International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on Effect of Alcohol on Liver

[1]Sudhir Nanasaheb Gorane, [2]Shubhangi Mali

[1,2]Pratibhatai Pawar College of pharmacy Shrirampur

Abstract:

The adverse use of alcohol is a worldwide problem. It has been probable that alcohol abuse represents the world's third major risk factor for disease and disability; it is a connecting factor of 60 types of diseases and injuries and a simultaneous cause of at least 200 others. Liver is the main organ responsible for metabolizing ethanol, thus it has been considered for long time the major object of the dangerous use of alcohol. Ethanol and its bioactive products, acetaldehyde-acetate, fatty acid ethanol esters, ethanol-protein adducts, have been stared as hepatotoxins that directly and indirectly exert their toxic effect on the liver. A similar mechanism has been assumed for the alcohol-related pancreatic damage. Alcohol and its metabolites directly injure acinar cells and stimulate stellate cells to produce and deposit extracellular matrix thus causing the "necrosis-fibrosis" sequence that finally leads to waste and fibrosis, morphological hallmarks of alcoholic chronic pancreatitis. Even if less attention has been paid to the upper and lower gastrointestinal tract, ethanol produces dangerous effects by inducing: (1) direct damaging of the mucosa of the esophagus and stomach; (2) alteration of the sphincterial pressure and impairment of motility; and (3) modification of gastric acid output. In the intestine, ethanol can damage the abdominal mucosa directly or indirectly by altering the occupant microflora and damaging the mucosal immune system.

❖ **Keywords:** Alcohol, liver, Function of liver, Alcoholic liver disease (ALD), Risk factor

Introduction

Alcohol consumption is one of the main risk factors for health, one of the major causes of liver cirrhosis, and the third leading cause of premature death in Europe. Additionally, it is listed as a cause of approximately 60 illnesses and pathological conditions, including cancer. In every country, the overall cost of alcohol-related problems every year accounts for more than 1% of the gross domestic product. Each year, at least 2.3 million people die with an alcohol related problem (6)

In Europe, 55 million people are alcohols consumers, and 23 are million alcohol dependent. Alcohol-related mortality represents approximately 6.3% of all deaths registered in 2002– twice the world average (7)

The majority of people in industrialized societies consume alcohol in moderate amounts, either daily or intermittently. For example, daily social consumption of wines is common in many European wine-producing countries such as Austria, France, and Italy. Although liver cirrhosis mortality rates in these wine-producing countries are among the highest in the world,' the contributions of moderate or "social" alcohol consumption the liver cirrhosis mortality rate, as well as to prevalence of liver diseases in general, has not been satisfactorily established. (1)

The quickly increasing prevalence of overweightness constitutes a major threat to modern health care. In most industrialized countries more than half of the population is currently overweight or obese Simultaneously, during the past decadesthetotal per capitaethanol consumption and associated medical disorders have increased rapidly. Both extreme alcohol consumption and heaviness are known to lead to increase of fat in hepatic tissue and to make changes in serum liver-derived enzymes. Clinically, measurements of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and glutamyl transferase (GGT) are widely used as markers in evaluating the degree of liver injury. However, more information is needed on the indicator enzyme behavior to recover their diagnostic and prognostic values in the early phases of hepatic injury and in distinguishing between alcohol-induced and nonalcoholic fatty liver disease, which continues to be problematic because of the unreliability of alcohol consumption history (5)

What is Alcohol:

Alcohol is a psychoactive ingredient with dependence-producing properties that has been commonly used in many cultures for centuries. The dangerous use of alcohol causes a high burden of disease and has significant social and economic concerns. The harmful use of alcohol can also result in harm to other people, such as family members, friends, co-workers and foreigners. Alcohol ingestion is a causal factor in more than 200 diseases, injuries and other health conditions. Drinking alcohol is sociated with a risk of developing health problems such as mental and behavioural disorders, including alcohol dependence, and major noncommunicable diseases such as liver cirrhosis, some cancers and cardiovascular diseases.

A significant proportion of the disease burden attributable to alcohol consumption appears from unintentional and intentional injuries, including those due to road traffic crashes, roughness, and suicide. Incurable alcohol-related injuries incline to occur in relatively younger age groups.

A primary relationship has been established between damaging drinking and incidence or conclusions of infectious diseases such as tuberculosis and HIV/AIDS. Alcohol consumption by an expectant mother may cause fetal alcohol syndrome (FAS) and pre-term birth complications. (2)

Alcohol Consumption and the Daily Clinical Practice:

Alcohol and alcohol-related diseases, in the present and for the foreseeable future, represent an increasingly major problem, both for general medical practice and for other specialties. However, their true impact is often underestimated, and their management is particularly difficult duet to a lack of resources and synergies within the structures of the Health Service in our country. In particular, we believe it will be very useful to look into what is, at present, the primary approach to the problem by general practitioners.

The data derived from analysis of the item "alcohol" in computerized registration folders for general practitioners, as reported in the Health Search database and generated by 908 researchers (data not published), report the following:

- The contribution of alcohol consumption is often underestimated in the anamnesis of the patient;

- Alcohol consumption is higher in males and increases with age, mostly in age classes above 35 years;

- The percentage of alcohol consumption was found to be higher in subjects with gout and fatty liver. (8)

Absorption of Alcohol

Once alcohol is devour, it is not digested like food. First, a small amount is absorbed straight by the tongue and mucosal coating of the mouth. Once in the stomach, alcohol is absorbed directly into your stream through the tissue lining of the stomach and small intestine Food in the stomach can inhibit the absorption of alcohol in two ways:

First, it physically hinders the alcohol from coming in contact with the stomach lining. Food can either engage alcohol, or simply "take up space" so the alcohol does not enter the bloodstream through contact with the wall of the stomach. Second, food in the stomach will avoid alcohol from transient into the duodenum, which is the upper percentage of the small intestine. The surface area of the small intestine is very big (about the size of a tennis court), so alcohol has more contact to enter the bloodstream once it leaves the stomach. If alcohol is taken in the stomach it will be absorbed slower. (4)

Disadvantages of Alcohol:

Physical effects - Of the top five disadvantages of current drinking, acute alcohol physical effects were most commonly cited. Most participants reported demanding to drink regularly throughout the day to avoid withdrawal, which was generally superficial as distressing. One participant noted,

"When I remained drinking all that vodka, I'd wake up…shaky like a leaf. And God prevent I drink a glass of water. It was just like [vomiting noise]." If a person does not receive adequate treatment, physical withdrawal can become more severe, leading to alcohol

Concerns about alcohol dependence - The second most regularly endorsed category of drinking disadvantages was anxiety about having alcohol dependence. One participant informed that alcohol has a "pretty good hold on me. I won't lie about it. There's not one morning I don't wake up that I-I have to have a drink. It's got a hold on me."

Some participants also pointed out the penalties of alcohol dependence: "It fucks up your life. I seen my dad expire of alcoholism.

Long-term health consequences -The health consequences of drinking, which covered the third most common disadvantage, raised to concerns about chronic conditions (e.g., liver cirrhosis). A few participants talked about initial, teratogenic effects of alcohol on their system: "I was born with a birth deficiency. I was a premature baby like my brother. My mama died at 36 years…She drank when she had me. She drank when she had my brother." Participants also recognized alcohol's continuing effects on their health, which often took the form of intestinal and liver disease

Legal concerns - Legal concerns involved the fourth most commonly mentioned disadvantage. Many participants regular that alcohol was often linked to their meetings with the illegal justice and legal systems. One member noted that "every legal problem [he'd] ever had has been due to alcohol." Because participants remained poor, drinking in public was a essential; however, it is a crime desecration in Washington State, where this study was absorbed (15)

Short-term effects of alcohol

Short-term effects you might notice while drinking alcohol (or shortly after) can contain:

- feelings of relaxation or sleepiness
- a sense of rapture or dizziness
- changes in mood
- lowered hang-ups

- spontaneous behavior
- slowed or unclear speech
- *nausea and vomiting*
- *diarrhea*
- *head pain*
- changes in hearing, vision, and awareness
- loss of organization
- trouble focusing or making results
- loss of awareness or gaps in memory

Long-term effects of alcohol

Some long-term effects of commonly drinking alcohol can include:

- determined changes in mood, including concern and irritability
- sleeplessness and other sleep concerns
- a weakened protected system, meaning you might get sick more often
- changes in libido and sexual function
- changes in taste and weight
- problems with memory and attention
- difficulty concentrating on tasks
- increased tension and struggle in romantic and family relationships.

Liver:

The liver is a major organ only found in vertebrates which performs many critical biological functions such as cleaning of the organism, and the synthesis of proteins and biological necessary for digestion and growth. In humans, it is placed in the right upper quadrant of the stomach, under the diaphragm. Its other roles in absorption include the regulation of glycogen storage,

The liver Is an attachment digestive organ that produces bile, an alkaline fluid comprising cholesterol and bile acids, which helps the failure of fat. The gallbladder, a small pouch that sits just under the liver, stores bile produced by the liver which is subsequently moved to the small intestine to complete digestion. The liver's highly focused tissue consisting mostly of hepaticfibrosis controls a wide variety of high-volume biochemical reactions, including the synthesis and collapse of small and complex molecules, many of which are necessary for normal vital functions Estimates concerning the organ's total number of functions vary, but is usually cited as being around 500. (16)

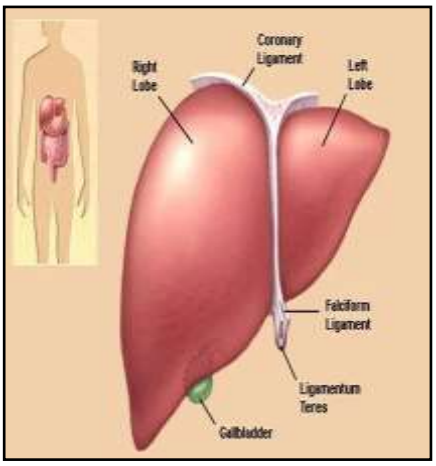


Fig: Human liver

Anatomy of liver

The liver is the largest organ, accounting for around 2% to 3% of average body weight. The liver has 2 lobes naturally described in two ways, by morphologic anatomy and by functional anatomy Located in the right upper quadrant of the abdominal cavity below the right hemi diaphragm, it is protected by the rib cage and maintains its position through peritoneal likenesses, referred to as ligamentous attachments. Although not true ligaments, these attachments are avascular and are in continuity with the Glisson capsule or the corresponding of the visceral peritoneum of the liver The falciform ligament is an attachment arising at or near the umbilicus and remains onto the anterior aspect of the liver in continuousness with the umbilical fissure. The falciform ligament courses cranially along the frontal surface of the liver, combination into the hepatic (17)

The liver is about 2% of body weight in the adult, which amounts to approximately 1400 g in females and 1800 g in males. The liver accepts its blood. Supply from two sources: 80% is transported by the portal vein, which drains the spleen and intestines; the remaining 20%, the oxygenated blood, is delivered by the hepatic artery. The portal vein is formed by the combination of the splenic and the superior mesenteric veins with the inferior mesenteric vein draining into the splenic vein (18)

Physiology of liver:

The liver rises as a part of the foregut. It branches from endodermal cells and starts as the hepatic diverticulum around the fourth week of improvement. It forms within the peritoneum and is anchored to the intestinal wall by the falciform ligament which arises from the ventral mesentery. The umbilical vein permits through the falciform ligament on its way from the umbilical cord to the liver.

The diverticulum is assumed to be induced by a combination of numerous pathways, mainly the Wnt/B-catenin pathway and fibroblast growth factors (FGF), which are unknown by fetal cardiac cells, which is induced by the MAPK pathway. The diverticulum then grows and networks with the septum transverses, a structure that distributes the heart from the abdominal cavity and later contributes to the development of the diaphragm. The diverticulum then distinguishes addicted to the primordium of the liver or the gallbladder. As the primordium liver grows, it develops into hepatic cords that anastomose around spaces lined by endothelium, creating the primordium of the hepatic sinusoids. VEGF plays an important role in the development of the hepatic sinusoids (19)

The liver theatres a role in nearly each organ system in the body. It cooperates with the endocrine and gastrointestinal systems by helping in digestion and metabolism. The liver is the storage locality for fat-soluble vitamins and handles cholesterol homeostasis. It stores iron and copper. It plays a role in hematology with clotting feature and protein synthesis. The liver theaters a role in heme breakdown into unconjugated bilirubin and conjugates it. It plays a role in sex hormone metabolism and produces carrier proteins that are important in reproduction and development. (20)

Functions of liver:

- ***Bile Production***

Bile is an vital fluid as it helps excrete material not excreted by the kidneys and helps in the absorption and digestion of lipids via secretion of bile salts and acids. Bile is produced by hepatocytes and is mainly collected of water, electrolytes, bile salts, bile acids, cholesterol, bile pigment, bilirubin, and phospholipids in adding to other substances. Bile is secreted from hepatocytes into the bile canaliculi where it travels from smaller ducts to the larger ducts finally ending up in the duodenum or being stored in the gallbladder for packing and absorption as determined by the vessel and sphincter of Oddi pressures.

- ***Fat-Soluble Vitamin Storage and/or Metabolism***

Most fat-soluble vitamins reach the liver via duodenal absorption in the form of chylomicrons or VLDL. The liver stores and/or metabolizes fat-soluble vitamins. As discussed prior, vitamin A is stored in Ito cells. It can suffer oxidation into retinal followed by retinoic acid for phototransduction, or retinoic acid can be conjugated into glucuronide for excretion into bile. Whether vitamin D3 comes from the skin, animal products, or plant products, it must undergo 25hydroxylation by the hepatic CYP-450 system, which is further hydroxylated in the kidney to accomplish its functional form. The hepatic CYP-450 system then hydroxylate carbon 24 to reduce vitamin D inactive. The liver accepts vitamin E in its alpha and gamma-tocopherol forms. Alpha-tocopherol is combined with VLDL or HDL in the liver and is then secreted back into transmission while the liver metabolizes the gamma-tocopherol form for. (20)

- ***Drug Metabolism***

Another critical function of the liver is metabolism and/or distillation of xenobiotics. The liver uses lysosomes for some of these substances, but a main route of metabolism and detoxification is through biotransformation. The liver functions to transform xenobiotics mainly by changing them from a lipophilic form to a hydrophilic form through 2 reactions: phase I and phase II. These reactions mostly take place in the flat endoplasmic reticulum of hepatocytes.

- ***Bilirubin Metabolism***

The liver plays a important role in the breakdown of heme. Hemolysis takes place in multiple locations through the body, including the liver, spleen, and bone marrow. Heme is cracked down into biliverdin, which is then compact to unconjugated bilirubin. The liver receives unconjugated bilirubin certain to albumin from the movement. The unconjugated bilirubin then undergoes conjugation via the uridine diphosphate glucuronosyltransferase (UGT) system, a phase II process, to develop hydrophilic. The newly conjugated bilirubin then is secreted via bile canaliculi into the bile or small volumes dissolve in the blood where it then gets filtered for excretion by the kidneys. Most conjugated bilirubin enters the bile and is defecated with bile in feces as it is not absorbable by the abdominal wall. Some bilirubin is changed to urobilinogen or unconjugated bilirubin by gut bacteria for reabsorption to undergo enterohepatic circulation.

The liver disruptions down most of the alcohol you drink so that it can be disconnected from the body. This creates substances that are even more injurious than alcohol. These substances can injury liver cells and cause serious liver disease.

Alcohol causes 4 out of 5 deaths from liver disease.

- ***How Alcohol Affects The liver:***

The liver breaks down and filter out injurious substances in the blood and manufactures the proteins enzymes and hormones the body uses toward of impurities. It also convert vitamins, nutrients and medicines into substance that our bodies can use. The liver is also responsible for scrubbing our blood, making bile for digestion, and storing glycogen for energy.

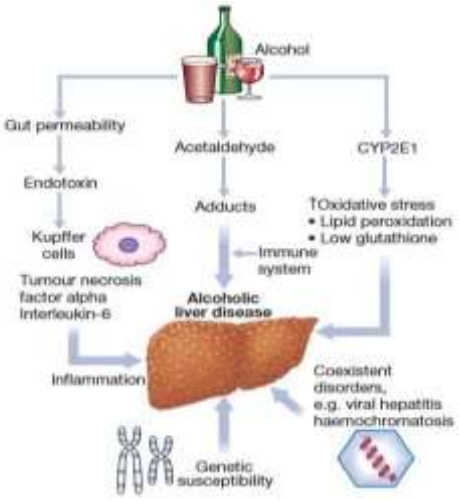
The liver processes over 90% of consumed alcohol, The rest exist the body via urine, sweat and breathing.

Types of liver disease produced by alcohol include:

- fatty liver (steatosis)
- inflammation of the liver (hepatitis)
- acute alcoholic hepatitis
- scarring of the liver (cirrhosis)
- liver failure and death

The first step of alcohol-induced liver damage is the growth of hepatic steatosis as a result of the impairment of fat synthesis, accumulation, mobilization and breakdown (9). The second step is the induction of inflammation, cell injury and apoptosis, all of which contribute to steatohepatitis. Stored free fatty acids encourage oxidative stress and hepatocyte apoptosis; ethanol induces cytochrome P4502E1, producing toxic acetaldehyde and reactive oxygen classes; gut-derived endotoxins (the translocation of which is promoted by alcohol-induced gut dysbiosis and mucosal barrier function impairment) activate Supercells, producing pro-inflammatory cytokines (14)

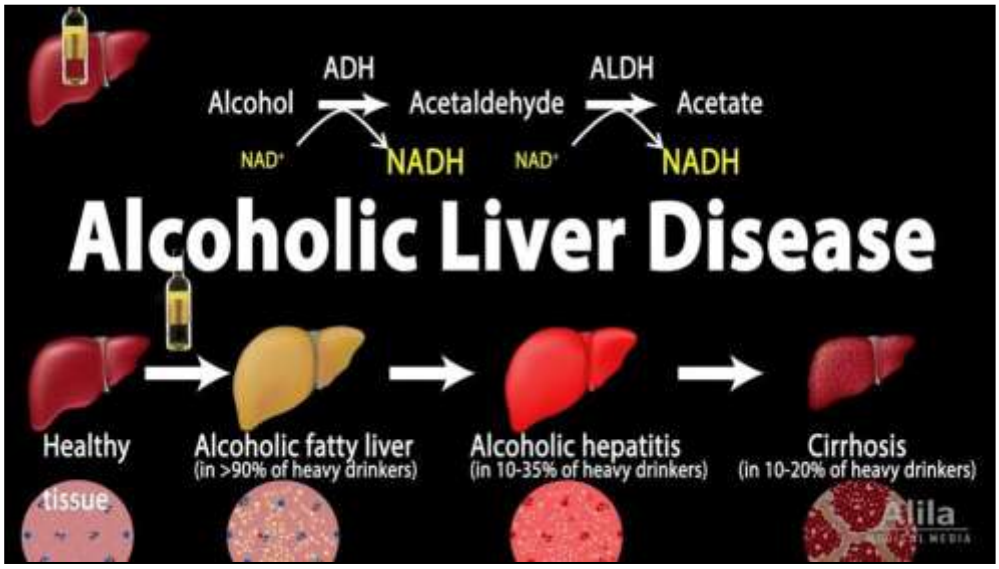
Although a dose–effect relationship between alcohol Intake and alcohol-encouraged hepatic damage has been Reported, there is no set amount of alcohol consumption that could surely forecast the development of ALD.2, 11, 15, 16 In fact, the majority of long-term Heavy drinkers develop fatty liver, but only 10–35% Develop hepatitis and only 8–20% will progress to Cirrhosis (24)



- ***Alcoholic liver disease:***

Alcoholic liver disease (ALD) is one of the major medical difficulties of alcohol abuse. Alcoholic liver disease (ALD) is a compound multi step chronic disease process which typically progresses through stages of alcoholic steatosis (AS), alcoholic hepatitis (AH), alcoholic cirrhosis (AC) to end-stage(ES) liver disease. Alcohol inductees liver damage by generation of oxidative and non-oxidative alcohol metabolites. With remaining alcohol use, the disease progresses via continuing cellular injury, inflammation, impairment of hepatic regeneration, and increasing fibrogenesis important to cirrhosis and its difficulties. Progression of fibrosis includes several mechanisms, linking remodelling of extracellular matrix (ECM). One of the proteolytic schemes involved in matrix degradation is the plasminogen activation system. (3)

Alcoholic liver disease (ALD) comprises a large spectrum of alcohol-related liver diseases, ranging from fatty liver or simple steatosis to alcoholics hepatitis, chronic hepatitis with hepatic fibrosis or cirrhosis(9)



Pathophysiology:

The pathogenesis of ALD can be theoretically divided into 1) Ethanol mediated liver injury, 2)

Inspiring Protected response to injury, 3) Abdominal permeability and microbiome changes. Corticosteroids may increase outcomes, but this is contentious and probably only impacts short term reality.

Fatty liver develops in approximately 90% of individuals who drink more than 60 g/day of alcohol, but this condition is completely adjustable after 4-6 weeks of abstinence, even if fibrosis and cirrhosis develop in 5-10% of patients, despite abstinence (9,10)

- ***PATHOGENESIS OF ALCOHOLIC LIVER DISEASE:***

The pathogenesis of alcoholic liver disease contains multiple factors including hepatocyte damage due to alcohol and its metabolites, cholestasis, recruitment and initiation of innate immune cells by gut-derived pro-inflammatory threat signals, Kupffer cells, and enlisted macrophages and neutrophils in the liver. The nonstop presence of these factors during chronic excessive alcohol use triggers ineffective anti-inflammatory pathways and results in beginning of stellate cells and myofibroblasts in the liver leading to fibrosis and alcoholic cirrhosis (26)

- ***Symptoms of alcohol-related liver disease (ARLD)***

ARLD does not usually cause any indications until the liver has been severely injured.

When this occurs, symptoms can include:

feeling sick weight loss loss of appetite yellowing of the whites of the eyes or skin (jaundice) swelling in the ankles and abdomen confusion or drowsiness vomiting blood or passing blood in your stools

- ***Stages of ARLD***

There are 3 main phases of ARLD, though there's often an overlap between each stage. These stages are:

-Alcoholic fatty liver disease

-Alcoholic hepatitis

-Cirrhosis

- ***Alcoholic hepatitis:***

represents a spectrum of diseases, ranging from mild injury to severe and life threatening damage, which occur only in a subdivision of alcoholics (approximately 10% to 35%). These typically occur in individuals with a long-standing history of consuming more than 100 g/day of alcohol for at least two decades (11)

This condition may occur even when alcohol consumption has been significantly condensed or stopped. Although alcoholic hepatitis can occur in a mild form, patients are at high risk for developing advanced liver injury, as cirrhosis develops in up to 50%. Abstinence from alcohol is associated with histological normalization in 27% of patients, with development to cirrhosis in 18% and with persistent alcoholic hepatitis in the Remainder (9)

As far as the type of beverages is concerned, beer and spirits seem to be more dangerous than wine (12), while drinking outside the meal and binge-drinking (defined as five drinks for men or four drinks for women in one sitting) increase the risk for ALD . Women appear to be twice as sensitive to alcohol-mediated hepatotoxicity and may advance more severe ALD at lower doses and with shorter durations of alcohol consumption than men. This can be a importance of their relative lower amount of gastric alcohol dehydrogenase, their higher proportion of body fat or the changes in alcohol absorption throughout the menstrual cycle. However, men are twice as likely to abuse alcohol compared to women, and so ALD is more common in men Obesity, protein and micronutrient deficiency and coexisting HCV infections represent factors that strengthen the injurious effects of alcohol on the liver(13)

The genetic polymorphisms of alcohol dehydrogenase and their communications with the genes involved in generating and detoxifying free radicals also influence the susceptibility to alcoholic liver disease(9)

- ***Causes:***

Alcoholic hepatitis is instigated by drinking too much alcohol. The liver breaks down alcohol. Over time, if you drink more alcohol than the liver can process, it can become totally damaged.

- ***Symptoms:***

Patients with alcoholic hepatitis symptoms including Jaundice abdominal pain fullness or distention fever GI bleeding changes in mental status. (26)

- ***Treatment:***

Treatment for alcoholic hepatitis includes Quitting drinking and therapies to ease the signs and symptoms of liver damage.

Quitting drinking

If you've been recognized with alcoholic hepatitis, you must stop drinking alcohol and never drink alcohol again. It's the only way to probably reverse liver damage or avoid the disease from worsening. People who don't stop drinking are likely to develop a variety of life-scaring health problems.

If you are dependent on alcohol and want to stop drinking, your doctor can recommend a treatment that's tailored for your needs. It can be dangerous to stop drinking rapidly so if you're dependent, be sure to discuss a plan with your doctor.

Treatment might include:

- Medications
- Counseling
- Alcoholics Anonymous or other support groups
- Outpatient or residential treatment program

Liver transplant

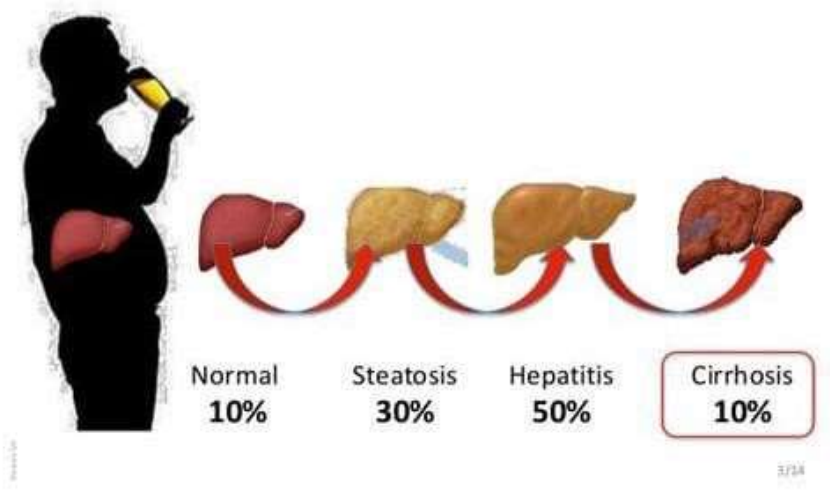
For many people with severe alcoholic hepatitis, the risk of death is high without a liver transplant.(27)

- ***Liver Cirrhosis :***

Cirrhosis is defined as the histological development of reformative nodules surrounded by fibrous bands in response to chronic liver injury, that leads to portal hypertension and end stage liver disease. Recent advances in the understanding of the natural history and pathophysiology of cirrhosis, and in

treatment of its difficulties, resulting in improved management, quality of life and life expectation of cirrhotic patients. At present, liver transplantation remains the only medicinal option for a selected group of patients, but pharmacological th-

-erapies that can halt progression to decompensated cirrhosis or even set aside cirrhosis are currently being developed.



- ***Pathogenesis and pathophysiology of cirrhosis:***

Fibrosis describes encapsulation or additional of damaged tissue by a collagenous scar. Liver fibrosis results from the perpetuation of the normal twisted healing response resultant in an abnormal continuation of fibrogenesis (connective tissue production and deposition). Fibrosis progresses at adjustable rates depending on the cause of liver disease, environmental and crowd factors. Cirrhosis is an advanced stage of liver fibrosis that is attended by alteration of the hepatic vasculature. It leads to shifting of the portal and major blood supply directly into the hepatic outflow (central veins), cooperating exchange between hepatic sinusoids and the touching liver parenchyma, i.e., hepatocytes. The hepatic sinusoids are lined by fenestrated endothelia which rest on a sheet of penetrable connective tissue (the space of Disse) which comprises hepatic stellate cells (HSC) and some mononuclear cells. The other side of the space of Disse is lined by hepatocytes which implement most of the known liver functions. In cirrhosis the space of Disse is filled with scar tissue and endothelial fenestrations are lost, a process termed sinusoidal CA pillarization. (Histologically, cirrhosis is characterized by vascularized fibrotic septa that link gateway tracts with each other and with dominant veins, leading to hepatocyte islands that are surrounded by fibrotic septa and which are devoid of a central vein(25)

- ***Symptoms:***

Early symptoms of cirrhosis may include

- feeling tired or weak
- poor appetite
- losing weight without trying
- nausea and vomiting
- mild pain or anxiety in the upper right side of your abdomen

As liver function gets inferior, you may have other symptoms, including

- bruising and bleeding easily
- confusion, difficulties thinking, memory loss, personality changes, or sleep disorders
- swelling in your lower legs, ankles, or feet, called edema
- bloating from buildup of melted in your abdomen, called ascites
- severe itchy skin
- darkening of the color of your urine
- yellowish tint to the whites of your eyes and skin, called jaundice

- ***Treatment:***

Treatment for cirrhosis depends on the cause and amount of your liver damage. The goals of treatment are to slow the movement of scar tissue in the liver and to prevent or treat symptoms and complications of cirrhosis. You may required to be hospitalized if you have severe liver damage.

Treatment for the underlying cause of cirrhosis

In early cirrhosis, it may be possible to minimize injury to the liver by treating the underlying cause. The options include:

- **Treatment for alcohol dependency.** People with cirrhosis caused by unnecessary alcohol use should try to stop drinking. If stopping alcohol use is difficult, your doctor may recommend a treatment database for alcohol addiction. If you have cirrhosis, it is condemnatory to stop drinking since any amount of alcohol is toxic to the liver.
- **Weight loss.** People with cirrhosis caused by nonalcoholic fatty liver disease may become improved if they lose weight and control their blood sugar levels.
- **Medications to control hepatitis.** Medications may limit further injury to liver cells caused by hepatitis B or C through specific treatment of these viruses.
- **Medications to control other causes and symptoms of cirrhosis.** Medications may slow the development of certain types of liver cirrhosis. For example, for people with primary biliary cirrhosis that is analyzed early, medication may significantly delay progression to cirrhosis.
- Other medications can relieve certain symptoms, such as itching, fatigue and pain. Nutritional additions may be prescribed to counter malnutrition associated with cirrhosis and to avoid weak bones (osteoporosis).

- ***Liver transplant surgery:***

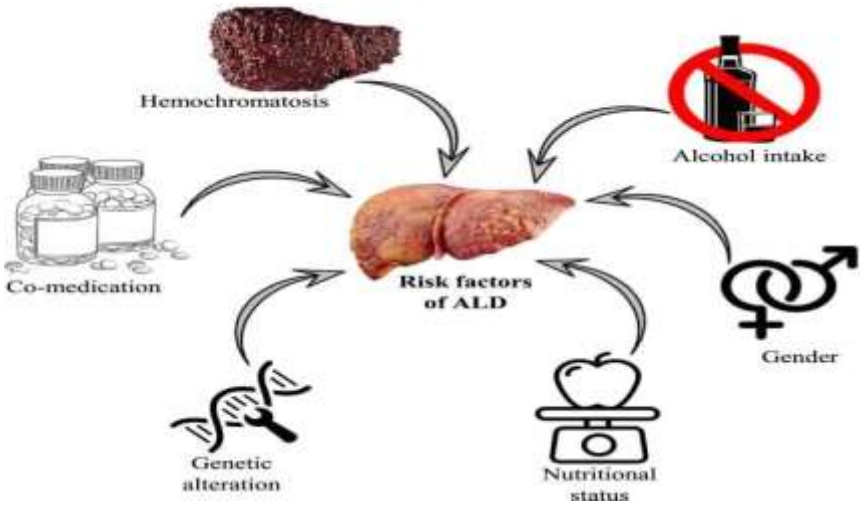
In advanced cases of cirrhosis, when the liver sources to purpose, a liver transplant may be the only treatment opportunity. A liver transplant is a tecnique to replaced your liver with a healthy liver from a Deceased contributor or with part of a liver from a living donor. Cirrhosis is one of the most common causes for a liver transplant. Candidates for liver transplant have extensive testing to determine whether they are healthy adequate to have a good outcome following surgery.

Historically, those with alcoholic cirrhosis have not been liver transplant applicants because of the risk that they will return to injurious drinking after transplant. Recent studies, however, suggest that carefully selected people with severe alcoholic cirrhosis have posttransplant survival rates similar to those of liver transplant receivers with other types of liver disease.

In industrialized countries, high alcohol consumption denotes one of the most important risk factors for developing liver cirrhosis and he- 1928 patocellular carcinoma (HCC). In general, alcohol consumption is related with a 2-fold increase in the individual risk of HCC enlargement, reaching an increase of 5 or 7- fold in cases of an intake >80 g/day for up to 10years. The swelling risk appeared to be doubled in the presence of HCV infection, thus underlying the synergistic effects of these two risk factors85. Chronic alcohol ingesting promotes hepatic carcinogenesis, not only inducing chronic irritation, hepatocyte necrosis and regenerations, but also leading to the exertion of the procarcinogenic effects of the main metabolite, acetaldehydes, due to its direct communication with the hepatocytes' DNA (13)

Many hypothesis have been progressive to explain the pathogenic mechanisms of ALD. Firstly, the liver is the main organ responsible for metabolizing ethanol, thus it is possible that ethanol and its metabolites [acetaldehyde-acetate, fatty acid ethanol esters (FAEEs), ethanol protein adducts] can exercise a direct cytotoxic effect acting a as hepatot oxins. Hepatic metabolism of the ethanol takings via oxidative and non-oxidative pathways The main steps of the oxidative pathway are refereed by alcohol dehydrogenase (ADH) and acetaldehyde dehydrogenase (ALDH) that convert ethanol to acetaldehyde and acetaldehyde to acetate, respectively. The end products of this reaction are acetaldehyde, acetate and higher levels of NADH. Acetaldehyde damages liver by direct triggering inflammation, extracellular matrix (ECM) conversion and fibrogenesis. Moreover, it covalently binds to proteins and DNA leading to the production of immunogenic adducts (i.e., malondialdehyde) in the hepatocytes. Finally, acetaldehyde stimulates transforming growth factor (TGF)-beta signaling in hepatic stellate cells that procure a pro-fibro genic and pro-inflammatory profile]. Electrons from alcohol are transferred to NADP+ by ADH. Changes in NADH/NAD+ ratio may affected biochemical reactions in the mitochondria and gene expression in nucleus. The burn of NADH requires added oxygen amount in the mitochondria; the hepatocytes take up in addition their normal share of oxygen from arteriosus blood but not enough to sufficiently supply all liver regions. Thus, alcohol consumption results in significant hypoxia of the pervious hepatocytes that are the first ones to show evidence of damage from chronic alcohol consumption(23)

Risk Factor:



- **Alcohol intake:** In our population, beer or wine drinkers were 41.1%, and their alcohol daily intake was less than others. Rural people tended to drink hard liquors. Multiple drinkers were 20.2%, 87.9% of the drinkers consumed alcohol only at mealtimes, the daily alcohol intake was significantly lower than that of alcohol consumed at any time (with and without food) ($P<0.05$). Daily alcohol intake of only hard liquors, also without food was significantly higher than that of all other categories of drinkers, the morbidity of ALD was also the highest, 2.7 times that of drinkers who drank only wine or beer at mealtimes(28)

  Consumption of 60–80 g per day (14 g is considered one standard drink in the US, i.e., 1.5 fl oz hard liquor, 5 fl oz wine, 12 fl oz beer; drinking a six-pack of 5% ABV beer daily would be 84 g and just over upper limit) for 20 years or more in men, or 20 g/day for women significantly increases the risk of hepatitis and fibrosis by 6% to 41%.(21)

- **Gender:** studies have shown that the relative risk of alcoholic cirrhosis rises in females much more steeply, with increasing levels of alcohol intake, than in males.44,45 It was reported that in women clinical liver disease occurs after a shorter period of alcohol intake.46 Pharmacoki netic studies indicated that in women blood levels after the ingestion of a standard dose of alcohol was significantly higher than in males, due either to a smaller distribution volume or to the lower gastric alcohol dehydrogenase (ADH) These gender related differences, however, were found only in selected populations. In large, open- population cohort studies no gender related differences were found in either the minimum quantity of alcohol necessary to increase the risk or the susceptibility to ALD.14 We therefore believe that the suggested greater susceptibility of women to ALD remains unproven and that further research is warranted.

- **Nutritional status:** Nutrition has long been known to be a factor modulating liver functions. Nutritional status, so difficult to define precisely and so easily grasped intuitively, is certainly related to the census of a given individual. Thus, the liver disease typical of protein malnutrition is more likely to interact with and to amplify the dam- age produced by alcohol abuse in lower income classes than in the wealthy groups. In a patient with liver failure, an adequate diet often induces a rapid clinical improvement even when up to 33% of the total calories are derived from alcohol. On the other hand, if protein intake remains below recommended levels, alcohol abstinence alone is not sufficient to improve liver function. Alcohol abuse increases the daily requirements of choline, folate and that of other important nutrients as well. Moreover, nutritional deficiencies, especially protein deficiency, might increase the toxic effects of alcohol because they bring about deficiencies of specific amino acids and interfere with the synthesis of specific liver proteins. Overall, malnutrition and alcohol abuse appear to have a synergistic effect.

- **Genetic Alterations:** The potential role of genetic factors in predisposing to ALD has long been investigated.39Twentyeight papers have compared the distribution of human leukocyte antigens (HLA) in heavy drinkers with that of normal individuals. 40 A meta analysis of these data 40 has concluded that no ne of the HLA phenotypes investigated so fail in Caucasian subjects is significantly more com- mon in any of the patient groups (heavy drinkers, subjects with ALD, cirrhotics) than in controls.

The genes encoding for alcohol dehydrogenase (ADH2, ADH3) and aldehyde dehydrogenase (ALDH2) as well those encoding for the microsomal ethanol oxidation system [cytochrome P4502E1 (CYP2E1)] have been, over the past few years, the object of intensive investigation.17±30 Unfortunately, these studies have yield contradictory results. Studies in Japanese and Chinese populations had indicated that the allele ADH2*2 of the ADH2 gene,

A meta-analysis of these data42 has concluded that the presence of ADH3 variations are capable of decreasing two-to-three-fold the risk of alcohol dependence and of increasing two-fold the risk of ALD among heavy drinkers. Unfortunately, the homogeneity test of the data used in the meta-analysis indicated a lack of statistical significance.(29)

- **Pattern of drinking:** Drinking outside of meal times increases up to 3 times the risk of alcoholic liver disease.(22)

Sex: Women are double as susceptible to alcohol-related liver disease, and may change alcoholic liver disease with shorter periods and doses of chronic consumption. The lesser amount of alcohol dehydrogenase unknown in the gut, higher proportion of the body fat in women, and changes in alcohol absorption due to the menstrual cycle may describe this phenomenon.(21, 22)

Ethnicity: Higher rates of alcohol-related liver disease, unrelated to differences in amounts of alcohol consumed, are seen in African-American and Hispanic males compared to Caucasian males Genetic factors: Genetic factors dispose both to alcoholism and to alcoholic liver disease. Both monozygotic twins are more likely to be alcoholics and to develop liver cirrhosis than both dizygotic twins. Polymorphisms in the enzymes complicated in the metabolism of alcohol, such as ADH,ALDH, CYP4502E1, mitochondrial dysfunction, and cytokine polymorphism may partly explain this genetic factor. However, no specific polymorphisms have currently been firmly linked to alcoholic liver disease(21)

Conclusion :

Alcohol abuse characterizes a serious public health anxiety in many countries. According to a "hepatocentric" vision of the problem, liver has been careful for long time the main victim of the injurious use of alcohol. However, growing evidence suggest that ALD have to be careful a true systemic disease. The "multisystemic scenarios" of the alcohol-related diseases inspires the urgent need to encourage research oriented to pathophysiology targeted therapies as well as preventive policy systems to reduce the clinical and economic weight of alcohol abuse.

❖ **Reference:**

1. V. T. Savolainen, K. Liesto, A. Mannikko, A. Penttila, and P. J. Karhunen, Alcohol Consumption and Alcoholic Liver Disease: Evidence of a Threshold Level of Effects of Ethanol, Alcohol Clin Exp Res, Vol 17, No 5, 1993: pp I 112-1 117
2. *https://www.who.int/news-room/fact-sheets/detail/alcohol*
3. Devanshi Seth, Philip J. Hogg5 , Mark D. Gorrell, Geoffrey W. McCaughan,Paul S. Haber,. Direct effects of alcohol on hepatic fibrinolytic balance: Implications for alcoholic liver disease, Journal of Hepatology 48 (2008) 614–627.
4. *https://www.bgsu.edu/recwell/wellness-connection/alcohol-education/alcoholmetabolism.html*
5. Pa¨ivikki I Alatalo, Heidi M Koivisto, Johanna P Hietala, Katri S Puukka, Risto Bloigu, and Onni J Niemela, Effect of moderate alcohol consumption on liver enzymes increases with increasing body mass index1–3, Am J Clin Nutr 2008;88:1097–103. Printed in USA. © 2008 American Society for Nutrition
6. BAUMBERG B, ANDERSON P. HEALTH, alcohol and EU law: understanding the impact of European single market law on alcohol policies. Eur J Public Health 2008; 18: 392-398
7. REHM J, ROOM R, MONTEIRO M, GMEL G, GRAHAM K,REHN N, SEMPOS CT, JERNIGAN D. Alcohol as a risk factor for global burden of disease. Eur Addict Res 2003; 9: 157-164.
8. LOGUERCIO C, TISO A, COTTICELLI G, DEL VECCHIO BLANCO C, ARPINO G, LARINGE M, NAPOLI L, PICCINOCCHI G, BONFRATE L,GRATTAGLIANO I, UBALDI E, PORTINCASA P. Management of chronic liver disease by general practitioners in southern Italy: unmet educational needs. Dig Liver Dis 2011; 43:736-741.
9. O'SHEA RS, DASARATHY S, MCCULLOUGH AJ; Practice Guideline Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Alcoholic Liver Disease. Hepatology 2010; 51: 307-328.
10. SCAGLIONI F, CICCIA S, MARINO M, BEDOGNI G, BELLENTANI S. ASH and NASH. Dig Dis Sci 2011; 29: 202-210.
11. BASRA S, ANAND BS. Definition, epidemiology and magnitude of alcoholic hepatitis. World J Hepatol 2011; 3: 108-113
12. BECKER U, GRØNBAEK M, JOHANSEN D, SORENSENTI. Lower risk for alcohol-induced cirrhosis in wine drinkers. Hepatology 2002; 35: 868-875
13. A. FEDERICO, G. COTTICELLI, D. FESTI, R. SCHIUMERINI, G. ADDOLORATO,A. FERRULLI, M. MERLI, C. LUCIDI, S. MILANI, C. PANELLA, M. DOMENICO,I. VANTINI, L. BENINI, E. UBALDI, M. ROMANO, C. LOGUERCIO, The effects of alcohol on gastrointestinal tract, liver and pancreas: evidence-based suggestions for clinical management, European Review for Medical and Pharmacological Sciences, 2015; 19: 1922-1940
14. STICKEL F, SEITZ HK. Alcoholic steatohepatitis. Best Pract Res Clin Gastroenterol 2010; 24: 683-693.
15. Susan E. Collins, Emily Taylor, Connor Jones, Laura Haelsig, Véronique S. Grazioli, Jessica L. Mackelprang, Jessica Holttum, Molly Koker, Alyssa Hatsukami, Madeline Baker,and n Seema L. Clifasefi, Content Analysis of Advantages and Disadvantages of Drinking Among Sherif Individuals with the Lived Experience of Homelessness and Alcohol Use Disorders, Department of Psychiatry and Behavioral Sciences University of Washington - Harborview Medical Center, 2018 January 02; 53(1): 16–25.

16. *https://en.m.wikipedia.org/wiki/Liver*

17. R. Z. Abdel-Misih, MD and Mark Bloomston, MD, Liver Anatomy, Surg Clin North Am. 2010 August ; 90(4): 643–653.

18. Lena Sibulesky, M.D, Normal liver anatomy, Clinical Liver Disease, Vol. 2, No. S1, March 2013.

19. Si-Tayeb K, Lemaigre FP, Duncan SA. Organogenesis and development of the liver. Dev Cell. 2010 Feb 16;18(2):175-89

20. Almazroo OA, Miah MK, Venkataramanan R. Drug Metabolism in the Liver. Clin Liver Dis. 2017 Feb;21(1):1-20.

21. O'Shea RS, Dasarathy S, McCullough AJ (January 2010). "Alcoholic liver disease: AASLD Practice Guidelines" (PDF). Hepatology. 51 (1): 307–28

22. Menon KV, Gores GJ, Shah VH (October 2001). "Pathogenesis, diagnosis, and treatment of alcoholic liver disease,Mayo Clin. Proc. 76 (10): 1021–9.

23. Alba Rocco, Debora Compare, Debora Angrisani, Marco Sanduzzi Zamparelli, Gerardo Nardone, Alcoholic disease: Liver and beyond, WJG 20th Anniversary Special Issues (10): Alcoholic liver disease, October 28, 2014|Volume 20|Issue 40|.

24. A. GRAMENZI, F. CAPUTO, M. BISELLI, F. KURIA, E. LOGGI, P. ANDREONE & M. BERNARDI, Review article: alcoholic liver disease – pathophysiological aspects and risk factors, Aliment Pharmacol Ther 24, 1151–1161.

25. Detlef Schuppan and Nezam H. Afdhal, 2009 Mar 8, Liver Cirrhosis,ncbi, 371(9615): 838– 851.

26.)Nooshin Hosseini, Julia Shor, and Gyongyi Szabo, 2019 Jun 20, Alcoholic Hepatitis: A Review 54(4): 408–416.

27. Mack C. Mitchell, MD and Craig J. McClain, MD, 2017 Jan, Medical Management of Severe Alcoholic Hepatitis,ncbi, 15(1): 5–12.

28. Xiao-Lan Lu, Jin-Yan Luo, Ming Tao, Yan Gen, Ping Zhao, Hong-Li Zhao, Xiao-Dong Zhang, Nei Dong, Risk factors for alcoholic liver disease in China, World J Gastroenterol August 15, 2004 Volume 10 Number 16.

29. STEFANO BELLENTANI,GIOCONDA SACCOCCIO, FLORA MASUTTI, MAURO GIACCA, LUCIA MIGLIOLI,ADRIANA MONZONI& CLAUDIO TIRIBELLI, Risk factors for alcoholic liver disease, Addiction Biology (2000) 5, 261 ±268.