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Alcoholic Liver Disease

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ABSTRACT

Alcoholism in excess is a problem for heath worldwide. Since the liver is the main site of ethanol metabolism, heavy drinking causes the most tissue damage to it. Steatosis, hepatitis, and fibrosis/cirrhosis are the most recognisable liver lesions that are caused by prolonged and heavy alcohol use. Excessive alcohol use is a major global health issue that has serious social, economic, and clinical ramifications. According to the WHO, it was responsible for 3.3 million fatalities in 2012. Nearly every organ in the body is damaged by years of excessive drinking. However, because it is the main site of ethanol metabolism, the liver experiences the quickest and most severe tissue damage from heavy drinking. This article will summarise the methods by which excessive alcohol use contributes to the development of various types of alcohol-induced liver damage after providing a basic overview of how alcohol is metabolised in the liver. Additionally, it will go through the modifying factors of alcoholic liver disease and go over current methods of treating ALD patients.

Keywords: Consumption of alcohol, heavy drinking, the effects and consequences of alcohol, abstinence, alcoholic liver disease, liver damage, hepatic lesions, steatosis, hepatitis, fibrosis, and cirrhosis, as well as treatment options such medication and nutritional therapy and liver transplantation.

Highlights

- Alcohol consumption that is sustained over time causes the release of cytokines and the creation of protein-aldehyde adducts, which are pathogenic processes.
- Alcohol dehydrogenase, cytochrome P4502E1, and genes linked to alcoholism may all be involved gene polymorphisms.
- Although there isn't a clear dose-response association, drinking alcohol may be associated with an increased risk of premature birth.
- Patients who abuse alcohol had less severe steatohepatitis thanks to oral pentoxifylline medications.

Introduction

Alcohol use has become practically accepted as a normative conduct in the social fabric of many adult communities. It is affordable, accessible, and legal. Continuously consuming too much alcohol is a brain-centered addictive behavioural illness that affects people of various ages, genders, and socioeconomic backgrounds. In many individuals, it can also result in alcoholic liver disease. Heavy drinking considerably raises the risk of cardiovascular, brain, pancreatic, renal, cerebral, and oncological disorders as well as morbidity and mortality from infectious infections. Alcoholic hepatitis, fatty liver, hepatic necrosis, and progressive fibrosis (alcoholic cirrhosis) are all examples of the clinical sickness and morphological alterations that make up alcohol-related liver disease. Additionally, persistently consuming too much alcohol encourages the growth of other liver conditions, such as virus-related chronic hepatitis, which also raises the risk of developing hepatocellular carcinoma.

This study tries to outline the latest theories about the causes, risk factors, prognosis, and therapy of ALD. Epidemiologic and experimental investigations have shown that alcohol consumption duration and intensity both contribute to the development and progression of liver injury. However, only a small percentage of heavy drinkers have clinical liver disease, indicating that additional genetic and environmental factors play a role in the onset and progression of ALD. Alcohol hepatotoxicity is caused by numerous, multifaceted mechanisms. It's likely that a number of primary and secondary variables work in concert to cause and maintain alcohol-related liver damage. Genetic background and its intricate interaction with direct ethanol hepatotoxicity and alcohol-induced metabolic and immunological alterations are undoubtedly important contributing factors. The onset of liver disease can be significantly influenced by secondary cofactors including nutritional deficiencies and hepatotoxic co-morbid diseases.

Alcoholic liver disease type

Although frequent, alcohol-related liver damage is preventable. There are 3 varieties.

- Fatty liver: Fatty liver is the accumulation of fat inside the cells of the liver. It causes the liver to grow larger. It is the most typical liver condition brought on by alcohol.
- Alcohol-related hepatitis:
- Alcoholic hepatitis is a severe liver inflammation. The liver cells are dying.
- Hepatocyte inflammation is a defining feature of alcoholic hepatitis. Heavy drinkers who get alcoholic hepatitis range from 10% to 35%.
- The dosage of a drug does not immediately affect the development of hepatitis.
- Alcohol seems to cause different reactions in different persons. Alcoholic steato necrosis is the medical term for this condition, and the inflammation may be a risk factor for liver fibrosis.
- It is believed that inflammatory cytokines (TNF-alpha, IL6 and IL8)
- To play a crucial role in the beginning and continuation of liver damage by triggering apoptosis and necrosis.

• Abdominal pain or tenderness, jaundice, spider-like veins on the skin, malaise, fever, nausea, and appetite loss are possible symptoms.

• Hair loss, dark urine, black or pale faeces, exhaustion, loss of libido, bleeding gums or nose, edoema, vomiting, muscle cramps, and weight loss are signs of the end stage.

• **Alcoholic liver disease:-** Alcoholic cirrhosis causes the destruction of healthy liver tissue. Scar tissue takes the place of the liver's functional tissue. Oat the right side of the abdomen below the ribs that place liver is located. The liver:

- Mai aim to cleansing the body of waste material
- To Create bile to aim that in meal digestion
- Preserves sugar, which the body uses as fuel.
- Produces proteins that are used throughout the body, such as those that produce blood clots.

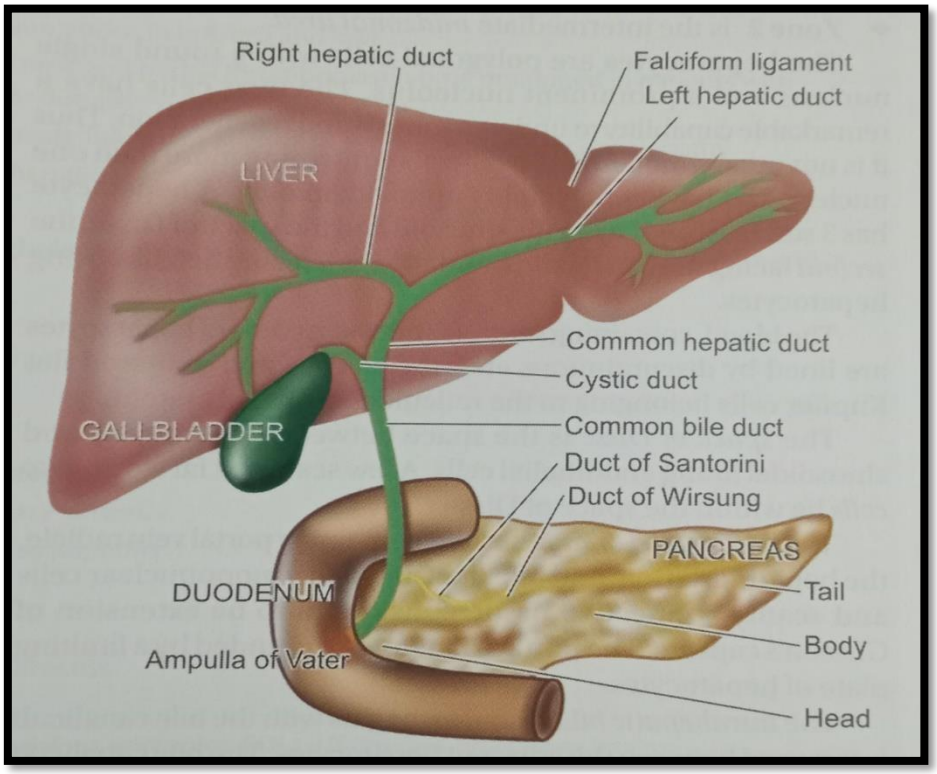

Fig. Liver anatomy

- Cirrhosis is a severe liver illness in its late stages that is characterised by inflammation (swelling), fibrosis (cellular hardening), and damaged membranes that stop the body's ability to rid itself of chemicals, end scarring, and cause necrosis (cell death).
- According to the NIAAA (1993), 10% to 20% of heavy drinkers will develop liver cirrhosis.
- Acetaldehyde may contribute to alcohol-induced fibrosis by encouraging hepatic stellate cells to deposit collagen; symptoms include jaundice (yellowing), hepatomegaly, discomfort, and tenderness from altered structural liver architecture.

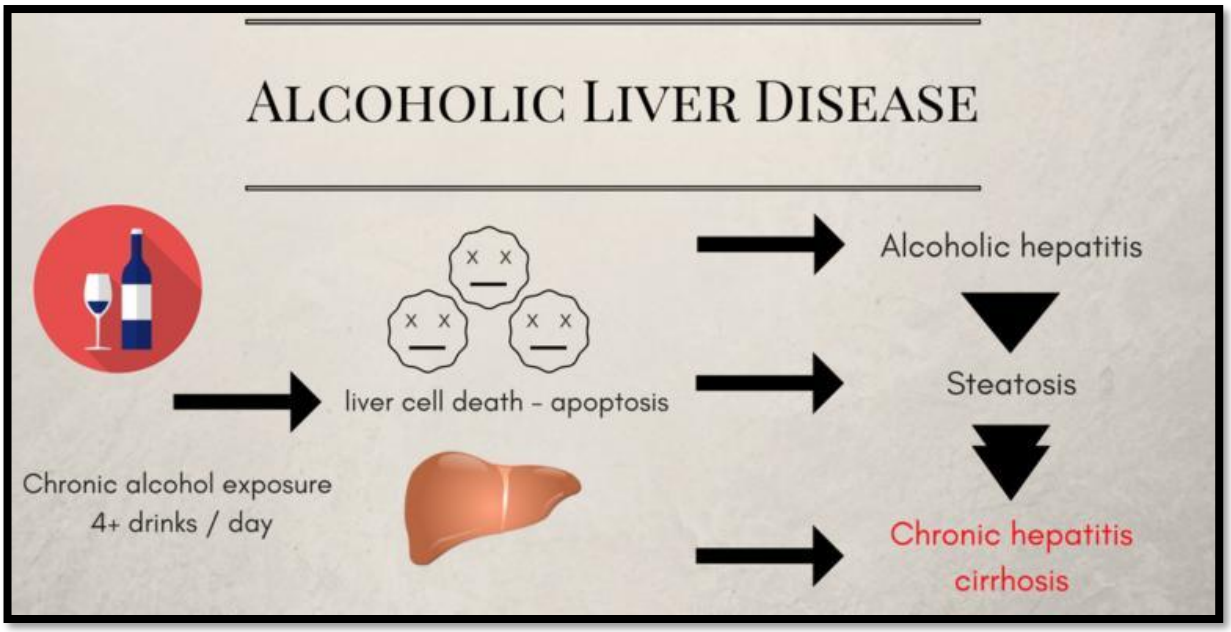

Fig Shows Alcoholic cirrhosis

Etiology

Alcoholic liver disease is caused by a variety of variables, including metabolic, genetic, environmental, and immunological factors. Mild alcohol use is tolerated by the liver, but as consumption increases, it causes problems with the liver's metabolic processes. The first stage involves steatosis, or the buildup of fat in the liver cells, often known as fatty liver. Alcoholic hepatitis can develop if alcohol drinking does not halted at this point. With continuous alcohol use, the alcoholic liver disease progresses to "alcoholic cirrhosis," a severe destruction to the liver cells. Hepatic fibrosis and nodules progress over time during the stage of alcohol-related cirrhosis. The most significant risk factors for the onset of liver disease are the quantity and frequency of the patient's alcohol consumption. The sort of beverage barely matters. Compared to men, women are more prone. The risk of alcoholic liver disease is further increased by obesity and a high-fat diet. Lower survival rates, earlier age of onset, and more severe histological damage are all related to concurrent hepatitis C infection. Alcoholic liver cirrhosis is linked to the protein PNPLAP3 (which contains a patatin-like phospholipase domain).

Epidemiology

In both the United States of America and the rest of the globe, alcohol is the drug that is most frequently abused.

It is the main contributor to liver disease in the US. Ten to twelve percent of the 61 percent of Americans who are affected by it are heavy drinkers.

The Centres for Disease Control and Prevention (CDC) defines an alcoholic beverage as containing half an ounce, or 13.7 grammes of pure alcohol, which is equal to the quantity of alcohol found in: 12 ounces of beer (5% alcohol); 8 ounces of malt liquor (7% alcohol).

• 5 ounces of 12% alcohol wine.

• 1.5 oz. of "hard liquor" at 80 proof (40 percent alcohol) The majority of cases of alcoholic liver damage occur in European nations. Alcoholic liver disease can be brought on by consuming 30 to 50 grammes of alcohol each day for more than five years. 90% of patients who drink more than 60 g/day may develop steatosis, and 30% of people who regularly consume more than 40 g/day may develop cirrhosis.

Definitions of at-risk drinking are as follows:

- Men: consume more than 14 drinks per week or four or more drinks per occasion
- For women and those over 65, more than seven drinks per week or more than three drinks on any particular occasion.

- The following are definitions of significant drinking from the perspective of liver toxicity (this history is crucial to distinguish between alcoholic fatty liver disease (AFLD) and non-alcoholic fatty liver disease (NAFLD))
- Men: more than 21 drinks per week
- Women: over 14 drinks per week

Metabolism Of Ethanol

- Alcohol provides 7 calories per gramme, however it cannot be stored by the body and must be oxidised, primarily in the liver. Thus, aside from providing energy, these empty calories have little nutritional value.
- After consumption and absorption from the small intestine, ethanol travels to the liver where 90% of it is converted to acetate by two enzymes in a two-step enzymatic process:

i. alcohol dehydrogenase (ADH) is found in the cytoplasm

ii. Acetaldehyde dehydrogenase (ALDH) is found in the mitochondria of hepatocytes

First step

- The liver uses one major mechanism and two minor pathways to convert ethanol to acetaldehyde:

i. In the cytosol, via alcohol Dehydrogenase's (ADH) primary rate-limiting route.

ii. In the smooth endoplasmic reticulum, where only a portion of ethanol is metabolised, via microsomal P-450 Oxidases (also known as the microsomal ethanol oxidising system, or MEOS).

iii. A small pathway via catalase, such as H2O2, exists in the peroxisomes.

iv. Acetaldehyde is poisonous and can harm membranes and lead to cell necrosis. Nicotinamide-Adenine Dinucleotide (NAD), a cofactor and hydrogen acceptor, is simultaneously reduced to NADH.

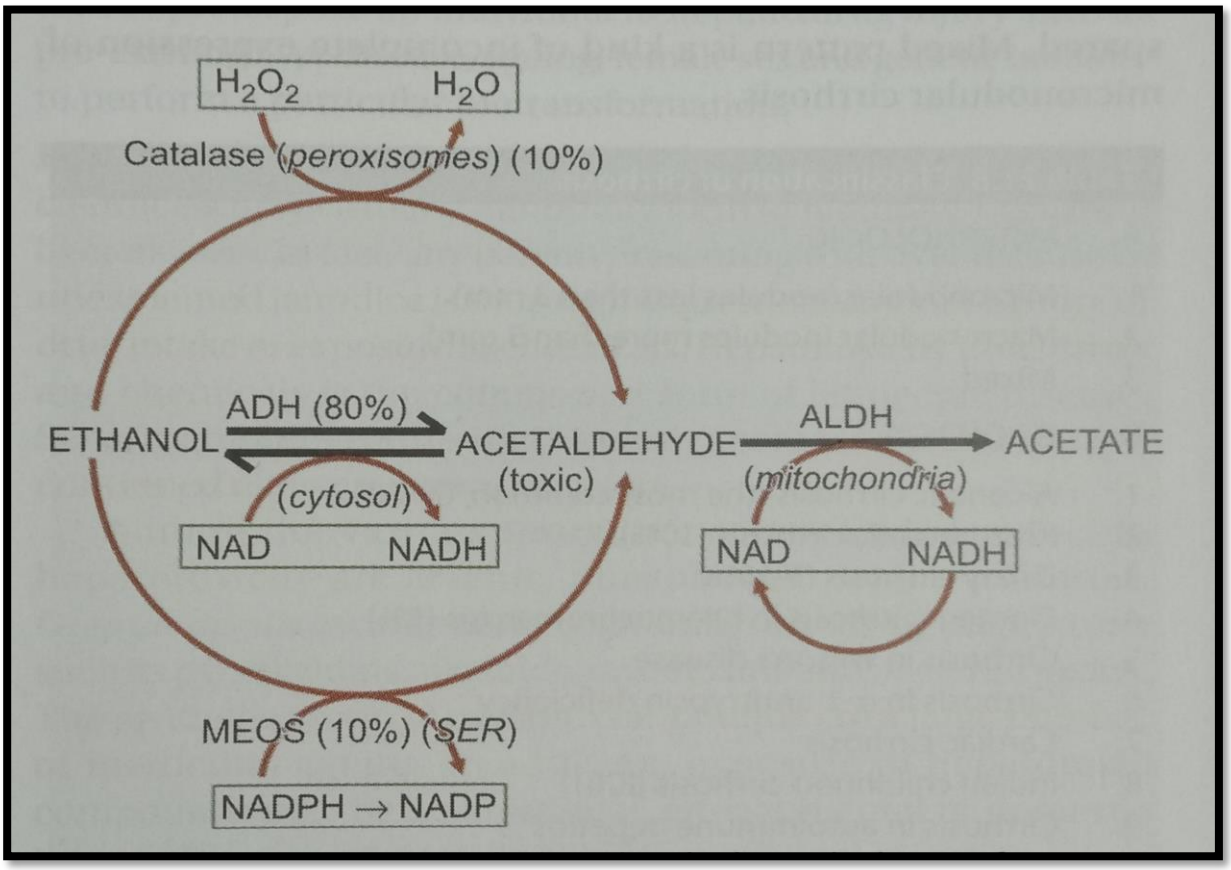

Fig Shows metabolism of ethanol in the liver

Second step

- Acetaldehyde is changed into acetate by ALDH, a c CO-enzyme, in the mitochondria. The majority of the acetate that leaves the liver is eventually oxidised to produce carbon dioxide and water or is changed into other fatty acids by the citric acid cycle.
- The same cofactor, NAD, is simultaneously reduced to NADH, increasing the NADH: NAD redox ratio, which is the fundamental biochemical change happening during ethanol metabolism.
- • The ratio of its oxidised and reduced metabolites, such as lactate-pyruvate ratio and ß-hydroxyl butyrate acetoacetate ratio, provides a good approximation of the NADH:NAD ratio.

Alcoholic Liver Disease Pathogenesis

It is well known that chronic alcoholics who are sensitive and who also have the risk factors indicated above will experience negative effects on their liver from ethanol and its metabolites. In a nutshell, the biomedical and cellular pathogenesis caused by prolonged alcohol consumption that results in the morphologic lesions of

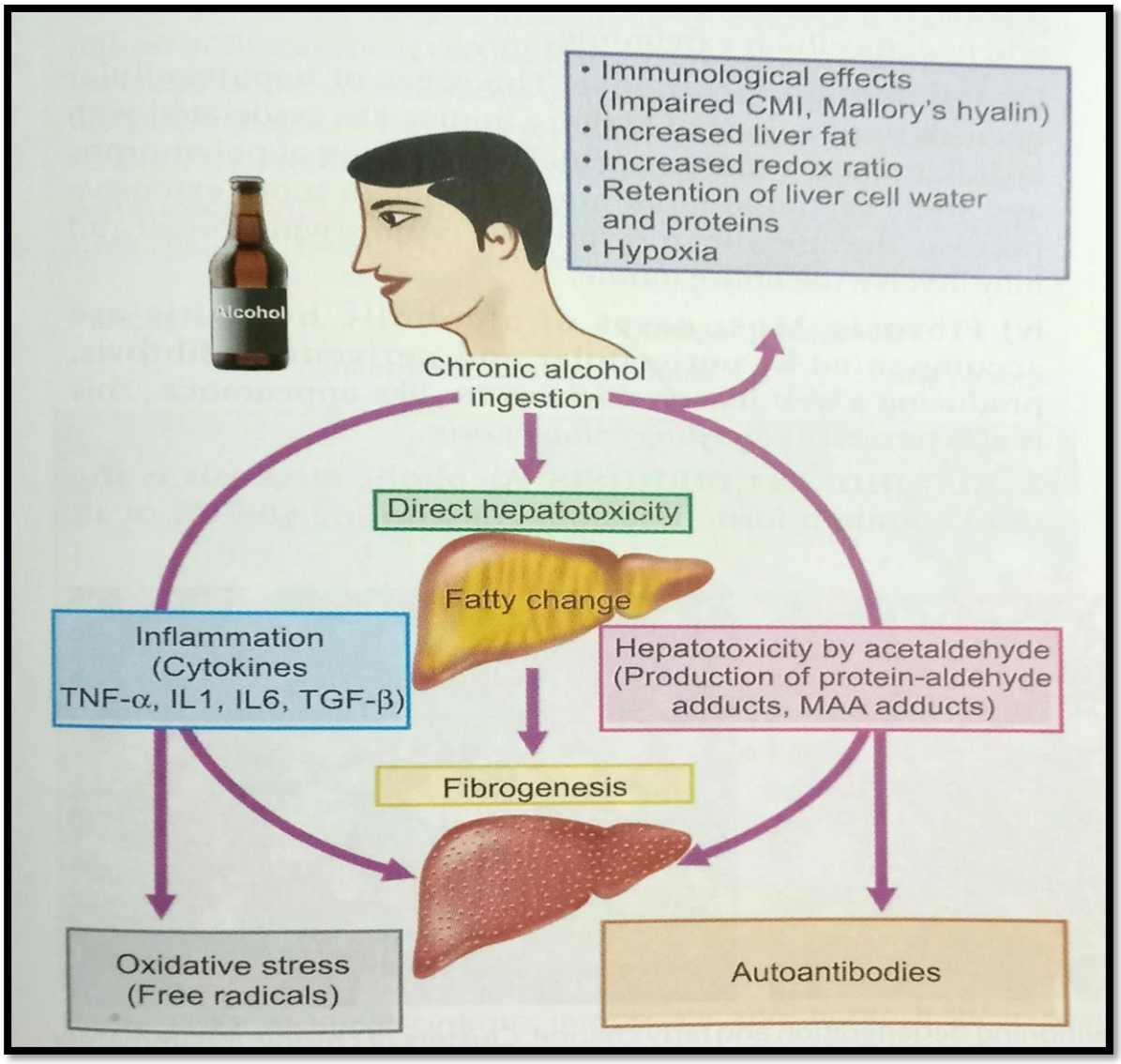

Fig Shows Pathogenesis of alcoholic liver disease

Processes in the ALD's pathogenesis

i. Direct ethanol damage to the liver

ii. Hepatotoxicity caused by metabolites of ethanol

iii. Stress from oxidation

iv. Immunological system

v. Inflammation

vi. Fibrogenesis

vii. Increased redox ratio

viii. Retention of proteins and water in liver cells

ix. Hypoxia

x. Increased liver fat

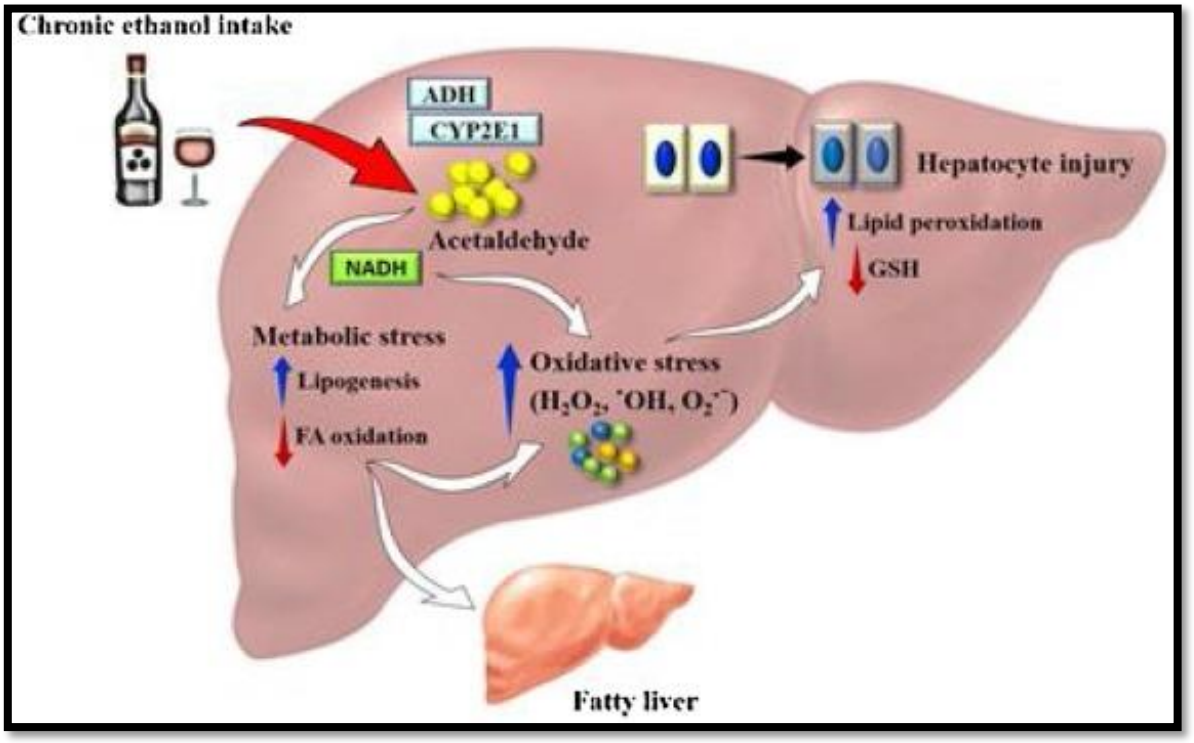

Fig Shows Hepatic metabolism of associated with oxidative stress

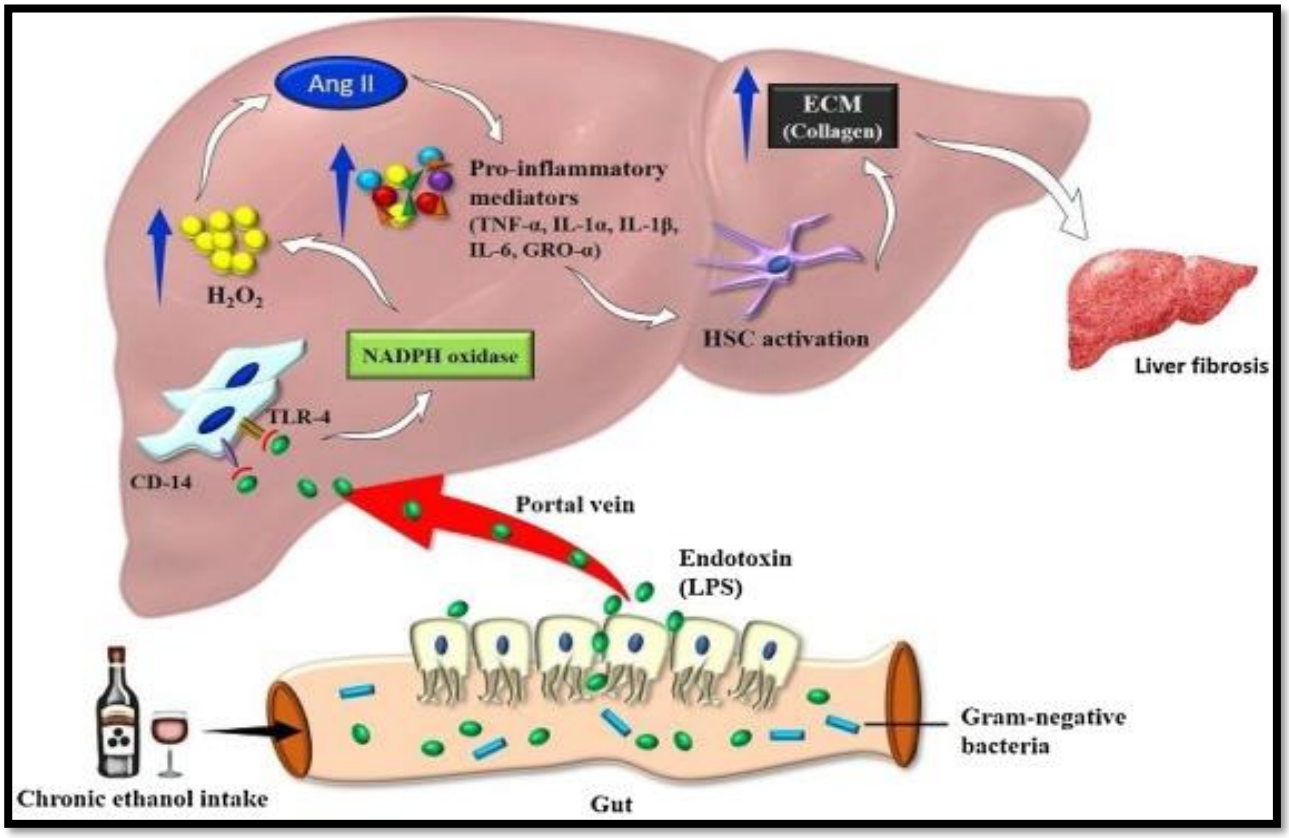

Fig. pathogenesis of alcoholic liver disease

Early Signs

A sick liver makes itself known by exhibiting a variety of symptoms. Due to the Early signs of alcoholic liver disease includes variety of bodily systems and are hazy. Signs as follows

- Pain in the abdomen.
- Nausea and vomiting.
- Diarrhea
- Decreased appetite.

These early symptoms are relatively treatable, but if they go untreated and alcohol use continues, the disease will grow more quickly.

Sign And Symptoms

How much and how long you've been consuming alcohol affects how it affects your liver. The most typical symptoms and warnings are as follows:

Fatty liver

- Often causes no symptoms
- As the liver enlarges due to a buildup of fat inside its cells, the right side of the upper abdomen becomes uncomfortable.
- Tiredness and weakness
- Weight loss

Alcoholic hepatitis

- Pain over the liver
- Fever
- Weakness

- Nausea and vomiting
- Appetite loss
- Yellowish the skin and eyes called (jaundice)

Alcoholic cirrhosis

- Portal hypertension, which increases the liver's blood flow resistance.
- Enlarged spleen
- Poor nutrition
- Bleeding in the intestines
- Ascites (fluid build-up in the belly)
- Kidney failure
- Confusion
- Liver cancer

The symptoms of alcoholic liver disease which looks like other health problem. Which is Always see to doctor for a diagnosis.

Diagnosis

Your healthcare professional that are perform a thorough physical examination test and health history. Other examinations as per follows

- Liver function tests, which determine if the liver is functioning properly, are among the blood tests.
- **Liver biopsy:-** surgical procedure to remove tiny tissue samples from the liver using needle. This type of liver illness is determined by the examining which samples under microscope.
- **Ultrasound:-** High frequency sound waves are used in this examination to see the organs.
- **CT scan:-** This imaging test creates images of the body—often referred to as slices—using X-rays and a computer. On the CT scan including body, muscles, fat, and organ can be seen in great detail. Compared the regular X-ray, CT scans are for the more detailed.
- **MRI:-** in the MRI that provides the precise image of inside body structure . And this technology combination of magnetic field, radio frequency, pulses, and a computer. Occasionally, dye injections into veins are utilised to create pictures of body sections. Due to the dye colour makes the liver and other abdominal organs more visible .

Diagnosis In Laboratory

The laboratory results as alcoholic liver disease progresses Quite variable, and in questionable cases, a liver biopsy is required. However, the disease's progressive stage typically exhibits the following biochemical and hematopoietic changes:

1) Increased transaminases; SGOT (AST) rise is greater than SGPT (ALT) increase.
2) Y-glutamyl transpeptidase (y-GT) serum levels are rising.
3) Increased serum alkaline phosphatase.
4) Hyperbilirubinaemia.
5) Hypoproteinaemia with reversal of albumin-globulin ratio.
6) Pro longed prothrombin time and the partial thromboplastin time.
7) Anaemia.
8) Neutrophilic leucocytosis in secondary infections and alcoholic hepatitis.

Alcohol-related Liver Disease Risk Factors

- Drinking pattern
- Gender

- Malnutrition
- Infection
- Genetic factors
- Hepatitis B and C infection

Management

- **Lactulose:**15-30ml orally 2-4 times per day.
- **Antibiotics:**

  Metronidazole:250mg orally 3 times daily.

  Neomycin: 0.5-1gm takes orally every 6-12 hrs for 7 days.

  Rifaximin:400mg orally 3 times daily. LOLA:
- **Lola**: L-ornithine L-aspartate 9gm takes orally 3 times daily.

Treatment

- Abstinence.
- Nutrition.
- Drug therapy.
- Liver transplantation.

Conclusion

ALD is largely to blame for the harmful effects of alcohol intake, which is a major contributor to illness and mortality worldwide. The diagnosis of ALD is made at advanced stages of the disease with increased rates of complications and mortality since the early stages of the disease are not well understood. The need for more accurate prognostic and natural history definitions, as well as the creation of trustworthy non-invasive ALD markers, cannot be overstated. This requirement would be met by early identification of the first signs of ALD in the primary care environment and subsequent behavioural therapies. Although there have been substantial advancements in our understanding of the pathophysiology and clinical features of ALD, there have been none in therapy over the past 40 years. Long-term alcohol abstinence is the mainstay of treatment for people with ALD, regardless of the illness stage. In all stages of ALD, from the asymptomatic early instances to the complex severe cases, abstinence is linked to better clinical results. The clinical endpoints vary according to the ALD stage. The end points for patients who have received compensation include the return to normalcy of aberrant laboratory results and the diminution of liver fibrosis. These end points are capable of non-invasive monitoring. One of the worst diseases, AH, has an unknown incidence. The mainstay of treatment is supportive therapy, as most medical therapies today are insufficient and ineffectual. The main endpoints for individuals with AH and decompensated cirrhosis are survival and liver disease compensation. The molecular and cellular elements that affect AH are not fully understood. Finding some possible treatment targets for severe AH has been made easier by recent translational research using human liver tissue. However, there hasn't been much progress in turning these discoveries into brand-new treatments. To enhance outcomes for this patient population, more thorough research is urgently required on these possible targets in both human and animal models.

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