DOI: https://doi.org/10.54393/pjhs.v2i01.22

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume2, Issue 1(Jan-Jun 2021)

Review Article

Pathophysiology and Diagnosis of Chronic Liver Disease

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Keywords:
Chronic liver disease, Pathophysiology, Biomarkers, Fibrosis, Aspartate Transaminase

How to Cite:
Shabbir, A., Arshad, M., Dar, A. J., & Khalid, S. (2021). Pathophysiology and Diagnosis of Chronic Liver Disease. *Pakistan Journal of Health Sciences, 2*(01). https://doi.org/10.54393/pjhs.v2i01.22

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Article History
Received: 13th January 2021
Accepted: 8th February 2021
Published: 30th June 2021

Chronic liver disease (CLD) is caused by an inflammatory damage to the liver that lasts six months or more. The development of new blood vessels, regardless of the underlying aetiology, is a fundamental process in the pathogenesis of chronic liver diseases (CLDs). Given the fact that CLDs often advance from hepatocyte injury to inflammation, fibrosis, cirrhosis, and, in rare circumstances, hepatocellular cancer, CLDs cannot be regarded a single illness (HCC). Neovascularisation and the creation of an aberrant angioarchitecture are linked in the pathological course of CLDs. Asymptomatic individuals with modestly increased liver enzymes such as Alanine Transaminase (ALT) and Aspartate Transaminase (ALT) are frequently found in basic care. Biochemical indicators include serum bilirubin, alanine amino transferase, aspartate amino transferase, aminotransferase ratio, alkaline phosphatase, gamma glutamyltransferase, 5' nucleotidase, ceruloplasmin, and alpha-fetoprotein. In conclusion, further epidemiological and pathophysiology research is needed. A better knowledge of the molecular pathways behind geriatric chronic liver disease will aid in determining the best diagnostic and treatment strategy for each older patient.

INTRODUCTION

Chronic liver disease (CLD) develops due to an inflammatory injury to the liver, which prolongs for six or more months [1]. Chronic liver disease is not a single disease, it normally progresses from cellular inflammation, carcinoma, fibrosis and cirrhosis [2]. According to the National Statistics Office, liver illnesses are now the fifth leading cause of mortality, behind heart disease, stroke, chest disease, and cancer (statistics). The prevalence of liver illnesses is high [3]. Various invasive and noninvasive methods are used in diagnosis of CLDs. A liver biopsy is an invasive procedure. Liver biopsy has always been regarded as critical for determining the degree of fibrosis since it allows for direct assessment of the entity. However, because of the inherent danger of problems, observer variability, and technological constraints connected with this approach, it can cause sample mistakes as a result of these alternative non-invasive procedures, which has motivated researchers to look for other options [4]. Noninvasive methods have been designed in the last few years. Serological markers and radiological tests are involved in these methods based on liver elasticity measurement. In the liver it allows to quantify the degree of fibrous tissue. These noninvasive methods are highly important in the early detection of liver diseases [5]. Liver function abnormality tests are used to explore the cause of disease. Increased ALT-immunoglobulin levels are directly linked with the severity of disease [6].

In recent decades with the advancement in technology the incidence of liver diseases has been reduced. Liver transplantation, biological therapies and surgeries reduced the mortality rate among liver patients. Early diagnosis is a major contributor in the reduction of disease progression [7]. HBV vaccination also help to overcome the incidence of viral hepatitis B and its complications. It also prevents from HCC progression [8]. Some preventive measures also control occurrence of hepatitis B and C such as avoid alcohol and promote safe blood transfusion. Consistency in liver disease leads toward major health outcomes. In western countries liver cancer and cirrhosis are major factor of disease and death among adults [9]. Statistically liver diseases are 5th common cause of death after stroke, cancer and heart disease [10].

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Recently a study showed that the number of men in with cirrhosis is more than women [11].
Hepatocellular carcinoma (HCC) is a major contributor to increase the incidence rate of chronic liver disease globally. Usually, it starts from a malignant tumor. Angiogenesis is most important pathophysiological factor of HCC [12]. Liver cancer also most common in Asian countries due to increased prevalence of viral hepatitis B and C [13]. Hepatitis C is more dangerous and leads toward liver cirrhosis [14]. Smoking is a pivotal risk factor which increase progression of disease [15].

Pathophysiology

Cirrhosis is considered as end stage of chronic liver diseases. Hepatocellular carcinoma, portal hypertension, and liver failure are among the numerous additional liver problems. All of these factors have a role in cirrhosis detection. In recent years many technologies and diagnostic measurements are invented to diagnose chronic liver diseases [16].
Repeated injury and inflammation of liver in cirrhosis make it irreversible. During inflammation large number of fibrous tissues are formed to repair the damage caused by injury. But these fibrous tissues interfere with the normal structure and make abnormal structures are called nodules throughout the liver. In this stage new blood vessels are also formed but can't manage large amount of blood. Higher pressure of blood in liver which remains un-control leads toward severity [17].
Mechanism behind the pathogenesis of CLD is the production of excessive blood vessels in the result of fibrosis, inflammation and hepatocellular carcinoma (HCC). In other words, abnormal angioarchitecture and neovascularisation are directly linked with chronic liver disease progression [18].

Diagnosis

In primary care asymptomatic patients normally have mild elevation in liver enzymes. These enzymes are Alanine Transaminase (ALT) and Aspartate Transaminase (ALT). In the absence of any historical and physical symptoms, patient's evaluation is started on the basis of prevalence of any disease which cause increase in transaminase levels (Fig1). Usually, elevation in transaminase levels is observed in patients with fatty liver disease. Other reasons behind the progression of chronic liver disease are hepatitis B, hepatitis C, alcoholic liver disease, hemochromatosis and medication-related liver disease. Otherwise, autoimmune hepatitis, Wilson disease and A1-antitrypsin deficiency also cause CLD but these are not common. Liver transaminase levels are also increased in some extrahepatic conditions such as hemolysis, muscle disorders, thyroid disorders and celiac disease. Initial tests use to detect chronic liver disease are blood glucose levels (fasting, random, HbAc1); serum iron; serum ferritin; hepatitis B; blood lipid profile; hepatitis C virus; LFTs; and total iron-binding capacity. Lifestyle and dietary modifications can help to reduce symptoms if test value is normal or mildly disturbed. Other diagnostic measurements are serum protein electrophoresis; α1-antitrypsin and ceruloplasmin; ultrasonography; antinuclear antibody, smooth muscle antibody, and liver/kidney microsomal antibody type 1 tests, when transaminase results remain high for more than six months, a liver biopsy is suggested [19].

Laboratory testing is very useful to detect liver diseases and also help to make a treatment plan. Liver is the metabolic organ that metabolites carbohydrates; proteins and fats so the end products of these metabolic pathway also help to expose liver abnormality. Serum alanine amino transferase, aminotransferases, bilirubin, aspartate amino transferase, 5' nucleotidase, ceruloplasmin and alkaline phosphatase levels are some other indicators to check liver dysfunction. Chronic liver disease diagnosis is very challenging because liver enzymes are also elevated in some other disorders as seen in figure 1. To detect hepatic function or liver injury "liver chemistry tests" are collectively used [20]. Increased ALT levels are mainly associated with hepatocytes and hepatic damage. In clinical practice serum liver chemistry tests are routinely acquired. Many individuals with abnormal test results have been identified by using widespread testing in symptomatic or asymptomatic condition. Up to 4% of the U.S. population is estimated to have asymptomatic liver chemistry test abnormalities [21, 22].

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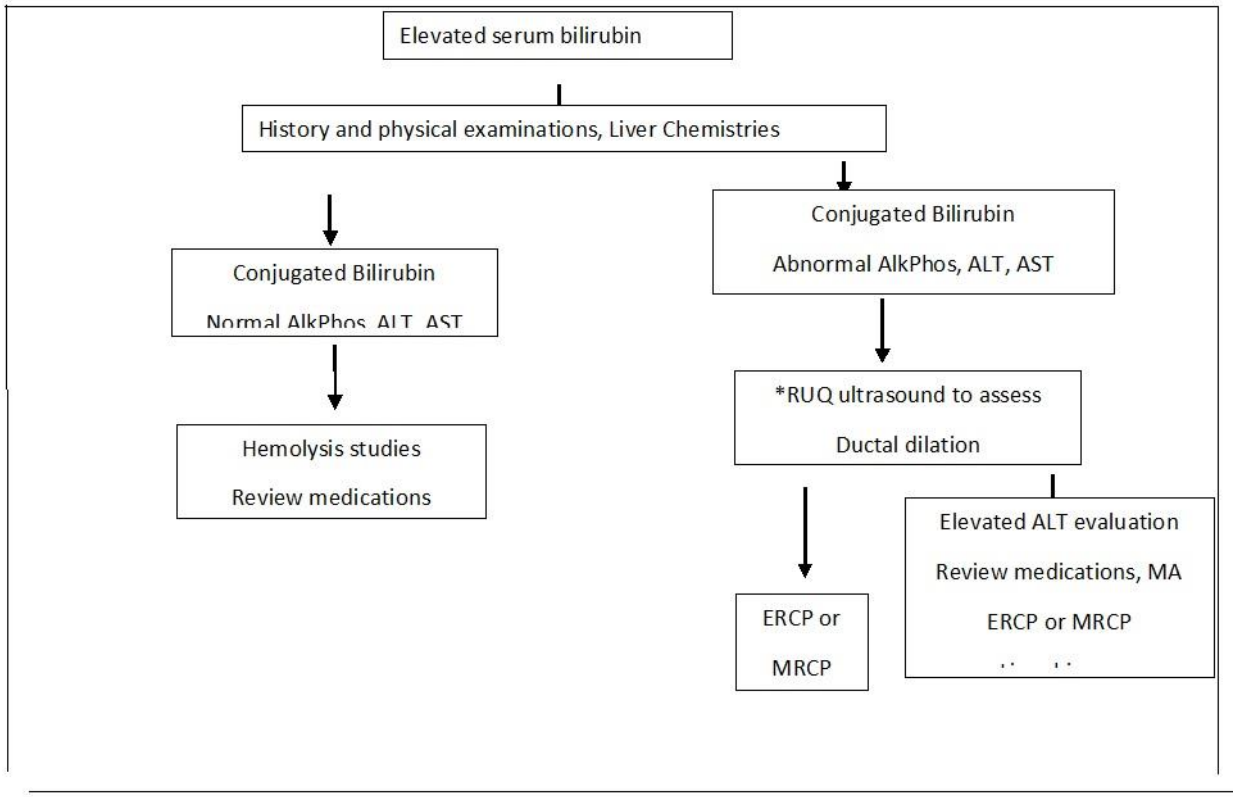

Figure 1: Elevated serum alkaline phosphate

*RUQ= Right upper quadrant

Figure 1 shows how to evaluate individuals with elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Non-invasive serologic testing should be used to rule out common hepatic disorders in patients with increased serum aminotransferases.

Evaluation of Abnormal Liver Transaminase Levels

ALT and AST levels that are too high (less than 5 times the average)

Examination of the patient's medical history and physical condition
Stop using hepatotoxic medications and drinking alcohol.
Recognize the signs of metabolic syndrome (consider fasting lipid profile and glucose level)
Consider testing again in 2 to 4 weeks.

ALT and AST abnormalities that are persistent or unexplained

Antibody testing for the hepatitis C virus
Surface antigen testing for hepatitis B
Total iron-binding capacity, serum iron and ferritin levels
Consider ultrasonography if you have a fasting lipid profile and a high glucose level
Consider collecting a full blood count including platelets, measuring prothrombin time, and testing prothrombin time.

CONCLUSION:

CLD is supposed to have a vital role in age-related liver disease, owing to an increased trend in metabolic disorders, especially those associated with reduced insulin sensitivity, such as obesity and T2D. It is linked to liver cirrhosis and hepatocellular carcinoma (HCC) in aged population. Treatment options will need to include the particular characteristics of an aging population and will require a multidisciplinary approach. Non-pharmacological treatment must be particularly

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designed due to the physical restrictions of older citizens and the need for an adequate caloric supply. More epidemiology and pathophysiology researches are required. Understanding the molecular mechanisms behind geriatric CLD will assist in selecting the appropriate diagnostic and therapeutic strategy for each older patient.

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