause of accidents and violence in society. Alcohol is also harmful to other people, such as family members, friends, co-workers, and neighbors (Osna et al., 2017).

## 6. Major Stages of ALD

In the USA, ALD affects at least two million people. Both the duration and the quantity of alcohol consumption are important risk factors for the development of ALD. With continued drinking, alcohol-induced liver disease can proceed to liver inflammation, fibrosis, cirrhosis, and even liver cancer (Cordero-Espinoza & Huch, 2018). ALD develops in three stages: alcoholic fatty liver disease, alcoholic hepatitis, and alcoholic cirrhosis (O'Shea et al., 2010). Frequently there is significant overlap between these three stages, and clinical presentation depends upon the stage of liver disease (Sharma & Arora, 2020).

### *6.1 Alcoholic Fatty Liver*

Alcohol consumption induces fatty acid synthesis and inhibits fatty acid oxidation, thereby promoting fat deposition in the liver (Seitz & Stickel, 2006). Fatty liver is a condition in which triglyceride accumulates in hepatocyte. As a result, the enlargement of hepatocyte and disturbances of blood circulation within the sinusoids are happened that create adverse effects on various metabolic processes within the cells (Ishii et al., 2010). When fat reaches 5-10% of the weight of liver, it becomes a matter of concerning (Sakhuja, 2014).

Alcoholic fatty liver (steatosis) is the earliest stage of alcohol-related liver disease, where extra fat is stored in the cytosol of hepatocytes. Steatosis is usually seen macroscopically and rarely microscopically. The lipid droplets in the cytoplasm of the hepatocytes (microvascular) expand and push the nucleus to the boundary of the cell (macrovascular). Moreover, macrovascular droplets have a low surface area to volume ratio, that is, they are less prone to lipases (Sakhuja, 2014).

It is common in 80-90% of heavy drinkers who take four to five standard drinks within two hours. In severe fatty liver, fat is distributed throughout the acinus (Singh et al., 2017). It develops among nearly all individuals who consume chronically more than 60g of alcohol per day even for a short period of time (Rubin & Lieber, 1968). In this stage many patients are asymptomatic and frequently never try for medical diagnostic and treatment. The early symptoms of steatosis are vague and sometimes have no symptoms. In severe fatty infiltration some

nonspecific symptoms of it are fatigue, malaise, anorexia, nausea, abdominal discomfort, weakness, and weight loss (Bouneva et al., 2003).

Drinking a large volume of alcohol can cause fatty acids in the liver. Sometimes, heavy drinking over a short period, even less than a week, can cause this. The alcoholic fatty liver disease is often reversible if the patient completely stops the alcohol consumption in onward (Ishii et al., 2010). If it develops once, it is not clear whether it will remain a fatty liver or progress to a more severe liver disease (Teli et al., 1995).

*6.2 Alcoholic Hepatitis*

Alcoholic hepatitis (AH) or alcoholic steatohepatitis is a clinical syndrome characterized by acute jaundice and liver enzyme abnormalities for long-term heavy alcohol use (Keating et al., 2022). It is associated with liver cell necrosis, impaired liver function, and progression to cirrhosis. It is a severe syndrome of ALD with swelling and inflammation in the centrilobular area of hepatic acinus of the liver to become damaged with a high risk of mortality. A smaller numbers of heavy alcohol users' liver function progress on to AH (Mathurin & Bataller, 2015). It is a severe manifestation of ALD and severity varies from mild to life-threatening. Women are at higher risk of developing AH (Dugum et al., 2015).

Ballooning of hepatocytes is classical that compress sinusoids and lead to portal hypertension which is reversible. Symptoms of it vary significantly with the severity of the disease and the age of the patient (Choi et al., 2012). Some possible symptoms of it are loss of appetite, nausea and vomiting, abdominal pain, bleeding from esophageal varices, ascites, hepatorenal syndrome, spontaneous bacterial peritonitis, hepatopulmonary syndrome, hepatic encephalopathy, and jaundice. Usually, the liver is enlarged and tender during AH (Bouneva et al., 2003; Keating et al., 2022). Anemia and leukocytosis are common in AH; also, thrombocytopenia may occur due to direct alcohol toxicity. Risk factors of AH are female sex, higher body mass index (BMI), comorbid liver diseases, etc. (Veryan & Forrest, 2019). Every year about 20-40% of AH develop to fibrosis and 10-20% progress to cirrhosis; and of those with cirrhosis, 1-2% are diagnosed with hepatocellular carcinoma (Dugum et al., 2015).

In severe or associated with liver cirrhosis, complications occur due to liver failure and portal hypertension, leading to a high short-term mortality (Galambos & Shapira, 1973). AH has got poor short-term survival, need hospital admission and constant monitoring with good nutrition (Sharma & Arora, 2020). Protein-calorie malnutrition is a common comorbidity to AH. Nutritional supports, such as thiamine to decrease risk of Wernicke encephalopathy; low-volume intravenous fluids for dehydration; and supplemental folate, vitamin $B_6$, vitamin $B_{12}$, riboflavin, and zinc for common vitamins and minerals deficiencies that can improve the condition of AH (McClain et al., 2021). Daily energy intake of 35-40 kcal and daily protein intake of 1.2-1.5g per kg of body weight are recommended for an adult AH patient. Also, sodium, potassium, phosphate, and magnesium need to sufficiently for the balance of fluids and electrolytes (Moreno et al., 2016). AH is reversible and prolonged abstinence from alcohol is the mainstay of treatment of it (Mohajan, 2024e). If the AH patient continues to drink alcohol may progress to cirrhosis over months to years. Liver transplantation is recommended for some patients with severe AH (Goel & Daugherty, 2021).

*6.3 Alcoholic Cirrhosis*

Alcoholic cirrhosis is the final stage of ALD and unfortunately it is irreversible. It is characterized by extensive liver fibrosis, micronodular regeneration, impaired liver function, portal hypertension, and predisposition to hepatocellular carcinoma. It is the deposition of abnormal amounts of extracellular matrix proteins (Morgan, 1994; Bouneva et al., 2003). It reportedly occurs in 10–30% of heavy drinkers who have at least 20 years of drinking history at the consumption level of 0.9 L/day and the liver has been inflamed for a long time (Ishii et al., 2010). But there is no clear dose-dependent relationship between alcohol dosage and risk of development of alcoholic cirrhosis (Corrao et al., 1998).

Various associated factors, such as viral hepatitis, obesity; and various metabolic factors, such as diabetes increase the risk of alcoholic cirrhosis (Hart et al., 2010). In severe cirrhosis, the liver is shrunken, irregular or nodular along with ascites, dilated portal vein varices and splenomegaly, suggesting portal hypertension. Some symptoms of this stage are jaundice, ascites, peripheral edema, gastrointestinal bleeding, abdominal swelling, malnutrition, and mental confusion (Jepsen et al., 2010).

The patient may experience weakness, fatigue, and weight loss. Lifelong abstinence of alcohol can improve liver function. To survive, liver transplantation is the best option for patients of liver cirrhosis with severe liver dysfunction. Alcoholic cirrhosis is the eighth most common cause of death in the USA (Mathurin & Bataller, 2015). A great concern is the rising incidence of hepatocellular carcinoma (HCC) which evolves in about 1-2% of alcoholic cirrhosis patients (Stickel, 2015).

**7. Laboratory Evaluation of ALD**

Diagnosis of ALD requires good reliable evidence of alcohol abuse to treat the disease properly. Laboratory abnormalities reflect the deterioration of ALD. No single laboratory or imaging study can confirm the diagnosis of ALD. A detailed history from relatives is crucial in suspecting liver disease due to alcohol consumption (Singal et al., 2018).

Liver enzymes aminotransferases aspartate transaminase (AST) and alanine transaminase (ALT) increase among ALD patients. Most causes of liver injury are associated with higher serum levels of ALT than AST (up to 2 to 6 times the upper limit of normal), but AST elevation is more prominent than that of ALT (Cohen & Kaplan, 1979). The absolute values of the ALT and AST usually do not exceed 300 IU/L unless a superimposed hepatic insult exists. Serum AST/ALT>2 indicates alcoholic hepatitis and cirrhosis and has a very high probability when it exceeds 3 (Giannini et al., 2002). Elevated serum levels of γ-glutamyl transpeptidase (γGTP) is common who consume over alcohol regularly. It occurs in 85-90% of persons who ingest more than 50g of alcohol daily (Seitz, 2006). An isolated raised γ-GTP in a heavy drinker with otherwise normal liver function tests is usually associated with only mild histological liver damage, which is reversible (Pol et al., 1990).

Ultrasonography (USG) is very useful for identifying steatosis and liver morphology, and splenomegaly can be used to evaluate the progression of liver disease. It can reveal the presence of fatty liver and hepatitis through changes in the reflectivity of the liver parenchyma (Ratziu et al., 2010). Characteristic findings on USG include a hyperechoic liver with or without hepatomegaly. USG is inexpensive, noninvasive, widely available, and informative. Usually, the steatosis stage is not detected by USG unless a substantial fat is accumulated. In alcoholic hepatitis, the liver appears enlarged and diffusely hyperechoic in USG report. In cirrhosis, nodularity, varices, splenomegaly, and ascites may be detected through USG. The USG may be useful to rule out biliary obstruction or hepatocellular carcinoma (Nicolau et al., 2002).

Radiologic tests are used to identify steatosis, evaluate the progression of liver disease and the presence of complications, and rule out biliary tract disease and liver tumors (Zoli et al., 1991). Computed tomography (CT) is more expensive than USG but provides optimal results for evaluating steatosis (d'Assignies et al., 2009). It provides good visualization of vascular structures and can detect portal vein thrombosis and vascular collaterals as well as other features of cirrhosis and portal hypertension. It is also useful for detecting hepatocellular carcinoma (Takashima et al., 1982). Magnetic resonance imaging (MRI) provides high resolution images of liver parenchymal, vascular, and biliary anatomy than those are provided by CT. High-quality MRI provides the single most accurate and comprehensive technique for noninvasive evaluation of the liver without exposure to ionizing radiation (Dodd et al., 1999).

Liver biopsy is generally not required in majority of patients to diagnose liver injury except when history of alcohol intake is not reliable (Trabut et al., 2008). It is useful in ALD to confirm a diagnosis, to exclude other unsuspected causes of liver disease, to assess the extent and severity of liver damage, and to define prognosis (Van Ness & Diehl, 1989). It may be useful in excluding steatohepatitis or fibrosis. It is used to identify mild alcoholic hepatitis or early cirrhosis that may escape detection on purely clinical grounds (Trejo et al., 1996).

Several models have been developed to assess the severity of ALD. Mean corpuscular volume (MCV) is the most important and valuable score for the detection of alcohol excess. It is elevated by heavy drinking that is occasionally observed when the daily alcohol consumption exceeds 60g. It returns to normal after several months of abstinence (Whitehead et al., 1978). Carbohydrate deficient transferrin (CDT) is a useful biochemical marker for heavy drinking, but it is not a popular measure due to its high specificity but low sensitivity (Salaspuro, 1999). The Maddrey discriminant function (MDF) system was the first scoring system developed and is still the most widely used. A score of MDF>32 indicates severe ALD (Maddrey et al., 1978). The Model for End-stage Liver Disease (MELD) score of greater than 21 have the highest sensitivity and specificity in predicting mortality (Sheth et al., 2002).

**8. Treatment of ALD**

During the last 20 years there is a tremendous progress in the treatment of ALD, yet the pathogenesis of ALD remains obscure, and at present no reliable drugs and no proper treatment strategy are approved for the treatment of ALD. An integrated approach is needed to deal for detoxification for patients. Hospital admission may be required for the evaluation by clinical assessment/investigation, initiate the management, and treating complications (Mackowiak et al., 2024).

Nutrient-based treatments are applied to regulate the functions of the gut system and prevent liver injury. At the early stage, the ALD is potentially reversible when a patient completely stops drinking alcohol. Abstinence from alcohol improves survival and long-term management of ALD. It is the cornerstone of treatment of ALD (Alexander et al., 1971). A completely stopping of alcohol takes a few weeks to reverse steatosis and it may take more than 6 months to complete resolution for AH. But, maintain of complete abstinence of alcohol is often difficult to them (Ishii et al., 2010).

Various agents, such as anabolic steroids, promoters of hepatic regeneration anti-fibrogenic agents, antioxidants, thyroid antagonists, phospholipids, calcium channel blockers, and hepatoprotective bile acids are used for the treatment of AH. But none of them have been found to be consistently beneficial for the survival (Cabre et al., 2000). When liver cirrhosis occurs, it is difficult to reverse even with abstinence from alcohol, but prevent further deterioration of the disease. Cirrhosis treatments rely on supportive care measures, such as ascites control and the treatment of esophageal varices (Maher, 2002).

A liver transplant is necessary when cirrhosis does not respond in medications and therapies. It is their only chance of survival. It is widely employed worldwide in patients with end-stage liver cirrhosis (Bravata et al., 2001). It is a complicated procedure and has become a topic of great medical and social controversy. Many countries restrict in allocating donor livers for ALD patients (Burra et al., 2010). Also, some countries require six months of abstinence from alcohol before placing a patient on the liver transplant list due to donor shortage and risk of recidivism, and many patients die within this period (Singal & Duchini, 2011). The patients require lifelong follow-up for prevention and management of complications of liver. Various effects of long-term abuse of alcohol, such as malnutrition, muscle wasting due to alcoholic myopathy, vitamin deficiencies, peripheral and central neural system abnormalities, etc. may be regularized among the patients (Lucey, 2014). Liver transplant listing should be considered for patients who develop liver dysfunction corresponding to a MELD score≥10, or in clinical decompensation, such as ascites, variceal bleeding, or hepatic encephalopathy (Murray et al., 2005).

## 9. Conclusions

From this study we have observed that chronic excessive alcohol consumption is the main cause of alcoholic liver disease (ALD). At present ALD becomes a major health problem in Europe and in the USA. Excessive alcohol intake also affects some other major organs of the body, such as brain, heart, pancreas, gastrointestinal tract, and immune system. Alcohol abuse is fully preventable. Therefore, both morbidity and mortality due to ALD is entirely preventable through the completely absenteeism of alcohol at the beginning of the disease. The governments and healthcare providers can make consciousness among the alcohol abuse patients. At present after treatment the complete recovery of alcohol-use disorder is not possible, especially in alcoholic hepatitis and alcoholic cirrhosis. Treatment of ALD is the combination of abstinence from alcohol, supportive care, such as adequate nutrition, and pharmacologic interventions. Usually, the ALD develops with no symptoms, so that a patient frequently misses in primary care, and expert services in secondary care. Despite of extensive research on ALD over the last four decades, there are still no full curable drugs for cirrhosis. At present there are few medications and therapies to support ALD; yet more scientific, medical and societal researches are needed to prevalent and fully cure this fatal and deadly disease. Therefore, economic, political, and scientific coordination is essential to do this job properly.

## References

Alexander, J. F., et al., (1971). Natural History of Alcoholic Hepatitis. II. The Long-Term Prognosis. *American Journal of Gastroenterology*, *56*(6), 515-525.

Askgaard, G., et al., (2015). Alcohol Drinking Pattern and Risk of Alcoholic Liver Cirrhosis: A Prospective Cohort Study. *Journal of Hepatology*, *62*(5), 1061-1067.

Bouneva, I., et al., (2003). Alcoholic Liver Disease. *Hospital Physician*, 31-38.

Bradley, K. A., et al., (1998). Medical Risks for Women Who Drink Alcohol. *Journal of General Internal Medicine*, *13*(9), 627-639.

Bravata, D. M., et al., (2001). Employment and Alcohol Use after Liver Transplantation for Alcoholic and Nonalcoholic Liver Disease: A Systematic Review. *Liver Transplantation*, *7*(3), 191-203.

Burra, P., et al., (2010). Liver Transplantation for Alcoholic Liver Disease in Europe: A Study from the ELTR (European Liver Transplant Registry). *American Journal of Transplantation*, *10*(1), 138-148.

Cabre, E., et al., (2000). Short and Long-Term Outcome of Severe Alcohol-Induced Hepatitis Treated with Steroids or Enteral Nutrition: A Multicenter Randomized Trial. *Hepatology*, *32*(1), 36-42.

Choi, G., et al., (2012). Alcoholic Hepatitis: A Clinician's Guide. *Clinical Liver Disease*, *16*(2), 371-385.

Cohen, J. A., & Kaplan, M. M., (1979). The SGOT/SGPT Ratio: An Indicator of Alcoholic Liver Disease. *Digestive Diseases and Sciences*, *24*(11), 835-838.

Cordero-Espinoza, L., & Huch, M., (2018). The Balancing Act of the Liver: Tissue Regeneration Versus Fibrosis. *Journal of Clinical Investigation*, *128*(1), 85-96.

Corrao, G., et al., (1998). Meta-analysis of Alcohol Intake in Relation to Risk of Liver Cirrhosis. *Alcohol Alcohol*, *33*(4), 381-392.

Creswell, J. W., (2007). *Qualitative Inquiry and Research Design: Choosing Among Five Approaches*. Thousand

Oaks, CA: Sage Publications.

d'Assignies, G., et al., (2009). Noninvasive Quantitation of Human Liver Steatosis Using Magnetic Resonance and Bioassay Methods. *European Radiology*, *19*(8), 2033-2040.

Dodd, G. D., et al., (1999). Spectrum of Imaging Findings of the Liver in End-Stage Cirrhosis: Part I, Gross Morphology and Diffuse Abnormalities. *American Journal of Roentgenology*, *173*(4), 1031-1036.

Dugum, M., et al., (2015). Alcoholic Hepatitis: Challenges in Diagnosis and Management. *Cleveland Clinic Journal of Medicine*, *82*(4), 226-236.

Friedman, S. L., et al., (2018). Mechanisms of NAFLD Development and Therapeutic Strategies. *Nature Medicine*, *24*(7), 908-922.

Galambos, J. T., & Shapira, R., (1973). Natural History of Alcoholic Hepatitis. IV. Glycosaminoglycuronans and Collagen in the Hepatic Connective Tissue. *Journal of Clinical Investigation*, *52*(11), 2952-2962.

Giannini, E., et al., (2002). The 1-Year and 3-Month Prognostic Utility of the AST/ALT Ratio and Model for End-Stage Liver Disease Score in Patients with Viral Liver Cirrhosis. *American Journal of Gastroenterology*, *97*(11), 2855-2860.

Goel, A., & Daugherty, T., (2021). Selection Criteria for Liver Transplantation for Acute Alcohol-Associated Hepatitis. *Clinical Liver Disease*, *25*(3), 635-644.

Hagstrom, H., et al., (2021). Mortality in Biopsy-Proven Alcohol-Related Liver Disease: A Population-Based Nationwide Cohort Study of 3453 Patients. *Gut*, *70*(1), 170-179.

Hallberg, L., (2006). The "Core-Category" of Grounded Theory: Making Constant Comparisons. *International Journal of Qualitative Studies on Health and Well-being*, *1*(3), 141-148.

Hart, C. L., et al., (2010). Effect of Body Mass Index and Alcohol Consumption on Liver Disease: Analysis of Data from Two Prospective Cohort Studies. *British Medical Journal*, 340, c1240.

Ishii, H., et al., (2010). Alcoholic Liver Disease and Its Relationship with Metabolic Syndrome. *Japan Medical Association Journal*, *53*(4), 236-242.

Jepsen, P., et al., (2010). Clinical Course of Alcoholic Liver Cirrhosis: A Danish Population-Based Cohort Study. *Hepatology*, *51*(5), 1675-1682.

Keating, M., et al., (2022). Alcoholic Hepatitis: Diagnosis and Management. *American Family Physician*, *105*(4), 412-420.

Kothari, C. R., (2008). *Research Methodology: Methods and Techniques* (2nd Ed.). New Delhi: New Age International (P) Ltd.

Legesse, B., (2014). *Research Methods in Agribusiness and Value Chains*. School of Agricultural Economics and Agribusiness, Haramaya University.

Lieber, C. S., & Leo, M. A., (1998). Metabolism of Ethanol and Some Associated Adverse Effects on the Liver and the Stomach. *Recent Developments in Alcoholism*, 14, 7-40.

Lucey, M. R., (2014). Liver Transplantation for Alcoholic Liver Disease. *Nature Reviews Gastroenterology & Hepatology*, *11*(5), 300-307.

Mackowiak, B., et al., (2024). Alcohol-Associated Liver Disease. *Journal of Clinical Investigation*, *134*(3), e176345.

Maddrey, W. C., et al., (1978). Corticosteroid Therapy of Alcoholic Hepatitis. *Gastroenterology*, *75*(2), 193-199.

Maher, J. J., (2002). Treatment of Alcoholic Hepatitis. *Journal of Gastroenterology and Hepatology*, *17*(4), 448-455.

Mathurin, P., & Bataller, R., (2015). Trends in the Management and Burden of Alcoholic Liver Disease. *Journal of Hepatology*, *62*(1 Suppl), S38-S46.

McClain, C. J., et al., (2021). Malnutrition and Alcohol-Associated Hepatitis. *Clinical Liver Disease*, *25*(3), 557-570.

Mohajan, D., & Mohajan, H. K., (2023a). Obesity and Its Related Diseases: A New Escalating Alarming in Global Health. *Journal of Innovations in Medical Research*, *2*(3), 12-23.

Mohajan, D., & Mohajan, H. K., (2023b). Basic Concepts of Diabetics Mellitus for the Welfare of General Patients. *Studies in Social Science & Humanities*, *2*(6), 23-31.

Mohajan, D., & Mohajan, H. K., (2023c). Historical View of Diabetics Mellitus: From Ancient Egyptian Polyuria to Discovery of Insulin. *Studies in Social Science & Humanities*, *2*(7), 26-34.

Mohajan, D., & Mohajan, H. K., (2023d). Body Mass Index (BMI) is a Popular Anthropometric Tool to Measure Obesity among Adults. *Journal of Innovations in Medical Research*, *2*(4), 25-33.

Mohajan, D., & Mohajan, H. K., (2023e). A Study on Body Fat Percentage for Physical Fitness and Prevention of Obesity: A Two Compartment Model. *Journal of Innovations in Medical Research*, *2*(4), 1-10.

Mohajan, D., & Mohajan, H. K., (2023f). Bulimia Nervosa: A Psychiatric Problem of Disorder. *Innovation in Science and Technology*, *2*(3), 26-32.

Mohajan, D., & Mohajan, H. K., (2023g). Binge-Eating: A Life-Threatening Eating Disorder. *Innovation in Science and Technology*, *2*(4), 62-67.

Mohajan, D., & Mohajan, H. K., (2023h). Effects of Metformin among Type 2 Diabetes Pregnant Women: A Preliminary Study. *Journal of Innovations in Medical Research*, *2*(12), 24-30.

Mohajan, D., & Mohajan, H. K., (2023i). Abdominal Elephantiasis: An Obstructive Disease Due to Extreme Obesity. *Journal of Innovations in Medical Research*, *2*(7), 13-15.

Mohajan, D., & Mohajan, H. K., (2023j). Long-Term Regular Exercise Increases $\dot{V}O_2$max for Cardiorespiratory Fitness. *Innovation in Science and Technology*, 2(2), 38-43.

Mohajan, D., & Mohajan, H. K., (2023k). Hyperosmolar Hyperglycaemic State: A Life-Threatening Complication of Type 2 Diabetes Patients. *Journal of Innovations in Medical Research*, *2*(10), 30-35.

Mohajan, D., & Mohajan, H. K., (2023l). Panniculus Morbidus: A New Global Health Crisis Due to Extreme Obesity. *Innovation in Science and Technology*, *2*(5), 1-6.

Mohajan, D., & Mohajan, H. K., (2023m). Hyperglycaemia among Diabetes Patients: A Preventive Approach. *Innovation in Science and Technology*, *2*(6), 27-33.

Mohajan, D., & Mohajan, H. K., (2023n). Bronze Diabetes: A Common Genetic Disorder Due to Systemic Iron Overload. *Journal of Innovations in Medical Research*, *2*(8), 1-7.

Mohajan, D., & Mohajan, H. K., (2023o). Hypoglycaemia among Diabetes Patients: A Preventive Approach. *Journal of Innovations in Medical Research*, *2*(9), 29-35.

Mohajan, D., & Mohajan, H. K., (2023p). Discovery of Insulin is a Great Achievement for the Diabetes Patients. *Studies in Social Science & Humanities*, *2*(8), 8-16.

Mohajan, D., & Mohajan, H. K., (2023q). Diabetic Ketoacidosis (DKA): A Severe Diabetes Mellitus Disorder. *Studies in Social Science & Humanities*, *2*(9), 29-34.

Mohajan, D., & Mohajan, H. K., (2023r). Prevention and Management Strategies of Pre-diabetes. *Frontiers in Management Science*, *2*(5), 32-36.

Mohajan, D., & Mohajan, H. K., (2023s). Management of Type-I Diabetes: A Right Procedure to Normal Life Expectancy. *Frontiers in Management Science*, *2*(6), 47-53.

Mohajan, D., & Mohajan, H. K., (2023t). Ponderal Index: An Important Anthropometric Indicator for Physical Growth. *Journal of Innovations in Medical Research*, *2*(6), 15-19.

Mohajan, D., & Mohajan, H. K., (2023u). Broca Index: A Simple Tool to Measure Ideal Body Weight. *Innovation in Science and Technology*, *2*(2), 21-24.

Mohajan, D., & Mohajan, H. K., (2023v). Metformin: An Oral Anti-hyperglycaemic Agent for the Treatment of Type 2 diabetes. *Journal of Innovations in Medical Research*, 2(11), 1-8.

Mohajan, D., & Mohajan, H. K., (2024a). Metformin is the First Choice of Oral Medicated Breastfeeding Mothers. *Innovation in Science and Technology*, *3*(2), 21-25.

Mohajan, D., & Mohajan, H. K., (2024b). Sulfonylureas: A Widely Used Oral Anti-Hyperglycaemic Medication for Type 2 Diabetes Management. *Journal of Innovations in Medical Research*, *3*(1), 14-19.

Mohajan, D., & Mohajan, H. K., (2024c). Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: New Oral Medications for the Treatment of Type 2 Diabetes. *Innovation in Science and Technology*, *3*(3), 31-35.

Mohajan, D., & Mohajan, H. K., (2024d). Visceral Fat Increases Cardiometabolic Risk Factors among Type 2 Diabetes Patients. Unpublished Manuscript.

Mohajan, D., & Mohajan, H. K., (2024e). Sodium-Glucose Cotransporter-2 (SGLT-2) Inhibitors: Antidiabetics Medications for Treating Diabetes. Unpublished Manuscript.

Mohajan, D., & Mohajan, H. K., (2024f). Peroxisome Proliferator-Activated Receptor γ (PPAR γ): A Systemic Insulin Sensitizer Associated with Decreased Risk of Type 2 Diabetes. *Journal of Innovations in Medical Research*, *3*(2), 18-24.

Mohajan, D., & Mohajan, H. K., (2024g). Glucagon-Like Peptide-1 Receptor Agonist (GLP-1R): An Important Therapy to Treat Type 2 Diabetes. Unpublished Manuscript.

Mohajan, D., & Mohajan, H. K., (2024h). Alpha-Glucosidase Inhibitors (AGIs): A New Class of Oral Medication for Treatment of Type 2 Diabetes Patients. Unpublished Manuscript.

Mohajan, D., & Mohajan, H. K., (2023i). Anorexia Nervosa: A Dreadful Psychosocial Health Complication. Unpublished Manuscript.

Mohajan, D., & Mohajan, H. K., (2024j). Oral Hypoglycaemic Agents: Non-Insulin Medications for Type 2 Diabetes Patients. *Innovation in Science and Technology*, *3*(1), 23-31.

Mohajan, H. K., (2017). Two Criteria for Good Measurements in Research: Validity and Reliability. *Annals of Spiru Haret University Economic Series*, *17*(3), 58-82.

Mohajan, H. K., (2018). *Aspects of Mathematical Economics, Social Choice and Game Theory*. PhD Dissertation, Jamal Nazrul Islam Research Centre for Mathematical and Physical Sciences (JNIRCMPS), University of Chittagong, Chittagong, Bangladesh.

Mohajan, H. K., (2020). Quantitative Research: A Successful Investigation in Natural and Social Sciences. *Journal of Economic Development, Environment and People*, *9*(4), 50-79.

Mohajan, H. K. (2024a). Alcoholic Hepatitis: Diagnosis and Management Procedures. Unpublished Manuscript.

Mohajan, H. K., (2024b). Anatomy of Human Liver: A Theoretical Study. Unpublished Manuscript.

Mohajan, H. K., (2024c). A Study on Functions of Liver to Sustain a Healthy Liver. Unpublished Manuscript.

Mohajan, H. K., (2024d). Liver Diseases: Epidemiology, Prevention, and Management Strategy. Unpublished Manuscript.

Mohajan, H. K., (2024e). Alcoholic Liver Cirrhosis: A Chronic Liver Failure Due to Alcohol Abuse. Unpublished Manuscript.

Moreno, C., et al., (2016). Intensive Enteral Nutrition is Ineffective for Patients with Severe Alcoholic Hepatitis Treated with Corticosteroids. *Gastroenterology*, *150*(4), 903-10.e8.

Morgan, M. Y., (1994). The Prognosis and Outcome of Alcoholic Liver Disease. *Alcohol Alcohol Suppl*, *2*, 335-343.

Murray, K. F., et al., (2005). AASLD Practice Guidelines: Evaluation of the Patient for Liver Transplantation. *Hepatology*, *41*(6), 1407-1432.

Mustika, S., & Arifah, N. N., (2017). Alcoholic Liver Cirrhosis in Young Female: Diagnostic and Therapeutic Challenge. *The Indonesian Journal of Gastroenterology, Hepatology and Digestive Endoscopy*, *18*(3), 206-211.

Nicolau, C., Bianchi, L., & Vilana, R., (2002). Gray-scale Ultrasound in Hepatic Cirrhosis and Chronic Hepatitis: Diagnosis, Screening, and Intervention. *Semin Ultrasound CT MR*, *23*(1), 3-18.

O'Shea, R. S., et al., (2010). Alcoholic Liver Disease. *Hepatology*, *51*(1), 307-328.

Osna, N. A., et al., (2017). Alcoholic Liver Disease: Pathogenesis and Current Management. *Alcohol Research*, *38*(2), 147-161.

Pandey, P., & Pandey, M. M., (2015). *Research Methodology: Tools and Techniques*. Bridge Center, Romania, European Union.

Parahoo, K., (2014). *Nursing Research: Principles, Process and Issues* (3rd Ed.). Basingstoke: Palgrave Macmillan.

Pol, S., et al., (1990). Diagnostic Value of Serum Gamma-Glutamyl-Transferase Activity and Mean Corpuscular Volume in Alcoholic Patients with or Without Cirrhosis. *Alcoholism: Clinical and Experimental Research*, *14*(2), 250-254.

Polit, D. F., & Hungler, B. P., (2013). *Essentials of Nursing Research: Methods, Appraisal, and Utilization* (8th Ed.). Philadelphia: Wolters Kluwer/Lippincott Williams and Wilkins.

Puri, P., et al., (2018). The Circulating Microbiome Signature and Inferred Functional Metagenomics in Alcoholic Hepatitis. *Hepatology*, *67*(4), 1284-1302.

Purohit, V., et al., (2008). Alcohol, Intestinal Bacterial Growth, Intestinal Permeability to Endotoxin, and Medical Consequences. *Alcohol*, *42*(5), 349-361.

Ratziu, V., et al., (2010). A Position Statement on NAFLD/NASH Based on the EASL 2009 Special Conference. *Journal of Hepatology*, *53*(2), 372-384.

Rehm, J., et al., (2009). Global Burden of Disease and Injury and Economic Cost Attributable to Alcohol Use and Alcohol-Use Disorders. *Lancet*, *373*(9682), 2223-2233.

Rehm, J., et al., (2013). Global Burden of Alcoholic Liver Diseases. *Journal of Hepatology*, *59*(1), 160-168.

Rossow, I., & Makela, P., (2021). Public Health Thinking Around Alcohol-Related Harm: Why Does Per Capita Consumption Matter? *Journal of Studies on Alcohol and Drugs*, *82*(1), 9-17.

Rubin, E., & Lieber, C. S., (1968). Alcohol-induced Hepatic Injury in Nonalcoholic Volunteers. *New England Journal of Medicine*, *278*(16), 869-876.

Russmann, S., et al., (2009). Current Concepts of Mechanisms in Drug-Induced Hepatotoxicity. *Current Medicinal Chemistry*, 16(23), 3041-3053.

Sakhuja, P., (2014). Pathology of Alcoholic Liver Disease, Can It be Differentiated from Nonalcoholic Steatohepatitis? *World Journal of Gastroenterology*, *20*(44), 16474-16479.

Salaspuro, M., (1999). Carbohydrate-Deficient Transferrin as Compared to Other Markers of Alcoholism: A Systematic Review. *Alcohol*, *19*(3), 261-271.

Seitz, H. K., (2006). Additive Effects of Moderate Drinking and Obesity on Serum Gamma-Glutamyl Transferase. *American Journal of Clinical Nutrition*, *83*(6), 1252-1253.

Seitz, H. K., & Stickel, F., (2006). Risk Factors and Mechanisms of Hepatocarcinogenesis with Special Emphasis on Alcohol and Oxidative Stress. *Journal of Biological Chemistry*, *387*, 349-360.

Sharma, P. & Arora, A., (2020). Clinical Presentation of Alcoholic Liver Disease and Non-Alcoholic Fatty Liver Disease: Spectrum and Diagnosis. *Translational Gastroenterology and Hepatology*, *5*, 19.

Sheth, M., Riggs, M., & Patel, T., (2002). Utility of the Mayo End-Stage Liver Disease (MELD) Score in Assessing Prognosis of Patients with Alcoholic Hepatitis. *BMC Gastroenterology*, *2*(2), 1-5.

Singal, A. K., et al., (2018). ACG Clinical Guideline: Alcoholic Liver Disease. *American Journal of Gastroenterology*, *113*(2), 175-194.

Singal, A. K., & Duchini, A., (2011). Liver Transplantation in Acute Alcoholic Hepatitis: Current Status and Future Development. *World Journal of Hepatology*, *3*(8), 215-218.

Singh, S. et al., (2017). Treatment Options for Alcoholic and Non-Alcoholic Fatty Liver Disease: A Review. *World Journal of Gastroenterology*, *23*(36), 6549-6570.

Stickel, F., (2015). Alcoholic Cirrhosis and Hepatocellular Carcinoma. *Advances in Experimental Medicine and Biology*, *815*, 113-130.

Stickel, F., et al., (2017). Pathophysiology and Management of Alcoholic Liver Disease: Update 2016. *Gut and Liver*, *11*(2), 173-188.

Subramaniyan, V., et al., (2021). Alcohol-associated Liver Disease: A Review on Its Pathophysiology, Diagnosis and Drug Therapy. *Toxicology Reports*, *8*(2021), 376-385.

Takashima, T., et al., (1982). Diagnosis and Screening of Small Hepatocellular Carcinomas. Comparison of Radionuclide Imaging, Ultrasound, Computed Tomography, Hepatic Angiography, and Alpha 1-Fetoprotein Assay. *Radiology*, *145*(3), 635-638.

Teli, M. R., et al., (1995). Determinants of Progression to Cirrhosis or Fibrosis in Pure Alcoholic Fatty Liver. *Lancet*, *346*(8981), 987-990.

Trabut, J. B., et al., (2008). Influence of Liver Biopsy on Abstinence in Alcohol-Dependent Patients. *Alcohol Alcohol*, *43*(5), 559-563.

Trejo, R., et al., (1996). The Applicability and Diagnostic Effectiveness of Transjugular Liver Biopsy. *Medicina Clínica* (Barc), *107*(14), 521-523.

Van Ness, M. M., & Diehl, A. M., (1989). Is Liver Biopsy Useful in the Evaluation of Patients with Chronically Elevated Liver Enzymes? *Annals of Internal Medicine*, *111*(6), 473-478.

Veldt, B. J., et al., (2002). Indication of Liver Transplantation in Severe Alcoholic Liver Cirrhosis: Quantitative Evaluation and Optimal Timing. *Journal of Hepatology*, *36*(1), 93-98.

Veryan, J., & Forrest, E. H., (2019). Recent Advances in Alcoholic Hepatitis. *Frontline Gastroenterology*, *11*(2), 133-139.

Whitehead, T. P., et al., (1978). Biochemical and Haematological Markers of Alcohol Intake. *Lancet*, *1*(8071), 978-981.

WHO, (2011). *Global Status Report on Alcohol and Health 2011*. Geneva, Switzerland: World Health

Organization.

WHO, (2014). Management of Substance Abuse Team. In: *Global Status Report on Alcohol and Health*. Geneva, Switzerland: World Health Organization.

Zoli, M., et al., (1991). Prognostic Indicators in Compensated Cirrhosis. *American Journal of Gastroenterology*, *86*(10), 1508-1513.