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Physiological Aspects on Liver Fibrosis

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Abstracts: Liver fibrosis resulting from long-standing liver damage represents a major health care burden worldwide. To date, there is no anti-fibrogenic agent available, making liver transplantation the only curative treatment for decompensated cirrhotic liver disease. Liver fibrosis can result from different underlying chronic liver disease, such as chronic viral infection, excessive alcohol consumption, fatty liver disease or autoimmune liver diseases. It is becoming increasingly recognised that as a result from different pathogenic mechanisms liver fibrosis must be considered as many different diseases for which individual treatment strategies need to be developed. Moreover, the pathogenic changes of both liver architecture and vascularisation in cirrhotic livers, as well as the lack of "true-to-life" in vitro models have impeded the development of an effective anti-fibrogenic drug. Thus, in order to identify an efficient anti-fibrogenic compound, novel in-vitro models mimicking the interplay between pro-fibrogenic cell populations, immune cells and, importantly, the extracellular matrix need to be developed.

Keywords: Liver Fibrosis, liver damage, autoimmune liver diseases

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Introduction:

The adult human liver typically weighs around 1.5 kg. It is the largest internal organ and plays many pivotal roles in intermediary metabolism and in the metabolism and clearance of xenobiotic (Yu, 2008). The liver is responsible for the disposal of bile pigments and for the generation of bile acids that are central to the maintenance of cholesterol homeostasis and the absorption of dietary lipid from the intestine (Tsuda et al., 2010). The liver also plays an important role in lipoprotein metabolism and cholesterol homeostasis. It is the site of synthesis for major serum proteins including albumin, complement and clotting factors, and of catabolism of amino acids and the generation of urea. In the normal state the liver is maintained at a size which provides substantial over capacity. It also has a remarkable ability to regenerate in response to functional parenchymal loss and can return to normal size and functional state even after 70% of the parenchyma is lost.

Chronic liver injury, irrespective of cause, is generally associated with the accumulation of matrix proteins – a process referred to as fibrosis (Yamada, 2011). In parallel with this there is a continued stimulus for regeneration leading to further distortion of the hepatic architecture and vascular structures (portal veins, hepatic veins) . This results in a transformation to a nodular architecture, so-called cirrhosis (Ryeom& Kim, 2004). Given the normal functional over capacity of the liver, patients with cirrhosis can have apparently normal (compensated) liver function for long periods of time but with many there is ultimately decompensation with catastrophic effects on the various strands of intermediary metabolism referred to above. In addition the altered vasculature leads to the development of portal hypertension (. To date most therapies for chronic liver disease have targeted the aetiological agent, for example, there are now several effective antiviral agents for the treatment of hepatitis B and C (Lee, 2011).Similarly there are a number of immunosuppressive agents that can be given for immune driven processes such as autoimmune hepatitis(Watanabe et al., 2011).While these agents often have a beneficial effect on the degree of fibrosis there are currently few agents that are specifically developed to interfere with fibrosis per se. For some patients with end-stage liver disease the only available option for treatment is orthotopic transplantation (Ashyraliyev, 2009).

Aim of the study

The objectives of this study were to determine the _ physiological aspects on Liver Fibrosis and Study of modern technologies used in diagnosing and treating disease and how to prevent it.

1-The liver

The liver is the largest internal organ in the body, constituting about 2.5% of an adult's body weight. During rest, it receives 25% of the cardiac output via the hepatic portal vein and hepatic artery. The hepatic portal vein carries the absorbed nutrients from the GI tract to the liver, which takes up, stores, and distributes nutrients and vitamins (Trauner, 2003).

the largest gland and one of the most vital organs that functions as a centre for metabolism of nutrients and excretion of waste metabolites(Dawson et al., 2009).

The liver Is located in the upper right part of the abdominal cavity below the diaphragm, above the stomach, right kidney and intestine (Grassl, 2007).

1.1- Structure of the liver

The liver consists of four lobes: the larger right lobe and left lobe, and the smaller caudate lobe and quadrate lobe. The left and right lobe are divided by the falciform (“sickle-shaped” in Latin) ligament, which connects the liver to the abdominal wall (Gu&Manautou, 2010)

The liver’s lobes can be further divided into eight segments, which are made up of thousands of lobules (small lobes). Each of these lobules has a duct flowing toward the common hepatic duct, which drains bile from the liver (Gerk et al., 2002).

Parts of the liver:

▪ Common Hepatic Duct: A tube that carries bile out of the liver. It is formed from the intersection of the right and left hepatic ducts.

▪ Falciform Ligament: A thin, fibrous ligament that separates the two lobes of the liver and connects it to the abdominal wall (Meier&pauli, 2006)..
▪ Glisson's Capsule: A layer of loose connective tissue that surrounds the liver and its related arteries and ducts.
▪ Hepatic Artery: The main blood vessel that supplies the liver with oxygenated blood (Kullak, 2002).
▪ Hepatic Portal Vein: The blood vessel that carries blood from the gastrointestinal tract, gallbladder, pancreas, and spleen to the liver.(cheng et al., 2008)
▪ Lobes: The anatomical sections of the liver.
▪ Lobules: Microscopic building blocks of the liver.
▪ Peritoneum: A membrane covering the liver that forms the exterior (Rockey, 2012).

1.2 Types of liver cells

1.2.1-Hepatocytes, the major parenchymal cells in the liver, play pivotal roles in metabolism, detoxification, and protein synthesis. Hepatocytes also activate innate immunity against invading microorganisms by secreting innate immunity proteins (Batts, 1995).

1.2.2-Endothelial Cells

Cells The sinusoidal endothelial cells line the walls of the hepatic sinusoid and perform a function of filtration due to the presence of fenestrae (Reddy et al., 2006).These cells also demonstrate large endocytic capacity for extracellular matrix components and immune complexes. In general they engulf smaller size particles and may play a role in clearance of viruses, but do not posses phagocytic function.

They may also function as antigen presenting cells and secrete certain cytokines and eicosanoids (Baranova,2011).

1.2.3-Kupffer Cells

respons The liver harbors large amounts of kupffer cells, which represent the largest tissue resident macrophage population of the body (Adams, 2012).. They are located within the sinusoid and are in constant contact with gut-derived particles that lead to low but constant amount of activation of these monocyte derived cells. Upon activation they are able to secrete a vast range of inflammatory mediators such as cytokines (Manizate et al, 2010).

1.2.4-Stellate Cells

The liver plays a central role in uptake and storage of vitamins A (Retinol) and stores about 95 % of retinoids found in the body (Morris, 2009). The fat storing perisinusoidal cells of the liver, stellate cells are the main vitamin A storing cells .They harbor large amounts of retinol and retinyl palmitate in lipid droplets within their cell cytoplasm (Fazakas et al., 2006).

1.3- Enzymes of liver

The liver makes proteins known as enzymes, whichh are substances that help the body perform Its functions by speeding up chemical reactions In the body. These enzymes help the body break down food, purify the blood from toxins, fight Infections, store energy, and then make proteins necessary for blood clotting (Williams,2014).

Elevated liver enzymes Indicate inflammation or damage to the liver, as these enzymes circulate In the bloodstream through leakage from inflamed or damaged liver cells(Asrani, 2013).

1.3.1-Gamma-glutamyltransferase (GGT)

Gamma-glutamyltransferase (GGT) is a membrane-bound glycoprotein enzyme derived mainly From the hepatocytes and biliary epithelial cells, renal tubules, pancreas and intestine(Manns et al, 2017).

Increased serum GGT activity has long been used in clinical practice as a marker of Both liver dysfunction and excessive alcohol In take (Marchesini, 2001). GGT in Known to increase In all forms of liver disease, especially In cases of biliary obstruction, with Small increases (2–5 times normal) observed In connection with fatty liver, so that GGT Is of. Limited value for the purpose of screening alcohol consumption per se In patients with non- Alcoholic liver diseases or In hospitalized patients, for Instance (Younossi& Abdelatife, 2016) ,

1.3.2-Alkaline phosphatase(ALP)

Is an enzyme that transports metabolites across cell membranes . Pathological elevations are commonly observed In liver and bone diseases, although the enzyme May originate from several other tissues (Puri, 2012) . The synthesis and release of hepatic ALP is stimulated by cholestasis, and when released, its half-life in the circulation is about 7 Days (Nasr et al., 2015). Since elevated ALP is a somewhat unspecific parameter, it needs to Be interpreted in the context of a clinical diagnosis and other laboratory markers(Karlsen, 2012).

1.3.3-Aspartate Aminotransferase(AST)

is an enzyme which like ALT Is also found in the liver however has also other Sites where its presence Is not as minimal as ALT. These sites are primarily skeletal Muscle, cardiac muscle, renal tissue, and brain (Lindor&Levy, 2012). It occurs as 2 isoenzymes that are not Differentiated on standard testing and hold little clinical value. AST facilitates amino Acid metabolismWhen it comes to AST, caution must be practiced when evaluating Abnormal levels due to Its presence in other tissues(Manns, 2012). The normal range for AST is < 35IU/L

1.3. 4-alanine transminase(ALT)

is an enzyme that Is found primarily In hepatocytes (lower concentrations In cardiac, renal, and muscle tissue) and thus is specific to the hepatocellular Injury(Navarro et al., 2006). ALT levels often fluctuate throughout the d. ALT facilitates the formation of glutamate and pyruvate in the hepatocyte whichh is important for energy production(Mac Donald, 2009).The normal range for ALT in males Is between 29-33 IU/L and 19-25 IU/L for female.

1.4-Function of the liver.

The liver makes proteins known as enzymes, whichh are substances that help the body perform its functions by speeding up chemical reactions in the body. These enzymes help the body break down food, purify the blood from toxins, fight infections, store energy, and then make proteins necessary for blood clotting(BonKovasky, 2012).

Elevated liver enzymes indicate inflammation or damage to the liver, as these enzymes circulate in the bloodstream through leakage from inflamed or damaged liver cells(Perlmutter et al., 2012).

1.4.1-Bile production

The liver produces about one litre of bile per day which passes into the gall bladder and gets concentrated to one fifth of its original volume. Bile consists of electrolytes, proteins, bilirubin, bile salts and Lipids (Goldin, 1996).. Bile acids are produced in the liver from cholesterol. .They are acted upon by bacteria in the gut to form secondary bile acids which are then conjugated to form bile salts (Kleiner, 2005).. Bile salts are important for emulsification of fat and absorption of the fat soluble vitamins A, D, E andK (Bedossa et al., 2003).

1.4.2-The Liver Is Important in Carbohydrate Metabolism

The liver is extremely important in maintaining an ade- quate supply of nutrients for cell metabolism and regulating blood glucose concentration (Rousselet, 2005).After the ingestion of a meal, the blood glucose increases to a concentration of 120 to 150 mg/dL, usually in 1 to 2 hours(Regev et al., 2002).. Glucose is taken up by hepatocytes by a facilitated carrier-mediated process and is converted to glucose 6-phosphate and then UDP- glucose. UDP-glucose can be used for glycogen synthesis, or glycogenesis(Griffin,2017). It is generally believed that blood glucose is the major precursor of glycogen (Poynard,2012) .recent evi- dence seems to indicate that the lactate in blood (from the peripheral metabolism of glucose) is also a major precursor of glycogen. Amino acids (e.g., alanine) can supply pyru- vate to synthesize glycogen(Godfrey et al., 2013).

1.4.3- The Liver Plays an Important Role in the Metabolism of Lipids

The liver plays a pivotal role in lipid metabolism .It takes up free fatty acids and lipoproteins (complexes of lipid and protein) from the plasma(Brown, 2014).Lipid is circulated in the plasma as lipoproteins because lipid and water are not mis- cible; the lipid droplets coalesce in an aqueous medium(Thomsen,1994).The protein and phospholipid on the surface of the lipoprotein particles stabilize the hydrophobic triglyceride center of particles(Reeder et al., 2011).

1.4.4-The Liver Produces Most of the Circulating Plasma Proteins

The liver synthesizes many of the circulating plasma pro- teins, albumin being the most important . It syn- the

sizes about 3 g of albumin a day (Dahlqvits, 2012).. Albumin plays an important role in preserving plasma volume and tissue fluid balance by maintaining the colloid osmotic pressure of plasma (Spinazzi, 1999). This important function of plasma proteins is illustrated by the fact that both liver disease and long-term starvation result in generalized edema and ascites. Plasma albu- min plays a pivotal role in the transport of many substances in blood, such as free fatty acids and certain drugs, includeing penicillin and salicylate (Gschwend et al., 2014)

1.4.5-The Liver Is Important in the Storage and Homeostasis of Iron

The liver is the major site for the synthesis of several pro- teins involved in iron transport and metabolism (The pro- tein transferrin plays a critical role in the transport and homeostasis of iron in the blood(Leonharted, 2010). The circulating plasma transferrin level is inversely proportional to the iron load of the body—the higher the concentration of ferritin in the hepatocyte, the lower the rate of transferrin synthesis (Pascolo, 2001). Dur- ing iron deficiency, liver synthesis of transferrin is signifi- cantly stimulated, enhancing the intestinal absorption of iron(Ulloa et al., 2013)..

1.4.6-THE METABOLISM OF DRUGS AND XENOBIOTICS

Hepatocytes play an extremely important role in the me- tabolism of drugs and xenobiotics—compounds that are foreign to the body, some of which are toxic (Fallon, 2016). Most drugs and xenobiotics are introduced into the body with food (Gerdle, 2013). The kidneys ultimately dispose of these substances, but for effective elimination, the drug or its metabolites must be made hydrophilic (polar, water-soluble). This is because re- absorption of a substance by the renal tubules is dependent on its hydrophobicity (Hamilton et al., 2009). .

2.1- Liver fibrosis

Is a disease that results In scarring of healthy liver tissue that affects its normal functioning (Longo, 1995).

Disease that, in advanced cases, can lead to a patient with more serious diseases, such as cirrhosis, renal failure, or portal hypertension (Reeder & Hu, 2012). It is an excessive accumulation of extracellular matrix proteins, including collagen, which occurs in most Types of chronic liver disease. Advanced fibrosis leads to cirrhosis, liver failure, and portal hypertension and often requires liver transplantation (Shields, 2015). Activated hepatic stellate cells, portal fibroblasts, and myofibroblasts of bone marrow origin were Identified as the major collagen-producing cells in the Injured liver These cells are activated by fibrogenic cytokines such as TGF-β1, angiotensin II, and leptin (lim et al., 2003).

2.2- Cause of liver fibrosis.

Fibrosis occurs when scarring occurs repeatedly or the infection persists for long periods of time, causing the accumulation of large amounts of scar tissue(Noren, 2005).In fact, the liver performs scarring as a natural response when there is an injury, wound, or inflammation in the area (Naressi et al., 2001).It should be noted that cirrhosis occurs in the majority of individuals who suffer from chronic liver injuries, but in varying proportions and rates, based on several factors, including; The underlying cause of liver disease, and other individual factors that belong to the patient himself Below is a statement of the causes of fibrosis (Vanhamme, 1997).

2.2.1- Alcoholic liver disease

Alcoholic liver disease results from drinking alcoholic substances that lead to damage to the liver tissue and Impair the ability of the liver to perform normal functions. (Glaser et al., 2012).Alcoholic liver disease usually occurs after several years of excessive drinking, and with the passage of time scars appear In the liver tissue, and the condition recedes The health of the liver gradually occurs until fibrosis of the liver occurs, and cirrhosis of the liver Is considered the last stage of alcoholic liver diseases (Forsgren, 2015).It should be noted that the possibility of developing this disease in an Individual increases the longer the period of drinking alcohol, and the greater the amount consumed of alcoholic substances, but alcoholic liver disease does not affect all Individuals who drink alcohol excessively, and It is not required for the Individual to drinks until he gets sick (Bonate et al., 2011).

2.2.2- Non-alcoholic fatty liver disease

The term non-alcoholic fatty liver disease refers to a group of liver health problems, which affect individuals who drink alcohol In small quantities or do not drink alcohol at all, and this disease is represented by the presence of

large amounts of fat stored In liver cells (Roll, 2009).In fact, although the presence of excessive amounts of fat within the liver Itself is abnormal, It may not cause damage to liver tissue, but this condition can develop In a small group of Individuals into a dangerous health condition. (Klipp et al., 2009).The liver plays a role similar to that of toxic substances, as this causes inflammation of the liver cells that Is not caused by drinking alcohol, whichh may lead to the accumulation of scar tissue In the liver. Others, and the reason behind the Infection of some individuals with inflammation of fatty liver cells, which worsens into cirrhosis of the liver, Is not sufficiently clear so far (Nyman, 2011).It is worth noting that the accumulation of fat In the liver Is associated with a group of health problems, namely; Obesity, and Insulin resistance, which Is represented by the Inability of body cells to receive sugar in response to the presence of the hormone insulin, in addition to a high blood sugar level as an indicator of pre-diabetes or type 2 diabetes, as well as a high level of fats In the blood, especially triglycerides (Berg et al., 2007).

2.2.3- Viral hepatitis

Viral hepatitis Is a viral Infection that affects the liver tissue and leads to Inflammation in it that Is represented by Its swelling (Raue, 2009).this Inflammation may lead to damage to the liver tissue, and it should be noted that there are several types of viruses that cause hepatitis, most notably the hepatitis A virus, And B, C, D, and E, A and E viruses usually cause acute and short-term infections only Where the body can fight and resist acute viral Infection and get rid of It, while virus B, C and D can cause acute Infection or long-term chronic infection, and chronic viral infection Is represented by the body's Inability to fight and get rid of the virus (Huwart, 2006).

In fact, fibrosis results from Chronic damage to the liver in addition to the continuous accumulation of fibrous proteins that make up the tissue outside the cell, and fibrosis In the liver tissue continues to progress and develop In patients who suffer from chronic viral hepatitis, because it is a vital and effective process that requires the response of liver cells to many genetic factors of the individual in addition to Proteins belonging to the virus, and It should be noted that there are many factors that accelerate the incidence of cirrhosis of the liver In a patient with viral hepatitis, Including; Alcohol use, fatty liver disease, and age at exposure to viral Infection (Sinkus et al., 2005).

2.2.4- Autoimmuned disorders

These are diseases that appear as a result of the immune system attacking the body's tissues(Turlin,1998). One of the most prominent autoimmune liver diseases Is; Autoimmune hepatitis, primary biliary fibrosis and primary sclerosing cholangitis In fact, biliary fibrosis and cholangitis are associated with Inflammation, scarring, and blockage of the bile ducts (Lee et al., 2011).Digestion of fats known as bile from the liver and gallbladder into the small intestine (Romu, 2016).

2.2.5- Hemochromatosis

It is a genetic medical condition represented by the absorption and storage of large amounts of Iron in the body, and In this case excess Iron accumulates in various organs of the body, especially the liver, which leads to serious damage to these organs. If this condition Is not treated, fibrosis of the liver may occur (Andersson et al., 2015).

2.3- Stages of Liver fibrosis

Fibrosis does not happen all at once, but Its degrees and stages are many and different, and end with serious cirrhosis In the last stage, and these are the most Important degrees of fibrosis (CC et al., 1957). .

2.3.1- The first stage

In this stage of liver fibrosis, harmful scar tissue begins to form In the liver in very small quantities, and the patient often does not show any symptoms, and he does not feel any defect In his physical health (Hamm et al., 1995)

2.3.2- The second stage:-

Scar tissue begins to spread more In the liver Whichh may be accompanied by the appearance of symptoms on the patient, such as: high blood pressure and esophageal varices (Cui, 1999) .

2.3.3- The third stage:-

At this stage of fibrosis , the amount of scar tissue In the liver becomes significantly and dangerously large, which results in the appearance of the following symptoms on the patient (Muhler et al., 1993). :Noticeable swelling

And bloating In the abdominal area Complete failure of various liver functions

2.3.4- The fourth stage:-

At this stage, the condition of fibrosis of the liver becomes very serious in a way that may lead to the death of the patient, and here the patIent may need a liver transplant Immediately, otherwise he may die at any moment (Kim et al., 2010).

2.4- Complications of liver fibrosis

2.4.1- High blood pressure

In the veins supplying the liver (portal hypertension). As fibrosis slows the normal blood flow through the liver, the pressure Increases in the vein that brings blood from the intestines and spleen to the liver (Shuter, 1996).

2.4.2 -Splenomegaly) Enlarged spleen

(splenomegaly). Portal hypertension can also cause changes and swelling of the spleen, and retention of white blood cells and platelets. A low level of white blood cells and platelets in your blood may be the first sign of fibrosis (Rohrer et al., 2005).

2.4.3- Bleeding.

Portal hypertension can cause blood to be rerouted to smaller veins. This extra pressure strains these smaller veins, Causing them to burst, causing dangerous bleeding (Levitt, 2003).Portal hypertension may cause enlarged veins (varices) In the esophagus (esophageal varices) or stomach (gastric varices) and lead to fatal bleeding (JR, 1983).The inability of the liver to make enough blood-clotting factors may also contribute to continued bleeding (Hume et al., 1971)..

2.4.4- Infection

If you have fibrosis , your body will have difficulty fighting infection. Ascites can lead to bacterial peritonitis, which is a serious infection (Nadler & Hidalgo, 1962).

2.4.5- Malnutrition

Fibrosis may make It difficult for your body to process nutrients. Which leads to feeling weak and losing weight (Singh, 2016).

2.4.6Buildup of toxins In the brain (hepatic encephalopathy)

A liver damaged by fibrosis will not be able to filter toxins from the. blood as well as a healthy liver (Runge, 2014).These toxins can build up in the brain, causing confusion and difficulty concentrating. Over time, hepatic encephalopathy can progress to unresponsiveness or coma (Forsgren et al., 2015).

2.4.7 - Jaundice

Jaundice occurs when a diseased liver can't remove enough bilirubin, a blood waste product, from your blood. Jaundice causes yellowing of the skin and the whites of the eyes and cloudy urine (O, 2008)

1.3 -Diagnosis of liver fibrosis disease

Like any other disease, it requires several important stages in its diagnosis which are family and clinical history and laboratory tests.

1.3.1-Clinical and family history: physical examination:

The doctor may ask you about your symptoms, your health, and your family's health history (Wallace, 2008). He or she may look for some physical telltale signs of fibrosis, such as: Flatulence، Liver size, sometimes enlarged, Redness in the palms of the hands، Yellowing of the skin or eyes، Prominence of red blood vessels on the skin (kipper,2013).

1.3.2-blood tests: Liver function tests It can show abnormal levels of liver enzymes, which may be a sign of liver damage(Beatriz, 2017).The doctor may suspect that you have cirrhosis if there is a decrease in the levels of blood

proteins and an increase in the levels of liver enzymes, which are:

1-ALT Enzyme: It is one of the liver function tests, as the ALT analysis may be useful in early detection of liver disease, as the alanine aminotransferase enzyme, which is produced in the liver, is measured, and in the event that the liver is damaged, this enzyme is secreted into the bloodstream, and it may indicate High levels of this enzyme in the blood indicate a problem with the liver even before signs and symptoms of the disease appear (Almpains et al., 2016).

2- AST Enzyme: Is used in laboratory tests to detect the presence of health problems and disorders in the liver, as it is based on the liver producing the (AST) enzyme in normal amounts in small quantities and within the normal limit, but when the liver cells are exposed to damage or health disorders based on secretion enzyme (AST) in large quantities exceedingthe normal limit (Karanjia&Crossy, 2016) .

3- ALP Enzyme: analysis is part of a group of routine liver tests called Liver function tests, and the doctor requests it when he suspects that there are symptoms indicating liver disease, and the values are high when he has liver disease (Seki et al., 2015).

4- GGT Enzyme: If liver damage is suspected, especially if you drink alcohol, this test is the most sensitive enzyme indicator currently available, used to detect liver damage(Tacke,2010).

5-Albumin protein test: It is one of the proteins that are manufactured in the liver, and measuring its levels contributes to determining the efficiency of manufacturing the proteins that the body needs in it. Its decrease indicates liver damage (Baloghe et al., 2016)

6-Bilirubin test: Liver function can be evaluated through a bilirubin test, and bilirubin is the yellow substance resulting from the body's breakdown of red blood cells (Aghemo, 2013). It is worth noting that this test measures the level of both total bilirubin and direct bilirubin, and liver disease may result in an increase in bilirubin levels (Paradis et al., 2013).

1.3.3- liver biopsy:

Liver biopsy is done either through a needle through the skin or through a vein, and it can be taken directly during abdominal surger then the liver sample is then examined under a microscope (Lencioni, 2012). A liver biopsy can diagnose fibrosis when other test reports are uncertain. A biopsy may show the cause of you. Sometimes your doctor may find that something other than fibrosis has caused your liver to become damaged or enlarged (Xu et al., 2016).

1.3.4-Imaging tests:

Imaging tests can show the size, shape, texture, and stiffness of the liver. Also, measuring the stiffness of the liver can show scarring (who, 2000). A specialist can place sclerosis measures to see if scarring is getting better or worse. Imaging tests can also show how much fat is in the liver (Poobalano, 2016) . A doctor may use one or more From the following imaging tests:

1-Magnetic resonance imaging of the liver MRI of the liver is a harmless examination that does not require surgery and gives a complete idea of the condition of the liver tissue by using magnetic currents and radio waves to create detailed images inside the liver or the body in general and display them on a computer (Wong, 2015). MRI of the liver makes cross-sectional images of the tissue The internal procedure of the liver, which allows doctors to examine the liver and the changes and diseases inside it without making any incision or wound to the patient (Lencioni et al., 2014).

2-Ultrasound imaging of the liver is a safe and harmless method for the patient and gives important results and information to the doctor (Gines, 1987). It helps the doctor to clearly see the liver tissue and blood movement in the veins.The doctor may ask the patient to do this test if there are abnormal values for the levels of liver enzymes (Bert, 2016).

3-CT Scan is defined as a method of imaging the body that uses X-rays and computer technology to create detailed images (Martinez et al., 2011). CT scan of the liver gives clearer and more detailed images of the liver compared to regular X-ray imaging of the abdomen.

Therefore, it provides more information for diagnosing liver disease (Tannapfel, 2012).

2.3- Treatment of liver fibrosis

Medicinal and non-pharmacological treatment of fibrosis depends on the cause of the problem. Fibrosis Is not considered a stand-alone disease, but rather a symptom of other liver diseases, such as chronic hepatitis, alcoholic liver disease, and others (Sporea, 2010).

Therefore, when treating fibrosis , the focus is on Identifying the cause and Its treatment to stop or slow the process of fibrosis , that Is, to prevent the progression of the disease and the occurrence of complications (Abdollahi et al., 2015).Several medications are available to treat fibrosis , including the following, according to the cause of fibrosis :

2.3.1-Antivirals

Used to treat chronic viral hepatitis, such as ribavirin, interferon-alpha, and lamivudine (Bedossa, 2003).

2.3.2- Medications that stimulate the immune system

Such as the immunotherapy interferon-alpha, and alpha-tocopherol, which is a form of vitamin E. These medications are used to treat hepatitis C virus infection (Rufat, 2000).

2.3.3- A group of drugs known as ACE inhibitors

Including lisinopril and ramipril, are used in cases of chronic hepatitis (Batts et al.,1995).

2.3.4- Medicines to treat metal poisoning

Used in cases of iron overload in the body, which causes damage to liver cells, and an example of them is deferoxamine (Wai, 2003).

2.3.5- Chelation therapy

Means the use of drugs that remove minerals, in the event that liver fibrosis is caused by hemochromatosis, which means an increase in the level of iron, or Wilson's disease (Bedossa, 1996).

2.3.6- Liver transplant

It is a treatment for advanced liver cirrhosis. If the patient reaches the stage of liver cirrhosis and his cirrhosis has not been previously treated, he will have to undergo a liver transplant, which is one of the most common organ transplant operations (Ishak et al., 1995).

The treatment in the liver transplant process requires part of the donor's liver and not the entire liver. The remaining part will replace the part that was taken. Also, in the transplant patient, the part of the liver that has been transplanted will also grow in a compensatory manner to suffice his needs, which is the advantage of the liver over the rest of the body's organs (Hui, 2007).

3.3- Recomme Dation for Patient With The liver Fibrosis

1-Refrain from alcoholic beverages so as not to increase the incidence of fibrosis

2-In the event that it is confirmed that there is cirrhosis in the liver, the doctor must be followed up and the appropriate treatment should be taken for the conditions.

3-Wash hands frequently and take vaccinations for pneumonia, influenza, and hepatitis A and B.

4- Eating more fresh vegetables and fruits.

5-Avoid eating raw seafood.

6- Eat a diet low in fat and sodium, because the excess amount of salt in the body can lead to fibrosis of the liver and fluid retention in the body.

7- Wear a protective mask to avoid inhaling toxic substances.

8-Avoid using any kind of recreational drug.

9-Do not take any medications without a doctor's prescription.

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