بسم الله الرحمن الرحيم

**Sudan University of Sciences and Technology**

**College of Graduated Studies**

# A Study of Non Alcoholic Fatty Liver Disease and its Associated Risk Factors in Sudanese using Computed Tomography

# دراسة مرض الكبد الدهنية غير الكحولية وعوامل الخطر المرتبطة بها لدى السودانيين باستخدام الأشعة المقطعية المحوسبة

***AThesis submitted in fulfillment of the requirements for the Ph.D degree in Diagnostic Radiologic Technology***

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# آيـــــــــــة

# Abstract

The study of Non Alcoholic Fatty Liver Disease (NAFLD) and identifying its risk factors would be critically important due to spread of these diseases worldwide. But, the prevalence of NAFLD in Sudan remains uncertain, due to lack of studies and there are no national surveys have been conducted. This study was aimed to determine the prevalence of and factors associated with NAFLD in Sudanese populations using unenhanced CT scans as diagnostic tools. About 292 adult participants, aged 18 ~ 88 years old, were enrolled in this study .The participants were selected from patients that scheduled to undergo abdominal CT scan. The following information was collected for each patient including sex, age, height; body weight (WT), BMI, Waist circumference, medical history, and abdominal CT scan. The participants those who had a history of alcohol consumption, hepatic mass and liver cirrhosis, were excluded. Liver-to-spleen ratio (L/S) <1.0 was used to diagnose the presence of liver fat. The overall prevalence of non alcoholic fatty liver in this study was (43) 14.7% using L/S ratio <1.0. There was no prevalent difference between males and females. Non alcoholic fatty liver in our population was 24.2% in obese participants (BMI >30), 20.4% and 10.3% in hypertensive and diabetic participants, respectively. Patient with NAFLD were older than Non-NAFLD (P=0.022) and there is significant relation between body weight and NAFLD (p=.031).

Non-alcoholic fatty liver disease is present in Sudan but is less than what one would expect based on American and European studies. Age and body weight are the major associated risk factors of NAFLD in Sudanese population. Unenhanced CT scan can be used as screening and diagnostic tools for NAFLD .And the disadvantage of the high radiation dose of the CT can be avoided by making a Single slice, low dose CT scan.

# الملخص


دراسة مرض الكبد الدهني غير الكحولي وتحديد عوامل الخطر المرتبطة به ذو اهمية بالغة وذلك بسبب انتشار هذا المرض في جميع أنحاء العالم. ولكن ، لا يزال انتشار مرض الكبد الدهني غير الكحولي في السودان غير مؤكد بالاضافة الى ان عوامل الخطر المرتبطة به غير معروفة لدى السودانيين ويعزى ذلك لنقص الدراسات البحثية فى هذا المجال بالاضافة الى انه لم يتم إجراء أي مسوحات وطنية لتحديد نسبة المرض ومعرفة عوامل الخطر فى السودان . أجريت هذه الدراسة لتحديد مدى انتشار مرض الكبد الدهني غير الكحولي لدى السودانيين وتحديد عوامل الخطر المرتبطة بـه وذلك باستخدام التصوير المقطعي المحوسب بدون صبغة كاداة تشخيصية للمرض . شارك فى هذه الدراسة حوالى 292 مشارك من البالغين ، تتراوح أعمارهم بين 18 و 88 سنة ، في هذه الدراسة. تم اختيار المشاركين من المرضى الذين كان من المقرر أن يخضعوا لفحص اشعة مقطعية محوسبة لمنطقة البطن والمناطق المجاورة . تم جمع المعلومات لكل مريض شملت البيانات التالية: الجنس ,العمر ,الطول,وزن الجسم ، مؤشر كتلة الجسم ، محيط الخصر ، والتاريخ الطبي بالاضافة لفحص الاشعة المقطعية . تم استبعاد المرضى الذين لديهم تاريخ من شرب الكحول , ومن لديهم اورام فى الكبد اوتليف الكبد. تم استخدام نسبة الكبد إلى الطحال اقل من واحد صحيح (L / S) <1.0 لتشخيص وجود الدهون في الكبد. كان الانتشار العام للكبد الدهني غير الكحولي في هذه الدراسة (43) 14.7٪ باستخدام نسبة .L / S <1.0 لم يكن هناك فرق فى انتشار المرض بين الذكور والإناث. كان الكبد الدهني غير الكحولي في السودانيين 24.2 ٪ في المشاركين الذين يعانون من السمنة(كتلة الجسم اكبر من 30) ، 20.4 ٪ و 10.3 ٪ في المشاركين الذين يعانون من ارتفاع ضغط الدم والسكري ، على التوالي. وجد ان المصابين بمرض الكبد الدهني غير الكحولي فى الدراسة اكبر سنا مقارنة بغير المصابين (P = 0.022) . بالاضافة الى ان الدراسة وجدت ان عوامل الخطر المرتبطة بمرض الكبد الدهنى غير الكحولى هما العمر ووزن الجسم .

خلصت الدراسة الى ان نسبة المصابين بمرض الكبد الدهني غير الكحولي في السودان اقل من النسبة العالمية المسجلة فى الدراسات الأمريكية والأوروبية.كما ان العمر ووزن الجسم هما عوامل الخطر الرئيسية المرتبطة بمرض الكبد الدهني غير الكحولي في السودانيين. يمكن استخدام التصزير المقطعى المحوسب بدون صبغة كأداة فحص وتشخيص لـمرض الكبد الدهني غير الكحولي ويمكن تجنب عيوب الجرعة الإشعاعية العالية من التصوير المقطعي المحوسب عن طريق عمل شريحة واحدة بالاضافة الى التصوير باستخدام جرعة منخفضة من الأشعة المقطعية.

# DEDICATION

To……..

My family

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My teachers

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My friends

**********

My colleagues

**********

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# List of Abbreviations

| | |
|---|---|
| **99mTc** | Technetium-99m |
| **ADC** | Analog-to-digital converter |
| **BH** | Body height |
| **BW** | Body weight |
| **CT** | Computed tomography |
| **DAS** | Data-acquisition system |
| **DM** | Diabetic mellitus |
| **EUS** | Endoscopic ultrasonography |
| **FNH** | Focal nodular hyperplasia |
| **HCC** | Hepatocellular carcinoma |
| **HT** | Hypertension |
| **Hu** | Hounsfield units |
| **L/S** | Liver-to-spleen ratio |
| **LAI** | liver attenuation index |
| **MDCT** | Multidetector CT |
| **MRCP** | Cholangiopancreatography |
| **MRI** | Magnetic resonance imaging |
| **MS** | Metabolic Syndrome |
| **NAFLD** | Non alcoholic Fatty liver disease |
| **NASH** | Non alcoholic steato hepatitis |
| **NBM** | Nil by mouth |
| **OP** | opposed phase |
| **SD** | Standard deviation |
| **SPSS** | Statistical Package for the Social Sciences |
| **TE** | Time to echo |
| **US** | Ultrasound |
| **wl** | window level |
| **ww** | window width |

# Chapter One

## 1.1 Introduction:

Non alcoholic Fatty liver disease ( NAFLD) is defined as the deposition of lipid , especially triglyceride in hepatocytes exceeding the normal range of 5% of liver wet weight, in the absence of other etiology of hepatic damage including hepatitis viruses, alcoholic consumption and metabolic diseases (Neuschwander & Caldwell, 2003).The term NAFLD refer to spectrum of hepatic disorders ranging from simple or bland fatty liver (NAFL: Non alcoholic Fatty liver) in which no inflammatory changes are seen except for macrovesicular or microvesicular steatosis to non alcoholic steato hepatitis (NASH ), which is characterized by an inflammatory reaction with hepatocystic injury , such as ballonnnic degeneration and necroapoptosis with or without fibrosis (Chalasani et al., 2012). It is reported that almost 10% ~ 20% of individuals with NAFLD have NASH, 10% ~ 15% of individuals with NASH progress to cirrhosis (Pasumarthy and Srour, 2010). In patients with cirrhotic NASH, HCC and liver failure are the main causes of morbidity and mortality (5-year cumulative HCC development rate 11.3%, 5-year Survival rate 75.2%, respectively) (Hashimoto & Tokushige, 2011).

NAFLD often has no symptoms and in the majority of patients, NAFLD is associated with metabolic risk factors such as obesity, diabetes mellitus, and dyslipidemia (Chalasani et al., 2012). NAFLD currently affects 20–30% of the general population in affluent industrialized Western countries (Angulo, 2002) (Bellentani, et al., 2010) .In china, the prevalence was 15.0% (Jian, 2013). In the Kingdom of Saudi Arabia, a prevalence of 7–10% has been documented in the general population (Al-hamoudi et al., 2012).

In Khartoum, Sudan according to study used the ultrasound as noninvasive measurement tool, the overall prevalence of NAFLD range between 15%to 20% (Elkhader & Mahmoud, 2013)( Almobarak et al. ,2014)

The diagnosis of NAFLD needs confirmation of hepatic steatosis based on either imaging studies or liver biopsy, Histologic examination (liver biopsy) is accurate in detection of hepatic fat content, but it is invasive and time consuming, and sampling errors can occur. Noninvasive methods for diagnosing fatty liver include sonography, MRI, and CT. Among these methods, sonography is the easiest, but it is only a qualitative assessment of the fatty liver (Levenson et al., 1991) in addition it is operator dependent and subject to significant intra- and interobserver variability (Strauss et al., 2007). MRI is probably the best method for detecting a small amount of fatty infiltration, but it is relatively expensive .CT allows for a more quantitative assessment with measurement of liver attenuation in Hounsfield units (HUs) compared to U/S. It appears that non contrast CT scanning is more useful for detecting steatosis than contrast enhanced scans (Jacobs et al., 1998; Piekarski et al., 1980)

The Hounsfield Unit (HU) attenuation of liver on CT scans is usually higher than the spleen; when this ratio is reversed, this can be used to diagnose the presence of liver fat (Jacobs et al., 1998). Liver-to-spleen ratio (L/S) <1.0 can be used effectively to diagnose the presence of liver fat (Kawata et al., 1984). Studies have also shown liver HU attenuation <40 HU to reliably represent >30% of liver fat content (Kodama et al., 2007 ; Park et al., 2006).Measurement of attenuation of liver only on unenhanced CT scans is best for prediction of pathologic fat content (Kodama et al., 2007).

## 1.2 The problem of the study:

Study of NAFLD and identify its risk factors would be critically important due to spread of these diseases worldwide. But, the prevalence of NAFLD in Sudan remains uncertain, due to lack of studies and there are no national surveys have been conducted. This study conducted to study NAFLD and its associated risk factors in Sudanese populations using unenhanced CT scans as diagnostic tool.

## 1.3 The objectives:

### 1.3.1 General objectives:

To study non alcoholic fatty liver disease among Sudanese and determine it associated risk factors of using computerize tomography.

### 1.3.2 Specific objectives:

- To determine the characteristic of NAFLD subject among Sudanese.
- To correlate between the age and non alcoholic fatty liver.
- To find out the relation between obesity and the disease
- To assess the relation between gender and non alcoholic fatty liver.
- To correlate hypertension to non alcoholic fatty liver.
- To correlate diabetes mellitus to non alcoholic fatty liver
- To determine the relation between the disease and ethnicity in Sudan.

## 1.4 Thesis outline:

This study is concerned with evaluation of prevalence and associated factors of Non alcoholic fatty liver disease in Sudanese population using unenhanced CT images, it falls into five chapters. Chapter one is an introduction, which include preparation of the problem of study and background about the Non alcoholic fatty

liver disease as well as statement of the problem and study objectives. While Chapter two include a comprehensive scholarly literature reviews (anatomy, physiology, pathology, equipment, technique) and the previous studies. Chapter three deals with the methodology, where it provides an outline of material and methods used to acquire the data in this study as well as the method of analysis approach. While the results presented in chapter four, and finally Chapter five include discussion of results, conclusion and recommendations followed by references and appendices.

# Chapter Two

# Theoretical Background and Literature review

## 2.1 Theoretical Background:

### 2.1.1Anatomy of the Liver:

The liver is the largest gland in the body, situated in the upper and right parts of the abdominal cavity, occupying almost the whole of the right hypochondrium, the greater part of the epigastrium and not uncommonly extending into the left hypochondrium. In the male it weighs from 1.4 to 1.6 kilogm , in the female from 1.2 to 1.4 kilogm (Gray, 1918).

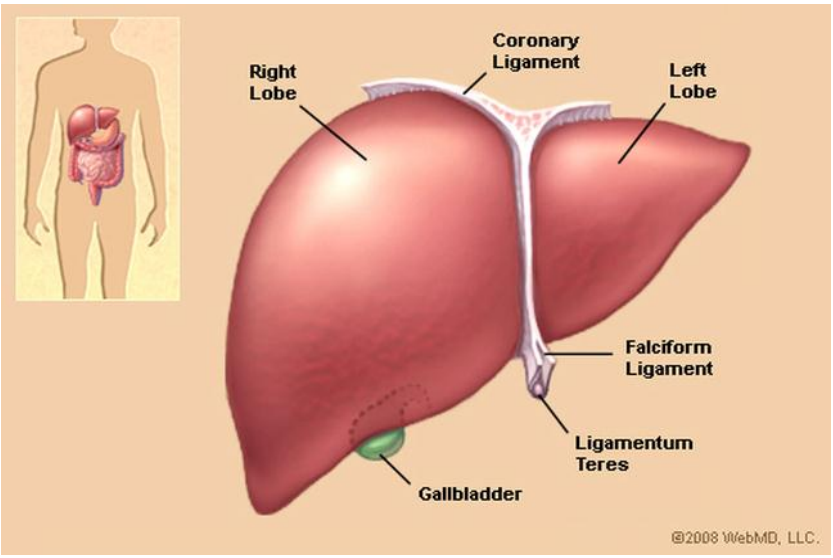



Figure (2.3): Show the Anatomy of the liver (http://www.webmd.com/digestive-disorders/picture-of-the-liver, 2006)

#### 2.1.1.1 Gross Anatomy:

The liver has four lobes called the right, left, quadrate, and caudate lobes. From an anterior view, we see only a large right lobe and smaller left lobe. They are separated from each other by the falciform ligament, a sheet of mesentery that suspends the liver from the diaphragm and anterior abdominal wall. From the

inferior view, we also see a squarish quadrate lobe next to the gallbladder and a tail-like caudate lobe posterior to that. An irregular opening between these lobes, the porta hepatis, is a point of entry for the hepatic portal vein and proper hepatic artery and a point of exit for the bile passages, all of which travel in the lesser omentum(Saladin, 2010).

The gallbladder adheres to a depression on the inferior surface of the liver between the right and quadrate lobes. The posterior aspect of the liver has a deep groove (sulcus) that accommodates the inferior vena cava. The superior surface has a bare area where it is attached to the diaphragm. The rest of the liver is covered by a serosa (Saladin, 2010).

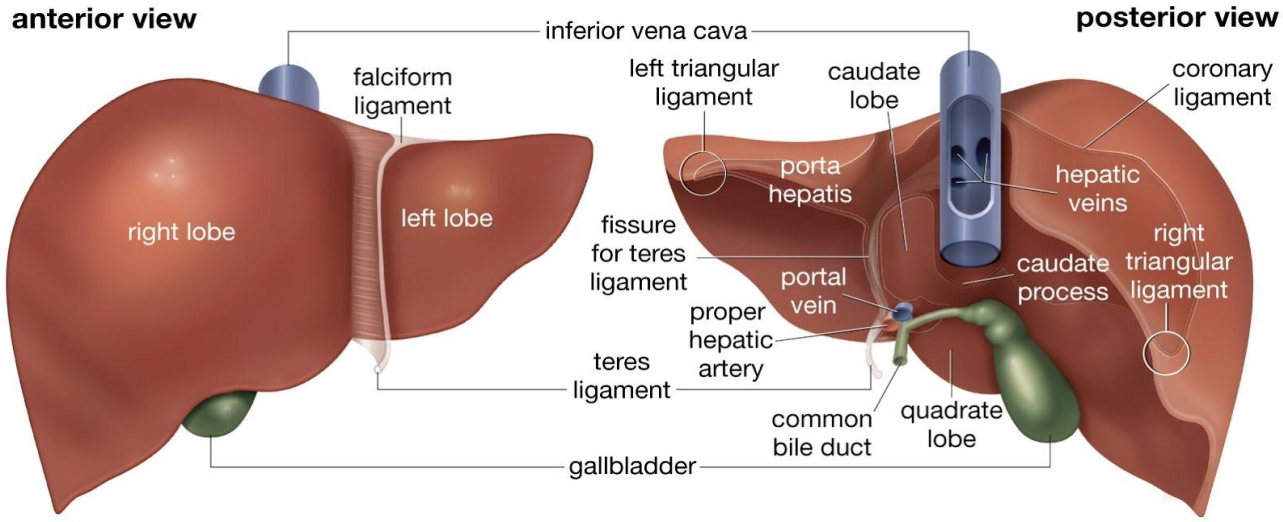



Figure (2.2): Demonstrate the Anterior and posterior views of liver https://sites.google.com/site/odettessonographyportfolio/dms-121---cross-sectional-anatomy/liver-anaotmy-normal

**2.1.1.1.1Surfaces:**

The liver possesses three surfaces, superior, inferior and posterior. (Gray, 1918)

**The superior surface,** is convex, and fits under the vault of the diaphragm which in front separates it on the right from the sixth to the tenth ribs and their cartilages,

and on the left from the seventh and eighth costal cartilages. Its middle part lies behind the xiphoid process, and, in the angle between the diverging rib cartilage of opposite sides, is in contact with the abdominal wall. Behind this the diaphragm separates the liver from the lower part of the lungs and pleura, the heart and pericardium and the right costal arches from the seventh to the eleventh inclusive. It is completely covered by peritoneum except along the line of attachment of the falciform ligament (Gray, 1918).

**The inferior surface (visceral surface),** is uneven, concave, directed downward, backward, and to the left, and is in relation with the stomach and duodenum, the right colic flexure, the right kidney and suprarenal gland. The surface is almost completely invested by peritoneum; except where the gall-bladder is attached to the liver, and at the porta hepatis. The inferior surface of the left lobe presents behind and to the left the gastric impression. The under surface of the right lobe is divided into two unequal portions by the fossa for the gall-bladder; the portion to the left, is the quadrate lobe, and is in relation with the pyloric end of the stomach, the superior portion of the duodenum, and the transverse colon. The portion of the under surface of the right lobe to the right of the fossa for the gall-bladder presents two impressions the colic impression, and the renal impression (Gray, 1918).

**The posterior surface** is rounded and broad behind the right lobe, but narrow on the left. Over a large part it is not covered by peritoneum and contact with the diaphragm. It is marked off from the upper surface by the line of reflection of the upper layer of the coronary ligament, and from the under surface by the line of reflection of the lower layer of the coronary ligament. (Gray, 1918)

### 2.1.1.1.2 Peritoneal Ligaments of the Liver:

The **falciform ligament,** which is a two-layered fold of the peritoneum, ascends from the umbilicus to the liver. It has free margin that contains the ligamentum teres, the remains of the umbilical vein. The right layer forms the upper layer of the

coronary ligament; the left layer forms the upper layer of the left triangular ligament. The right extremity of the coronary ligament is known as the right triangular ligament of the liver. It should be noted that the peritoneal layers forming the coronary ligament are widely separated, leaving an area of liver devoid of peritoneum. Such an area is referred to as a bare area of the liver (Snell, 2011).

The ligamentum teres passes into a fissure on the visceral surface of the liver and joins the left branch of the portal vein in the porta hepatis.The ligamentum venosum, a fibrous band that is the remains of the ductus venosus, is attached to the left branch of the portal vein and ascends in a fissure on the visceral surface of the liver to be attached above to the inferior vena cava .The lesser omentum arises from the edges of the porta hepatis and the fissure for the ligamentum venosum and passes down to the lesser curvature of the stomach .(Snell, 2011)

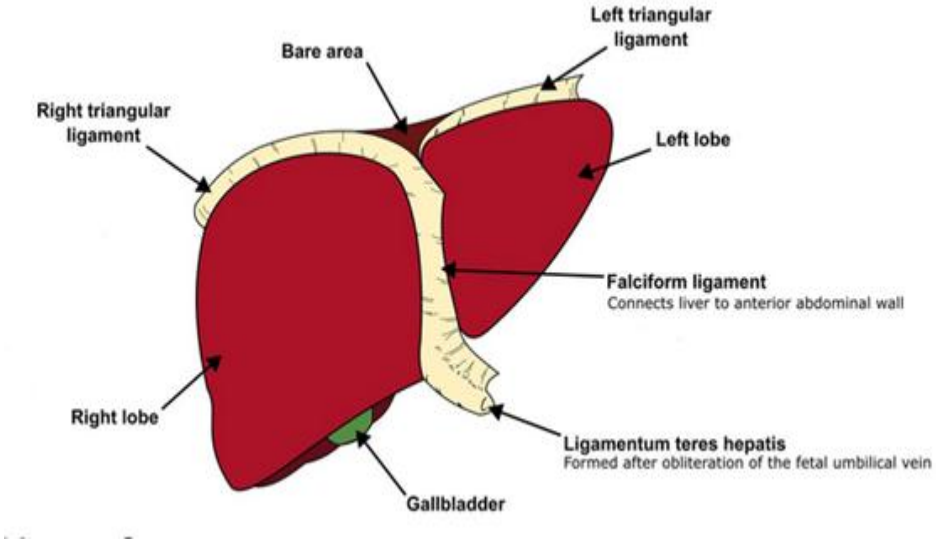



Figure (2.4): Ligaments of the liver
(https://upload.medbullets.com/topic/10003/images/lig%20of%20liver.jpg)

### 2.1.1.2 Segmental Anatomy:

Division of the liver at the falciform ligament and umbilical fissure does not correspond to division based on branch points in the vascular supply. Surgical

imperative has led to the search for functional divisions within the liver. The anatomic studies of Rex and others demonstrated that the liver can be divided on a different plane into right and left livers (or hemilivers), each with its own blood supply and duct drainage. The right hemiliver comprises 50–70% of the liver mass. The liver can be further divided into a total of eight segments based on the vascular or bile duct distribution. The segmental nomenclature devised by Couinaud has received the widest acceptance. This classification was based on the divisions of the portal veins. However, the branching of the PVs to the left lobe is irregular because of the entry of the umbilical vein, making it desirable to adopt a nomenclature based on the divisions of the arteries or ducts, as suggested by Strasberg. This can be done without modification of the segments defined by. Couinaud and rationalizes the diverse nomenclature used in different parts of the world. Most hepatic resections can be achieved by division either on the Cantlie line (between the gallbladder and vena cava) or near the falciform ligament. Surgical dissection along the planes between segments is relatively bloodless. Because the segments do not have surface landmarks, small resections are usually performed without attempting to identify the segmental boundaries. The segments vary greatly in size and shape among individuals, so that each operation is empirical and may be based on ultrasonography (Schiff, Sorrell, & Maddrey, 2007).

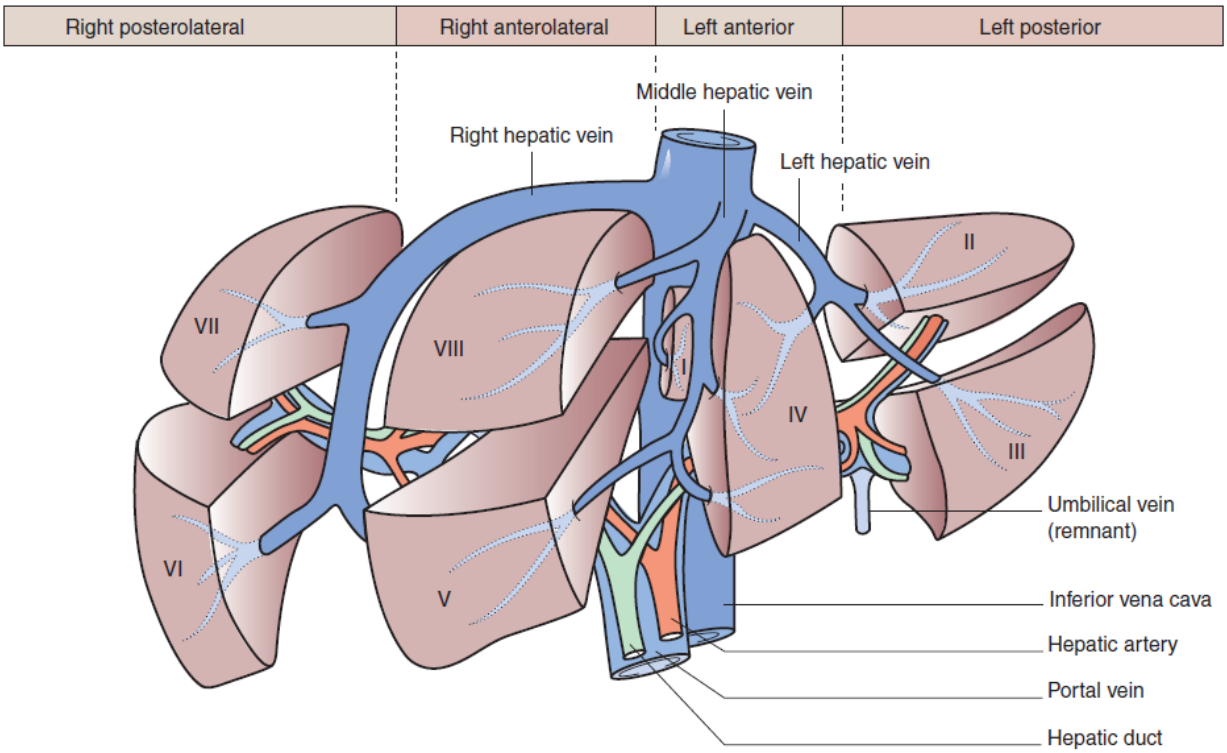



Figure (2.4): Demonstrate the Segmental anatomy of the liver (Schiff et al., 2007).

### 2.1.1.3 Histology of Liver:

#### 2.1.3.1. Hepatocytes:

Hepatocytes are the major functional cells of the liver and perform a wide array of metabolic, secretory, and endocrine functions. These are specialized epithelial cells with 5 to 12 sides that make up about 80% of the volume of the liver. Hepatocytes form complex three-dimensional arrangements called hepatic laminae . The hepatic laminae are plates of hepatocytes one cell thick bordered on either side by the endothelial-lined vascular spaces called hepatic sinusoids. The hepatic laminae are highly branched, irregular structures. Grooves in the cell membranes between neighboring hepatocytes provide spaces for canaliculi into which the hepatocytes secrete bile. (Tortora & Derrickson, 2008)

**2.1.1.3.2. Bile Canaliculi:**

These are small ducts between hepatocytes that collect bile produced by the hepatocytes. From bile canaliculi, bile passes into bile ductules and then bile ducts. The bile ducts merge and eventually form the larger right and left hepatic ducts, which unite and exit the liver as the common hepatic duct. The common hepatic duct joins the cystic duct (cystic = bladder) from the gallbladder to form the common bile duct. From here, bile enters the small intestine to participate in digestion. (Tortora at el., 2008)

**2.1.1.3.3**. **Hepatic Sinusoids**:

These are highly permeable blood capillaries between rows of hepatocytes that receive oxygenated blood from branches of the hepatic artery and nutrient-rich de-oxygenated blood from branches of the hepatic portal vein. Recall that the hepatic portal vein brings venous blood from the gastrointestinal organs and spleen into the liver. Hepatic sinusoids converge and deliver blood into a central vein. From central veins the blood flows into the hepatic veins, which drain into the inferior vena cava. In contrast to blood, which flows toward a central vein, bile flows in the opposite direction. Also present in the hepatic sinusoids are fixed phagocytes called stellate reticuloendothelial (Kupffer) cells, which destroy worn-out white and red blood cells, bacteria, and other foreign matter in the venous blood draining from the gastrointestinal tract. (Tortora at el., 2008)

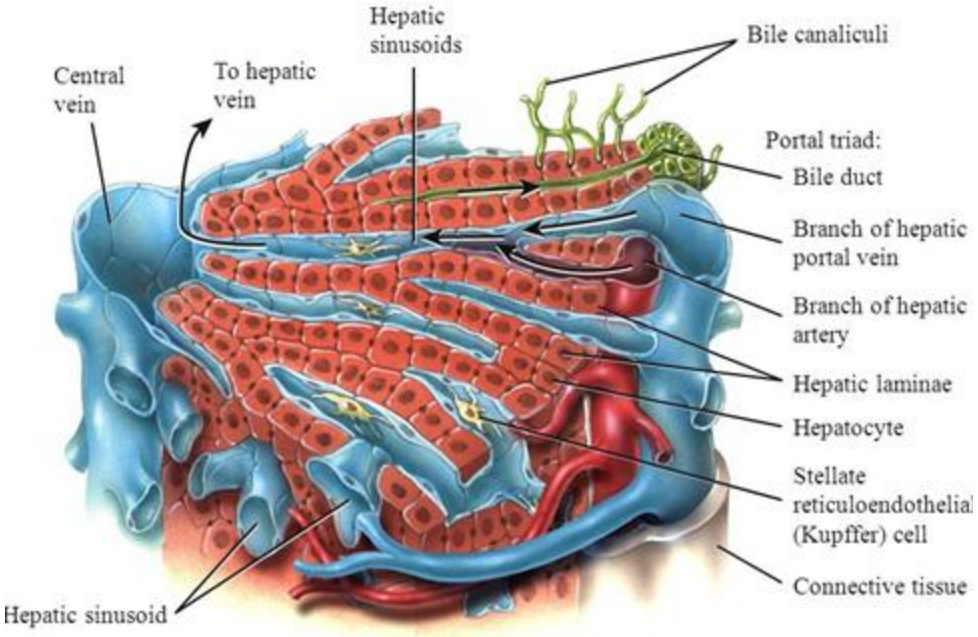



Figure (2.5): Show the histological components of liver

http://slideplayer.com/slide/5258442/16/images/33/(b)+Details+of+histological+components+of+liver.jpg

**2.1.1.4 Blood Supply:**

The liver has a dual blood supply from the portal vein and the hepatic artery. Approximately 25% of the liver's blood supply is supplied by the hepatic artery, which originates from the celiac axis. The portal vein provides 75% of the liver's blood supply and returns venous blood from the gastrointestinal tract and spleen. Both vessels enter the liver through the portahepatis (liver hilum). Inside the hilum, the portal vein and hepatic artery divide into the right and left branches supplying their respective lobes before being distributed to the segments and flows into the sinusoids via the portal tracts. Blood leaves the sinusoids and then enters tributaries of the hepatic veins (middle, right and left) before entering the inferior vena cava. The caudate lobe receives a separate blood supply from the portal vein and hepatic

artery while its hepatic vein drains directly into the inferior vena cava (Josh & Brind, 2015)

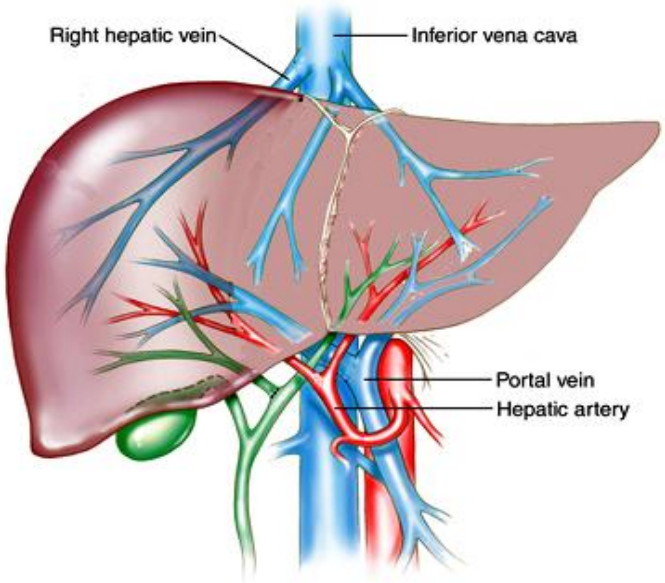



Figure (2.6): Describe the Blood supply of the liver

https://academic.amc.edu/martino/grossanatomy/site/Medical/CASES/GI/pop%20ups/pop%20up%20images/Liver%20blood%20flow.jpg

### 2.1.1.5 Lymph Drainage and Nerve Supply:

The liver produces a large amount of lymph—about one third to one half of all body lymph. The lymph vessels leave the liver and enter several lymph nodes in the portahepatis. The efferent vessels pass to the celiac nodes. A few vessels pass from the bare area of the liver through the diaphragm to the posterior mediastinal lymph nodes. While it get the Sympathetic and parasympathetic nerves form the celiac plexus. The anterior vagal trunk gives rise to a large hepatic branch, which passes directly to the liver. (Snell, 2011)

## 2.1.2 Physiology of the Liver:

The liver is a remarkable organ, and only the brain is capable of a greater variety of functions. The liver cells (hepatocytes) produce many enzymes that catalyze many different chemical reactions. These reactions are the functions of the liver. As blood flows through the sinusoids (capillaries) of the liver materials are removed by the liver cells, and the products of the liver cells are secreted into the blood. (Scanlon & Sanders, 2015)

### 2.1.2.1. Carbohydrate Metabolism:

The liver regulates the blood glucose level. Excess glucose is converted to glycogen (glycogenesis) when blood glucose is high; the hormones insulin and cortisol facilitate this process. During hypoglycemia or stress situations, glycogen is converted back to glucose (glycogenolysis) to raise the blood glucose level. Epinephrine and glucagon are the hormones that facilitate this process. The liver also changes other monosaccharides to glucose. Fructose and galactose, for example, are end products of the digestion of sucrose and lactose. Because most cells, however, cannot readily use fructose and galactose as energy sources, they are converted by the liver to glucose, which is easily used by cells. (Scanlon et al., 2015)

### 2.1.2.2. Amino Acid Metabolism:

The liver regulates blood levels of amino acids on the basis of tissue needs for protein synthesis. Of the 20 different amino acids needed for the production of human proteins, the liver is able to synthesize 12, called the non-essential amino acids. The other 8 amino acids, which the liver cannot synthesize, are called the essential amino acids.

All 20 amino acids are required in order to make body proteins. Excess amino acids, those not needed right away for protein synthesis, cannot be stored. However, they do serve another useful purpose. By the process of deamination,

which also occurs in the liver, the NH2 group is removed from an amino acid and the remaining carbon chain may be converted to a simple carbohydrate molecule or to fat. Thus, excess amino acids are utilized for energy production: either for immediate energy or for the potential energy stored as fat in adipose tissue.

The NH2 groups that were detached from the original amino acids are combined to form urea, a waste product that will be removed from the blood by the kidneys and excreted in urine. (Scanlon et al., 2015)

#### 2.1.2.3 Lipid Metabolism:

The liver forms lipoproteins, which are molecules of lipids and proteins, for the transport of fats in the blood to other tissues. The liver also synthesizes cholesterol and excretes excess cholesterol into bile to be eliminated in feces. Fatty acids are a potential source of energy, but in order to be used in cell respiration they must be broken down to smaller molecules. In the process of beta-oxidation, the long carbon chains of fatty acids are split into two-carbon molecules called acetyl groups, which are simple carbohydrates. These acetyl groups may be used by the liver cells to produce ATP or may be combined to form ketones to be transported in the blood to other cells. These other cells then use the ketones to produce ATP in cell respiration. (Scanlon et al., 2015)

#### 2.1.2.4 Synthesis of Plasma Proteins:

The liver synthesizes many of the proteins that circulate in the blood. Albumin, the most abundant plasma protein, helps maintain blood volume by pulling tissue fluid into capillaries. The clotting factors are also produced by the liver. These include prothrombin, fibrinogen, and Factor 8, which circulate in the blood until needed in the chemical clotting mechanism. The liver also synthesizes alpha and beta globulins, which are proteins that serve as carriers for other molecules, such as fats, in the blood. (Scanlon et al., 2015)

### 2.1.2.5 Formation of bilirubin:

The liver contains fixed macrophages that phagocytize old red blood cells (RBCs). Bilirubin is then formed from the heme portion of the hemoglobin. The liver also removes from the blood the bilirubin formed in the spleen and red bone marrow and excretes it into bile to be eliminated in feces. (Scanlon et al., 2015)

### 2.1.2.6 Phagocytosis by Kupffer cells:

The fixed macrophages of the liver are called **Kupffer cells** (or stellate reticuloendothelial cells). Besides destroying old RBCs, Kupffer cells phagocytize pathogens or other foreign material that circulate through the liver. The bacteria that enter the blood with the water absorbed by the colon are carried to the liver by way of portal circulation. The Kupffer cells in the liver phagocytize and destroy these bacteria, removing them from the blood before the blood returns to the heart and are pumped to the lungs. (Scanlon et al., 2015)

### 2.1.2.7 Storage:

The liver stores the fat-soluble vitamins A, D, E, and K, as well as the water-soluble vitamin B12. Up to a 6- to 12-month supply of vitamins A and D may be stored, and beef or chicken liver is an excellent dietary source of these vitamins. Also stored by the liver are the minerals iron and copper. Which is part of some of the proteins needed for cell respiration and is part of some of the enzymes necessary for hemoglobin synthesis. (Scanlon et al., 2015)

### 2.1.2.8 Detoxification:

The liver is capable of synthesizing enzymes that will detoxify harmful substances, that is, change them to less harmful ones. Alcohol, for example, is changed to acetate, which is a two-carbon molecule (an acetyl group) that can be used in cell respiration. Medications are all potentially toxic, but the liver produces enzymes that break them down or change them. When given in a proper dosage, a medication exerts its therapeutic effect but is then changed to less active

substances that are usually excreted by the kidneys. An overdose of a drug means that there is too much of it for the liver to detoxify in a given time, and the drug will remain in the body with possibly harmful effects. This is why alcohol should never be consumed when taking medication. Ammonia is a toxic substance produced by the bacteria in the colon. Because it is soluble in water, some ammonia is absorbed into the blood, but it is carried first to the liver by portal circulation. The liver converts ammonia to urea, a less toxic substance which excreted by the kidneys. (Scanlon et al., 2015)

**2.1.2.9 Excocrine Function:**

The liver also has an exocrine function. About 500 mL of bile is secreted each day. Patients who have jaundice due to intra- or extrahepatic obstruction of the bile duct usually have raised blood levels of cholesterol and alkaline phosphatase. Bile is an alkaline solution containing bicarbonate (secreted by both hepatocytes and biliary duct cells) and aids in the neutralisation of acid chime entering the duodenum from the stomach. Two major primary bile acids are synthesised in the liver from cholesterol at the rate of 0.5 g/day (cholic acid and chenodeoxycholic acid). Secondary bile acids are produced within the gut by the action of bacteria on primary bile acids. Cholica cid is converted to deoxycholic acid and chenodeoxycholic acid to lithocholic acid. Bile is continuously secreted by hepatocytes into biliary canaliculi. Between meals contraction of the sphincter of Oddi causes bile to accumulate in the gallbladder where the bile salts are concentrated. The most important trigger for relaxation of the sphincter of Oddi and release of bile is return of bile salts to the liver from the splanchnic circulation. The majority of bile salts (90–95%) are reabsorbed from the small intestine, most from the terminal ileum (meaning that a large proportion remains throughout the small intestine to promote fat absorption). The remaining bile salts enter the colon where more are reabsorbed. Those lost in the stool are replaced by synthesis in the

liver. The total pool of bile salts (approx 2.5 g) is recycled up to six to eight times in a day. (Sargent, 2009)

### 2.1.3. Non-Alcoholic Fatty Liver Disease:

#### 2.1.3.1. Definition:

The term "non-alcoholic fatty liver disease" (NAFLD) refers to hepatic steatosis accounting for more than 5–10% of the total weight of the liver or macrosteatosis of the same extent, which is not caused by excessive consumption of alcohol (women ≤20 g/d, men ≤30 g/d) . The term NAFLD refers to a spectrum of hepatic disorders, ranging from simple or bland fatty liver (NAFL, non-alcoholic fatty liver)—in which no inflammatory changes are seen except for macrovesicular or microvesicular steatosis to non-alcoholic steatohepatitis (NASH), which is characterized by an inflammatory reaction with hepatocytic injury, such as balloonic degeneration and necroapoptosis with or without fibrosis. (Weib & Geier, 2014).

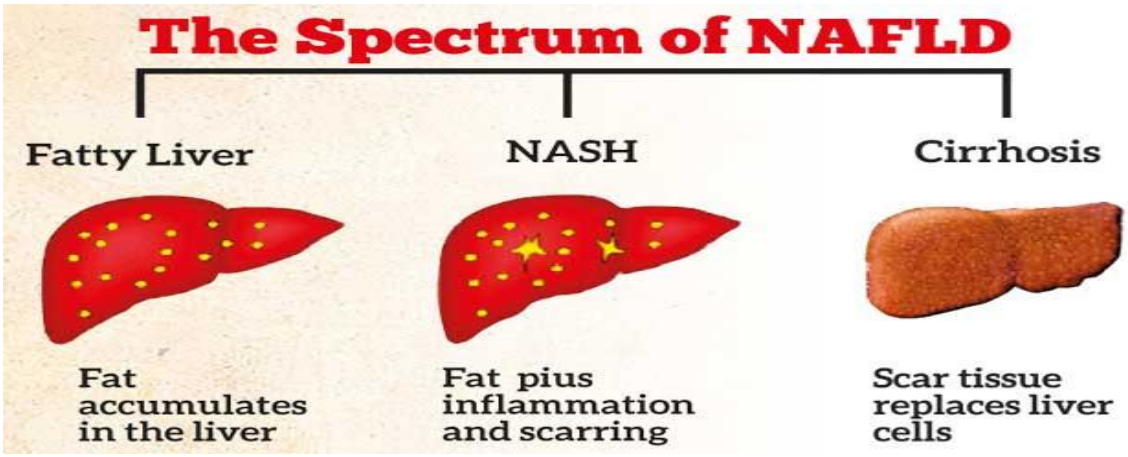



Figure (2.7): Show the spectrum of NAFLD

http://www.dailymirror.lk/110507/Preventing-non-alcoholic-fatty-liver

### 2.1.3. 2 Epidemiology:

In Europe, it is estimated 12–18% of the population have NAFLD, and of those 3–16% have NASH. The incidence of NAFLD is increasing and it is now the most

common cause of liver disease in Western populations and an increasingly common indication for liver transplantation. Risk factors for NASH include obesity, diabetes, metabolic syndrome, male sex, old age and ethnicity. (Josh & Brind, 2015)

### 2.1.3. 3 Pathophysiology:

NAFLD is increasingly recognised as the hepatic component of the multisystemic metabolic syndrome. In some cases, hepatic steatosis causes hepatocellular injury (ballooning of the hepatocytes and inflammatory infiltrate), leading to fibrosis, cirrhosis and ultimately HCC. However, why progression of the disease only occurs in a minority of patients with NAFLD remains unclear. A potential explanation is that progression occurs following a second liver injury ('second hit'), which is triggered by oxidative stress, mitochondrial abnormalities or changes hormones, such as adiponectin and leptin. Ultimately, this results in the activation of hepatic stellate cells, which produce collagen, leading to fibrosis and cirrhosis. (Josh et al., 2015)

### 2.1.3. 4 Prognosis:

Patients with NAFLD have a good prognosis. However, those with NASH have a 5–20% risk of progression to cirrhosis within 10 years. Overall mortality results from complications of advanced liver disease and cardiovascular manifestations of the underlying metabolic syndrome. Obesity and NAFLD are strongly associated with HCC; prevalence is estimated to be <0.5% in NAFLD and 2.8% in NASH (Josh et al., 2015)

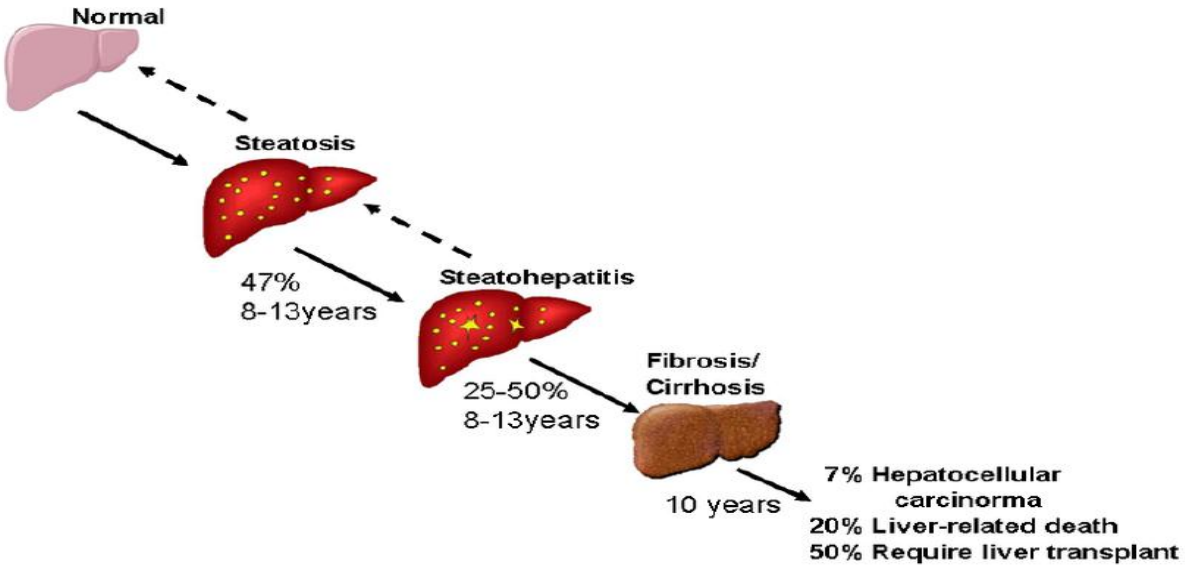



Figure (2.8): Show the prognosis of Non Alcoholic Fatty Liver Disease.

www.google.com

**2.1.3. 5 Symptoms:**

Most patients with NAFLD are asymptomatic. The disease is discovered incidentally during routine laboratory examination in subjects treated with hypolipidaemic drugs and during sonographic examination for suspected gallstone disease. The most common signs and symptoms are fatigue and right upper quadrant discomfort. During physical examination there are no pathognomic signs and the most common abnormalities are obesity and hepatomegaly, which has been reported in up to 50% of subjects. A smaller fraction of patients experience symptoms indicative of more serious liver disease such as ascites, jaundice and liver encephalopathy. (Neuschwander et al., 2003)

**2.1.3. 6 CT Criteria of Fatty Liver:**

**Fatty infiltration** lowers the CT attenuation of the involved liver parenchyma. The findings are most accurately assessed on non contrast CT. The attenuation of normal liver is at least 10 HU greater than that of the spleen. With fatty infiltration,the attenuation of the involved liver is at least 10 HU lower than that of

the spleen.Hepatic vessels course through areas of fatty infiltration unaltered. Fatty change is more difficult to judge on postcontrast CT because of the variability in scan timing and the fact that maximum liver enhancement is delayed compared to maximum spleen enhancement. CT attenuation below –40 HU is strong evidence of hepatic steatosis but excludes mild cases (Webb et al, 2014).

**2.1.3. 6.1 Diffuse Fatty Infiltration:**

In most cases of diffuse fatty infiltration, the entire liver is uniformly reduced in density. Vessels stand out in prominent relief but run their normal course through the liver without displacement or narrowing by a mass effect. The liver is usually enlarged, and the parenchyma is minimally enhanced. This pattern is the most common and is the easiest to recognize. In some cases the fatty infiltration is diffuse throughout the liver but is nonuniform and patchy in severity (Webb et al, 2014).

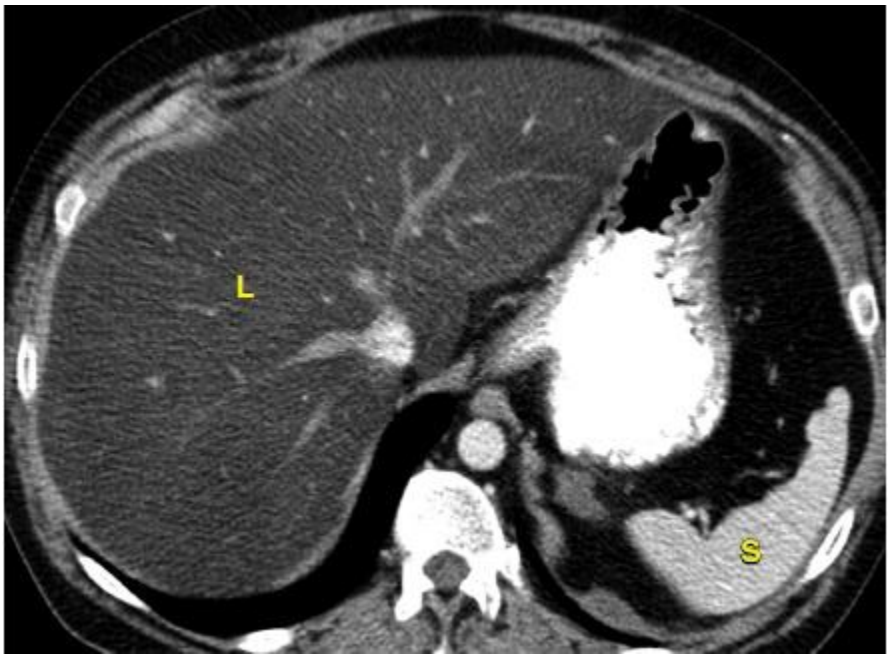



Figure (2.9): CT image for diffuse fatty liver (Webb et al, 2014).

### 2.1.3.6.2 Focal Fatty Infiltration:

A geographic or fan shaped portion of the liver shows fat infiltration, whereas the remainder of the liver is of normal density. The low-density area may extend to the liver surface, but no bulge in contour is seen. Vessels run their normal course through the area of involvement. Margins between fat-infiltrated and normal liver are frequently straight and well defined, reflecting blood-flow territories. Fat infiltration is confined to segments and sub segments. Areas of the liver supplied by third inflow systemic veins are commonly affected; these are adjacent to the gallbladder, the fissure of the ligamentum teres, and the porta hepatis. (Webb et al, 2014).

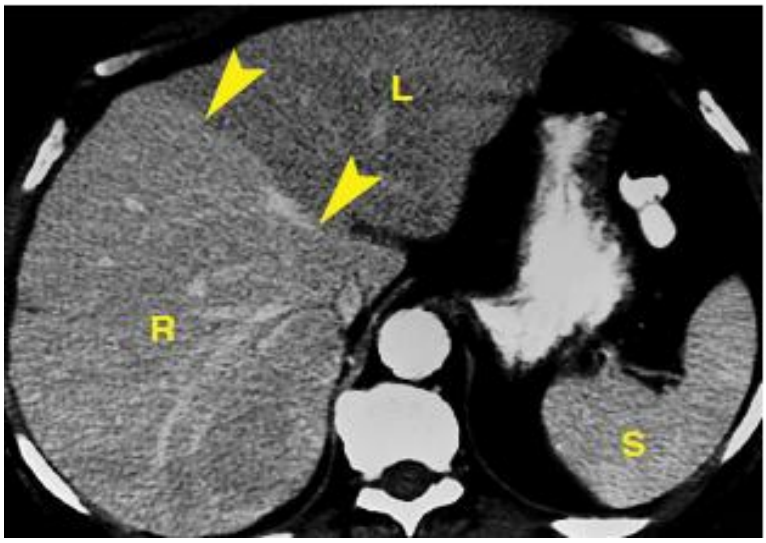



Figure (2.10): CT image of Focal fatty liver .The left lobe of the liver (L) is lower in density than the right lobe of the liver (R) and the spleen (S). A strikingly sharp boundary (*arrowheads*) separates the left and right lobes. This appearance is characteristic of focal fatty infiltration. (Webb et al, 2014).

### 2.1.3.6.3 Multifocal Fatty Infiltration:

Patchy areas of decreased attenuation are scattered throughout the liver. Tumors may be simulated by islands of fatty infiltration surrounded by normal parenchyma

or by islands of normal parenchyma surrounded by fatty infiltration (Webb et al, 2014).

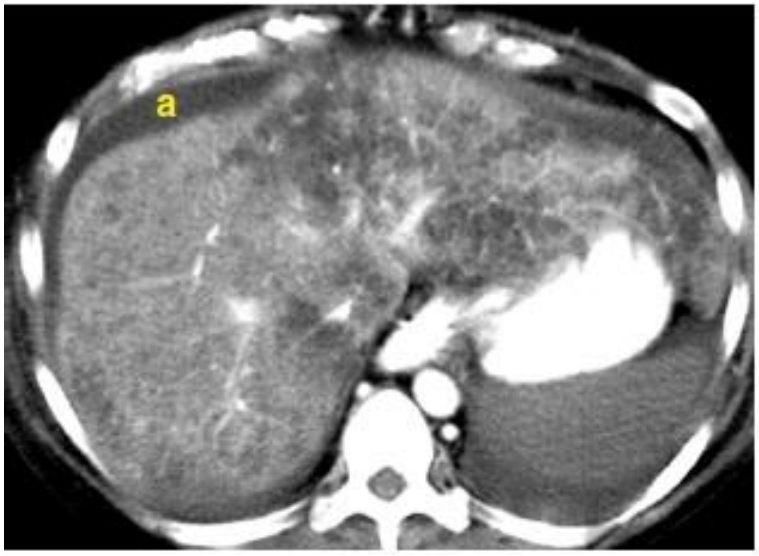
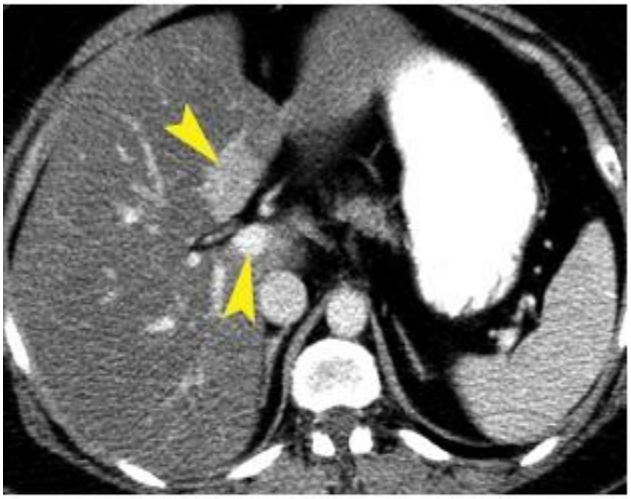



Figure (2.11): Multifocal Fatty Infiltration (Webb et al, 2014).

**2.1.3.6.4 Focal Sparing:**

Islands of normal parenchyma are surrounded by large areas of diffuse fatty infiltration and may simulate neoplasms . Focal sparing is most common in the same areas of the liver most often affected by focal steatosis (Webb et al., 2014).



Figure( 2.12): Focal Sparing (Webb et al., 2014).

### 2.1.3.7 Diagnosis and Evaluation Tools:

The diagnosis of NAFLD needs confirmation of hepatic steatosis based on either imaging studies or liver biopsy, together with the clinical exclusion of individuals who regularly consume >20 g ethanol per day. (Neuschwander & Caldwell, 2003)

#### 2.1.3.7.1 Liver Biopsy:

Liver biopsy is regarded as the gold standard for the assessment of NAFLD and is the only reliable method for differentiating NASH from simple steatosis. This method, however, is invasive and is, therefore, unsuitable for screening large numbers of subjects at risk, or for follow-up of patients with NAFLD after therapeutic intervention. Furthermore, as liver biopsy samples are small in size, they are subject to sampling variability. (Ratziu et al., 2005)

#### 2.1.3.7.2 Imaging modalities:

##### 2.1.3.7.2.1 Ultrasonography:

Hepatic steatosis on US appears as a diffuse increase in hepatic echogenicity, or "bright liver", due to increased reflection of US from the liver parenchyma, which is caused by intracellular accumulation of fat vacuoles. The normal liver parenchyma has a homogeneous echotexture with echogenicity equal to or slightly greater than that of the renal cortex and spleen. The liver shows echogenicity higher than the renal cortex and spleen due to fatty infiltration. (Valls et al., 2006) Various (0-3) grades of steatosis have been proposed based on visual analysis of the intensity of the echogenicity, provided that the gain setting is optimum. When the echogenicity is just increased, it is grade I; when the echogenic liver obscures the echogenic walls of portal vein branches, it is grade II, and, when the echogenic liver obscures the diaphragmatic outline, it is grade III fatty infiltration. (Saadeh et al., 2002)These are however subject to inter-observer variation. The sensitivity of USG in detecting hepatic steatosis ranges from 60 to 94% and the specificity from 84 to 95 %. (Joseph et al., 1991)

Hepatorenal sonographic index, which is the ratio between the mean brightness level of the liver and the right kidney, has also been proposed as a measure of hepatic steatosis with a cut-off of 1.49, yielding very high sensitivity (100%) and specificity (91%) for the diagnosis of steatosis >5%.(Webb M, et al., 2009) Transient elastography/Fibroscan and acoustic radiation force impulse (ARFI) elastography can be integrated into the conventional USG system. These have emerged as new kids on the block to grade the extent of liver stiffness.

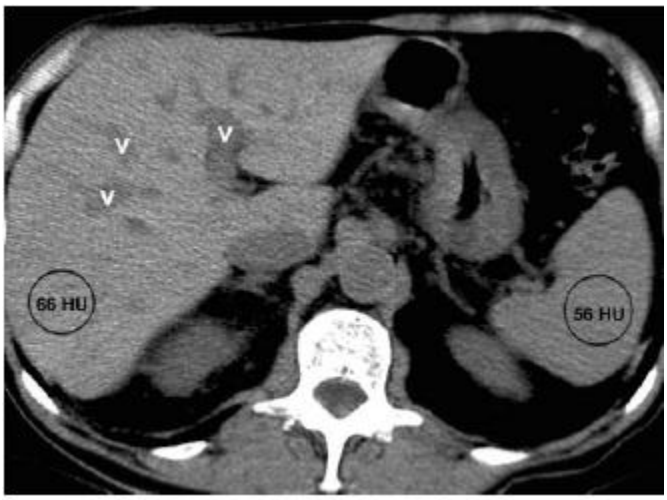
**2.1.3.7.2.2 Computed Tomography:**

CT evaluation of hepatic steatosis is based on the attenuation values of the liver parenchyma, evaluated as Hounsfield units (HUs), and dependent on tissue composition. As the attenuation value of fat (i.e., approximately -100 HU) is much lower than that of soft tissue.

Hepatic steatosis lowers the attenuation of liver parenchyma.Steatosis causes reduced attenuation of liver on CT, which can be represented quantitatively by comparing it with the attenuation of spleen on unenhanced scans.

A liver-to-spleen attenuation ratio of <0.8 has a high specificity (100%) for diagnosis of moderate to severe steatosis. From the assessment of hepatic steatosis in transplant donors, it has been concluded that unenhanced CT performs very well in diagnosing steatosis of ≥ 30%, with 100% specificity and 82% sensitivity.[ Park et al., 2006] Calculating the difference between the attenuation of the spleen and that of the liver can also be used to evaluate steatosis. The attenuation of the spleen is approximately 8-10 HU less than that of the liver in a normal individual, whereas a liver-to-spleen attenuation difference >10 HU is a strong predictor of hepatic steatosis (Piekarski et al, 1980). Also Fatty liver can be diagnosed if the attenuation of the liver is less than 40 HU. (Hamer et al., 2005) It is a quick, non-operator dependent technique. Radiation exposure can be kept at a minimum by using low-dose protocols.The degree of decrease in attenuation on unenhanced CT

is the best predictor of the degree of fatty infiltration in the liver. (Kodama et al., 2007)




Figure( 2.13): Normal appearance of the liver at unenhanced CT. The attenuation of the liver (66 HU) is slightly higher than that of the spleen (56 HU), and intrahepatic vessels *(v)* appear hypoattenuated in comparison with the liver.( ***www.rsna.org/rsnarights.)***

At contrast material–enhanced CT, the comparison of liver and spleen attenuation values is not as reliable for the diagnosis of fatty liver, because differences between the appearance of the liver and that of the spleen depend on timing and technique and because there is overlap between normal and abnormal attenuation value ranges Fatty liver can be diagnosed at contrast-enhanced CT if absolute attenuation is less than 40 HU, but this threshold has limited sensitivity. (Johnston et al., 1998)

Technique: Low-dose, unenhanced CT (80 kV, 100 mAs with dose modulation, collimation of 128 × 0.625, 10-mm section thickness) is performed. For each case, the hepaticattenuation [Figure 5] is measured by means of a random selection of circular regions of interest (ROIs) on both lobes. For each ROI, the largest possible ROI is selected by avoiding areas of visible hepatic vascular and biliary structures. ROIs may range from 200 to 400 $mm^2$. The ROI values are averaged as a mean hepatic attenuation. To provide an internal control, the mean splenic attenuation is also calculated by averaging three random ROI values of splenic attenuation

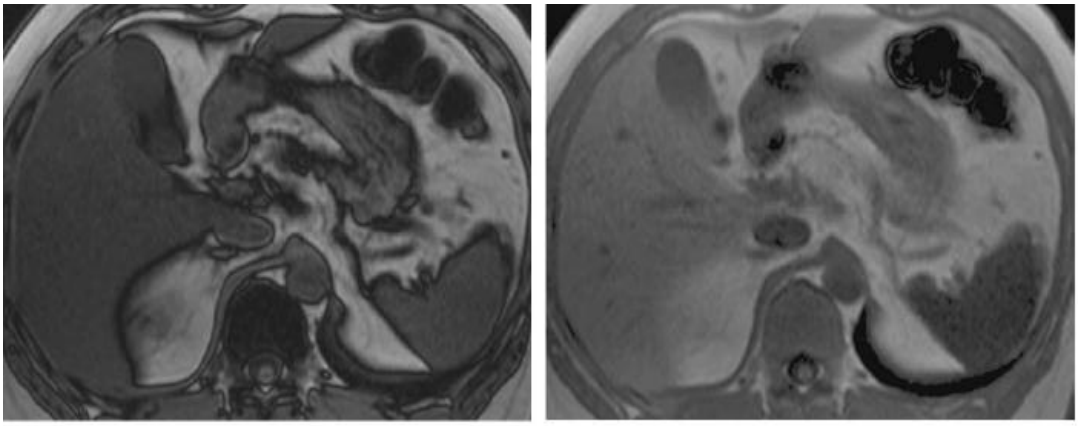
measurement. The largest possible ROI (size range: 200-400 mm2) is selected to represent splenic parenchymal attenuation. The liver attenuation index (LAI) is derived from the difference between mean hepatic attenuation and mean splenic attenuation and can be used as a parameter for prediction of the degree of macrovesicular steatosis. A difference in attenuation of the liver and spleen of 10 HU is taken as normal. (Johnston et al., 1998)

**2.1.3.7.2.3 Magnetic Resonance Imaging:**

MRI is a radiation-free modality to detect hepatic fat even in microscopic quantity. Various techniques like CSI, protonspectroscopy, and MR elastography can be utilized. The sensitivity and specificity of CSI is 90% and 91%, while that of spectroscopy is 91% and 87%, respectively.( Werven et al., 2010)

MR elastography can be used to measure liver stiffness. However, MRI is a relatively time consuming and costly procedure.

CSI is based on the fact that during echo time (TE), the transverse magnetization vectors of fat and water develop a phase difference that results in decreased overall length of the magnetization vector under opposed phase (OP) conditions. At the main magnetic field strength of 1.5 T, the frequency shift between fat and water is approximately 220 Hz, which results in OP condition at a TE of about 2.4 ms and in-phase (IP) condition at a TE of about 4.8 ms. Typically, the fatty liver shows increase in signal intensity (SI) on IP images and shows diffuse signal drop in OP image. The fat fraction can then be determined by calculating the loss of SI in OP images as compared to IP images




Figure( 2.14): Diffuse fat accumulation in the liver at MR imaging. Axial T1-weighted GRE images show a marked decrease in the signal intensity of the liver on the opposed-phase image **(a)**, compared with that on the in-phase image **(b)**. ***www.rsna.org/rsnarights***

### 2.1.3.8 Risk Factors :

It is well recognized that NAFLD is closely associated with metabolic risk factors like obesity, dyslipidemia, systemic hypertension, glucose intolerance, and insulin resistance. Indeed, NAFLD is now considered as a hepatic manifestation of the metabolic syndrome. (Koh et al., 2009; Kotronen & Yki-Jarvinen, 2008)

#### 2.1.3.8.1 Age and Sex:

Previous studies found that male had high prevalence than female (Fan et al., 2005; Lin et al., 2011; Fan J, 2001) supported by explanation of a role for endocrine determinants in the development of this condition. Most Asian and European studies strongly confirm such a view. In males, NAFLD tends to increase from younger to middle-aged groups of individuals and the prevalence of disease begins to decline at the age of 50 or 60. This has been defined as an "inverted U shaped curve". Of interest, a study by Nakajima, although conducted in a restricted series of liver biopsies, was nevertheless able to demonstrate that advancing age was inversely correlated with steatosis. ( Nakajima et al., 2012)

Consistent with a protective role of estrogens, during their fertile period, women tend to be spared from NAFLD compared to men. However, although they tend to

develop the disease approximately 10 years later than men, post-menopausal women are no longer spared from NAFLD. The prevalence of NAFLD in women tends to decrease after the seventh decade of life based on both epidemiological and clinical studies (Carulli et al., *2006*) While hormonal changes have consistently been proposed to account for the varying prevalence rates of NAFLD in either gender, the explanation of decreased rates of NAFLD in the elderly is deemed to reflect either selectively decreased survival in those with NAFLD or decreased fatty changes in advanced NASH. (Koehler et al., 2012)

**2.1.3.8.2 Obesity:**

NAFLD was earlier reported exclusively among obese individuals. Thus, until recently, it was generally assumed that NAFLD occurs only in obese individuals. However, more recently, it is being recognized that NAFLD may also occur in nonobese subjects (i.e., those with normal body mass index [BMI] (Margariti et al., 2013).

The prevalence of NAFLD in obese adults is estimated from 39 to 95% (A´ lvarez-Martı´nez & Pe´rez-Campos, 2002). Some studies have suggested that individuals with obesity or overweight and with central distribution of fatty are more likely to develop NAFLD (Ruhl & Everhart, 2003; Hu et al., 2004).

**2.1.3.8.3 Diabetes Mellitus Type 2:**

NAFLD and type 2 diabetes mellitus (T2DM) frequently coexist because they share the risk factors of excess adiposity and insulin resistance. The prevalence of T2DM or impaired fasting glucose ranges from 18–33% in patients with NAFLD, whereas it ranges from 49–62% in T2DM patients who have NAFLD ( Browning et al., 2004; Fan et al.,2005; Jimba et al., 2005; Gupte et al., 2004)

NASH is present in 12.2% of patients with T2DM, as compared to 4.7% in those without T2DM ( Wanless & Lentz, 1990). Moreover, T2DM increases the risk of

liver-related death by up to 22-fold as well as overall death by 2.6–3.3-fold in patients with NAFLD.

**2.1.3.8.4 Metabolic Syndrome:**

Metabolic syndrome was defined according to the National Cholesterol Education Program (NCEP) adult treatment panel III (ATP III) guidelines as the presence of any 3 of the following 5 components: (1) Waist circumference >102 cm [men] and > 88 cm [women], (2) Fasting triglycerides > 150 mg/dL, (3) High density lipoprotein cholesterol < 40 mg/dL [men] and < 50 mg/ dL [women], (4) blood pressure > 130/85 mm Hg, (5) fasting glucose >110 mg/dL. Patients with features of MS are at high risk for NAFLD. Additionally, ethnicity influences the prevalence of NAFLD: even with a lower degree of obesity, Hispanics and Asians are at higher risk than African Americans, who despite features of MS are known to have less severe NAFLD and a lower prevalence of NAFLD. (Puri & Sanyal , 2012)

**2.1.4 Computed Tomography:**

**2.1.4.1 Introduction:**

The word tomography has as its root *tomo,* meaning to cut, section, or layer from the Greek *tomos* (a cutting). In the case of CT, a sophisticated computerized method is used to obtain data and transform them into "cuts," or cross-sectional slices of the human body.

Computed tomography uses a computer to process information collected from the passage of x-ray beams through an area of anatomy. The images created are cross-sectional each CT slice represents a specific plane in the patient's body. The thickness of the plane is referred to as the *Z* axis. The *Z* axis determines the thickness of the slices (Hsieh, 2009).

### 2.1.4.2 CT Scanner:

CT scanners are complex, with many different components involved in the process of creating an image. It consists of a scanning gantry, x-ray generator, computer system, operator's console, and physician's viewing console.

#### 2.1.4.2.1 Gantry:

Houses many of the components necessary to produce and detect x- Components are mounted on a rotating scan frame. Gantries vary in total size as well as in the diameter of the opening, or aperture. The range of aperture size is typically 70 to 90 cm. The CT gantry can be tilted either forward or backward as needed to accommodate a variety of patients and examination protocols. The degree of tilt varies among systems, but ±15° to ±30° is usual. The gantry also includes a laser light that is used to position the patient within the scanner. Control panels located on either side of the gantry opening allow the technologist to control the alignment lights, gantry tilt, and table movement. In most scanners, these functions may also be controlled via the operator's console. A microphone is embedded in the gantry to allow communication between the patient and the technologist throughout the scan procedure (Romans, 2011).

#### 2.1.4.2.2 Slip Rings:

Early CT scanners used recoiling system cables to rotate the gantry frame. Current systems use electromechanical devices called slip rings. Slip rings use a brushlike apparatus to provide continuous electrical power and electronic communication across a rotating surface. They permit the gantry frame to rotate continuously, eliminating the need to straighten twisted system cables (Romans, 2011).

#### 2.1.4.2.3 Generator:

High-frequency generators are currently used in CT. They are small enough so that they can be located within the gantry.. The power capacity of the generator is listed in kilowatts (kW). The power capacity of the generator determines the range of

exposure techniques (i.e., kV and mA settings) available on a particular system. CT generators produce high kV (generally 120–140 kV) to increase the intensity of the beam, which will increase the penetrating ability of the x-ray beam and thereby reduce patient dose. In addition, a higher kV setting will help to reduce the heat load on the x-ray tube by allowing a lower mA setting. Reducing the heat load on the x-ray tube will extend the life of the tube. (Romans, 2011)

**2.1.4.2.4 Cooling Systems:**

Cooling mechanisms are included in the gantry. They can take different forms, such as blowers, filters, or devices that perform oil-to-air heat exchange. Cooling mechanisms are important because many imaging components can be affected by temperature fluctuation. (Romans, 2011)

**2.1.4.2.5 X-ray Source:**

X-ray tubes design is a modification of a standard rotating anode tube, such as the type used in angiography. Tungsten, with an atomic number of 74, is often used for the anode target material because it produces a higher-intensity x-ray beam. CT tubes often contain more than one size of focal spot; 0.5 and 1.0 mm are common sizes. Just as in standard x-ray tubes, because of reduced penumbra small focal spots in CT tubes produce sharper images (i.e., better spatial resolution), but because they concentrate heat onto a smaller portion of the anode they cannot tolerate as much heat. A CT tube must be designed to handle such stress. The way a tube dissipates the heat that is created during x-ray production is critical (Romans, 2011).

**2.1.4.2.6 Filtration:**

Compensating filters are used to shape the x-ray beam. They reduce the radiation dose to the patient and help to minimize image artifact. Filtering the x-ray beam helps to reduce the range of x-ray energies that reach the patient by removing the long-wavelength (or “soft”) x-rays. In addition, creating more uniform beam

intensity improves the CT image by reducing artifacts that result from beam hardening. Human body anatomy typically has a round cross section that is thicker in the middle than in the periphery. Hence, body-scanning filters are used to reduce the beam intensity at the periphery of the beam, corresponding to the thinner areas of a patient's anatomy (Romans, 2011).

**2.1.4.2.7 Collimation:**

Collimators restrict the x-ray beam to a specific area, reducing scatter radiation. Improve the image quality and reduce the radiation dose to the patient. Collimators control the slice thickness. The source collimator is located near the x-ray source and limits the amount of x-ray emerging referred to as prepatient collimation. The source collimator affects patient dose. The source collimator resembles small shutters with an opening that adjusts, dependent on the operator's selection of slice thickness. In MDCT systems, slice thickness is also influenced by the detector element; Scanners vary in the choices of slice thickness available. Choices range from 0.5 to 10 mm. Some CT systems also use predetector collimation. The primary functions of predetector collimators are to ensure the beam is the proper width as it enters the detector and to prevent scatter radiation from reaching the detector (Romans, 2011).

**2.1.4.2.8 Detectors:**

As the x-ray beam passes through the patient it is attenuated to some degree. To create an x-ray image we must collect information regarding the degree to which each anatomic structure attenuated the beam. In CT, we use detectors to collect the information. Specifically, the detector array comprises detector elements situated in an arc or a ring, each of which measures the intensity of transmitted x-ray radiation along a beam projected from the x-ray source to that particular detector element (Romans, 2011).

### 2.1.4.2.8 .1 Xenon Gas Detectors:

Pressurized xenon gas fills hollow chambers to produce detectors that absorb approximately 60% to 87% of the photons that reach them. Xenon gas is used because of its ability to remain stable under pressure. Compared with the solid-state variety, xenon gas detectors are significantly less expensive to produce, somewhat easier to calibrate, and are highly stable. A xenon detector channel consists of three tungsten plates. When a photon enters the channel, it ionizes the xenon gas. These ions are accelerated and amplified by the electric field between the plates. The collected charge produces an electric current. This current is then processed as raw data. A disadvantage of xenon gas is that it must be kept under pressure in an aluminum casing. This casing filters the x-ray beam to a certain extent. Loss of x-ray photons in the casing window and the space taken up by the plates are the major factors hampering detector efficiency. (Romans, 2011)

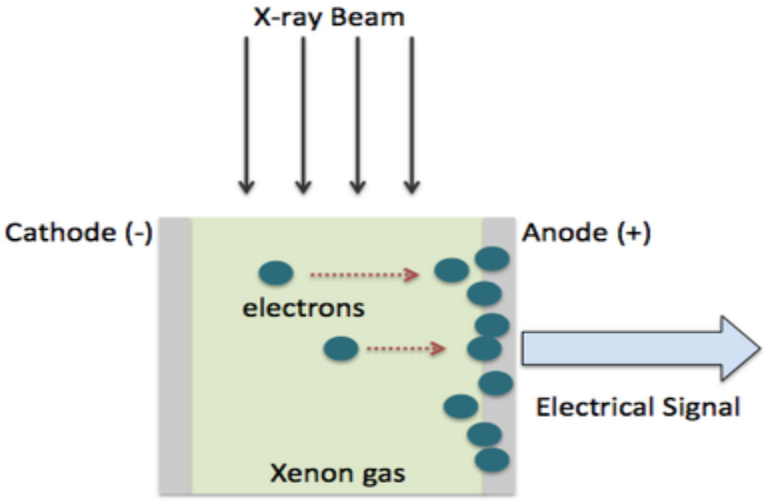



Figure (2.15): Demonstrates the basic structure of a xenon gas detector http://199.116.233.101/images/thumb/a/a9/Fig_4_Xenon_Detector.png/400px-Fig_4_Xenon_Detector.png

### 2.1.4.2.8 .2 Solid-State Crystal Detector:

Solid-state detectors are also called scintillation detectors .A photodiode is attached to the crystal and transforms the light energy into electrical (analog) energy. The

individual detector elements are affixed to a circuit board. Solid-state crystal detectors have been made from a variety of materials, including cadmium tungstate , bismuth germinate, cesium iodide, and ceramic rare earth compounds such as gadolinium or yttrium. Because these solids have high atomic numbers and high density in comparison to gases, solid-state detectors have higher absorption coefficients. They absorb nearly 100% of the photons that reach them. In addition, there is no loss in the front window, as in xenon systems. This increased absorption efficiency is the chief advantage of solid-state detectors. Solid-state detectors may produce a brief afterglow. However, this has been greatly reduced or eliminated in modern CT detectors. Solid-state detectors are more sensitive to fluctuation in temperature and moisture than the gas variety. (Romans, 2011)

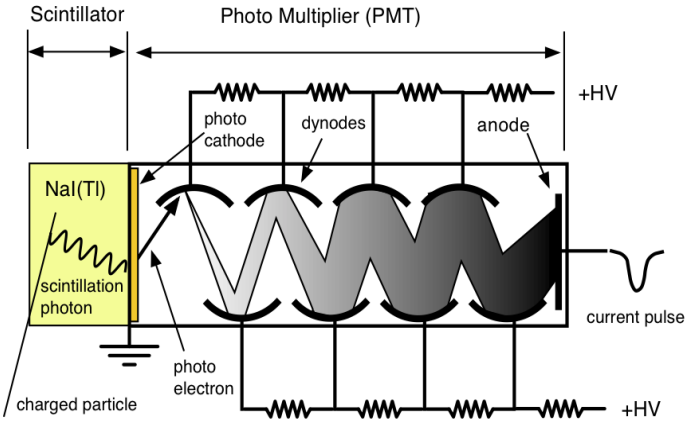



Figure (2.16): Schematic of scintillator and photo multiplier http://wanda.fiu.edu/teaching/courses/Modern_lab_manual/_images/PMT.png

### 2.1.4.3 CT Image Formation:

The formation of a CT image is a distinct three phase process:The scanning phase produces data, The reconstruction phase processes the acquired data and forms a digital image.and The visible and displayed analog image (shades of grey) is produced by the digital-to analog conversion phase (Karthikeyan, 2005).

#### 2.1.4.3.1 Data-Acquisition System:

X-ray photons that strike the detector must be measured, converted to a digital signal, and sent to the computer. This is accomplished by the data-acquisition system (DAS), which is positioned within the gantry near the detectors. Signals emitted from the detectors are analog (electric), whereas computers require digital signals. Therefore, one of the tasks of the DAS is to convert the analog signal to a digital format. This is accomplished with the aptly named analog-to-digital converter or ADC To measure the x-ray photons that have penetrated the patient, the detectors are sampled many times, as many as 1,000 times per second by the DAS. The number of samples taken per second from the continuous signal emitted from the detector is known as the sampling rate, sample rate, or sampling frequency. Artifacts, such as streaking, can appear on the image if the number of samples is insufficient. (Hsieh, 2009)

#### 2.1.4.3.2 Image Reconstruction:

The computer receives a signal in analog form and converts it to a binary digit by using a analog to digital convertor. The digital signal is stored and the image is reconstructed after the scan is over. Each picture is displayed on a matrix, each square in a matrix is called a pixel, its assigned a number based on the amount of energy reaching the detector. This number is called as Hounsfield unit. The reconstructed anatomy of an object is in the digital format composed of a large number of Tiny elongated blocks. Representing a volume of tissue called voxel and 1.13). Voxel it is 3D tissue element that has a width, height and depth. Depth of a voxel is a important parameter which depends on the slice thickness and each unit is assigned a shade of grey. Pixel is the 2D projection of a voxel on the computer screen and it has only height and width. (Karthikeyan, 2005)

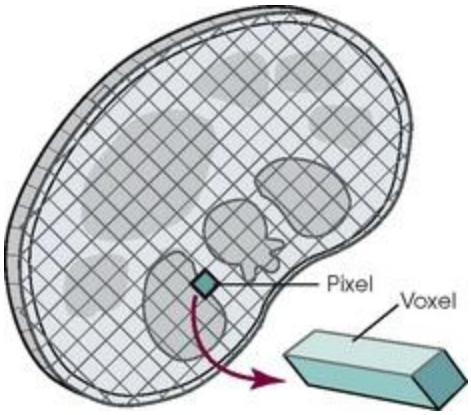



Figure (2.17): Demonstrates the Main component of CT image

(https://radiologykey.com/computed-tomography-8/

### 2.1.4.3.3 CT Numbers and Hounsfield Units:

The digital value ascribed to each pixel is called the Hounsfield units or HU, which lies on a scale were water has a value of 0 and air has a value of –1000. Bone has a value in order of +1000. HU values reflect the electron density and thus the physical composition of the voxel of tissue that the pixel represents. Reconstruction yields linear attenuation coefficients, usually relative to that of water and scaled to a large number, the CT number. (Karthikeyan, 2005)

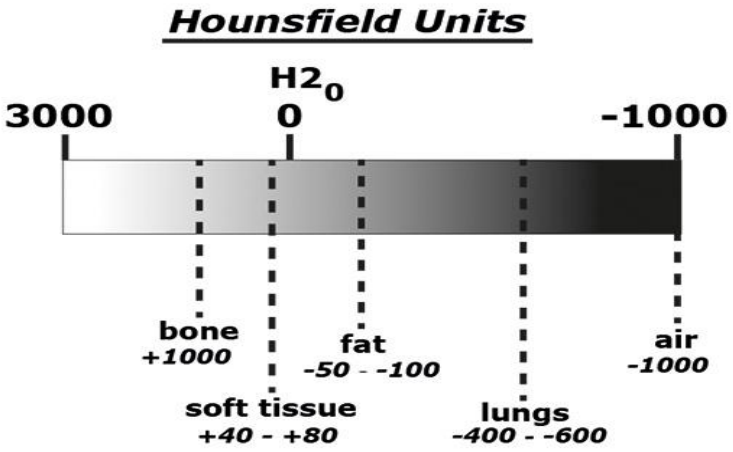



Figure ( 2.18): Shows the hounsfield units and gray scale

http://www.startradiology.com/internships/neurology/brain/ct-brain-hemorrhage/

### 2.1.4.4 CT Protocols:

#### 2.1.4.4.1 Patient Preparation:

Ideally the patient should have remained nil by mouth (NBM) for 2 hours prior to scanning if intravenous contrast is to be given and for 6 hours if oral contrast is required. Scanning can be carried out on unfasted patients if necessary. If contrast agents are to be used, check that the patient has no contraindications to these before they are administered. Refer to the manufacturer's leaflet for a list of contraindications

The pregnancy status of female patients under 50 years old should be checked. An alternative imaging procedure must be sought if there is any chance of pregnancy. The only exception is in cases of severe trauma. As for all CT scanning, the area to be examined must be free from articles that may cause artifact on the resultant images. Ideally, the patient should be asked to undress and put on a cotton gown.

The patient must be given an adequate description of the scanning procedure in order that they may cooperate to the best of their ability. **(**Henwood, 1999**)**

#### 2.1.4.4.2 CT Abdomen Technique:

Center the patient within the gantry in supine positioning (feet or head first). Scan range Scan from the top of liver to either iliac crest or pubic symphysis, depending on clinical indications. Suspension of respiration Patient should be instructed to hold his \her breath at end of inspiration. Oral contrast is often used to enhance CT images of the abdomen and pelvis. There are two different types of substances used for oral CT contrast. The first, barium sulfate, is the most common oral contrast agent used in CT. The second type of contrast agent is sometimes used as a substitute for barium and is called Gastrografin and kidneys. "Intravenous" means that the contrast is injected into a vein using a small needle. Some imaging exams of the abdomen and gastrointestinal system use both the intravenous iodine and orally administered barium contrast for maximum sensitivity .The intravenous

CT contrast is clear like water and has a similar consistency. It is typically packaged in glass bottle or vial. A sterile syringe is used to draw it from the bottle or a power injector is used to administer the contrast. Typically between 75 cc to 150 cc (about 2.5 oz. to 5 oz) of contrast is used depending upon the patient's age, weight, area being imaged and cardiovascular health{Thomsen, 2003).

**2.1.4.4.3 Liver CT Technique:**

Multidetector CT (MDCT) allows scanning of the entire liver with thin collimation during single breath hold of 10 to 25 seconds. Acquisition is routinely repeated several times during various phases of contrast medium enhancement.

Dynamic contrast-enhanced liver CT offers the opportunity to accurately characterize lesion enhancement patterns and significantly improve the specificity of diagnosis. Various lesions are detected best or sometimes only, in specific phases of postcontrast scanning. Intravenous contrast is administered via a power injector at a contrast concentration of 300 mg iodine (I)/mL at a rate of 4 to 5 mL/second for a volume of 100 to 150 mL. Routine scan delays for MDCT are 25seconds following initiation of contrast injection for the arterial phase and 65 seconds following initiation of contrast injection for the portal venous phase. With MDCT, images are routinely acquired at collimation of 1.25 to 2.50 mm but are viewed at a slice thickness of 5 mm. Image acquisition at thin collimation allows for highly detailed multiplanar reconstructions. Enhancement of the normal liver is homogeneous throughout the parenchyma for all enhancement phases

• **Noncontrast** scans are commonly obtained to provide a baseline for the degree of lesion enhancement. Many liver lesions are detected, but small lesions are often mistaken for unopacified vessels. Noncontrast scans are superior to postcontrast scans for diagnosis of fatty infiltration and other alterations in parenchymal attenuation.

• **Arterial-phase** acquisition is optimal for visualization of hypervascular lesions supplied by the hepatic artery such as hepatoma, carcinoid metastases, and focal nodular hyperplasia (FNH). Lesions are conspicuous because they enhance more than the surrounding parenchyma. A variety of perfusion abnormalities is seen only on arterialphase images.

• **Portal venous-phase** imaging yields the best lesion detection overall because parenchymal enhancement is maximum during this phase. Lesions are conspicuous because they are of low attenuation against a background of maximally enhanced liver parenchyma.

• **The equilibrium phase** occurs at 2 to 3 minutes after initiation of contrast injection. During the equilibrium phase, the concentration of contrast agent is approximately equal between the intravascular and extravascular spaces, rendering most liver lesions invisible.

• **Delayed-phase images**, acquired at 10 to 20 minutes after contrast injection, are used to demonstrate delayed contrast fill-in of hemangiomas and to detect fibrotic tumors such as cholangiocarcinoma (Webb et al., 2014) .

**2.2 Previous Studies:**

A cross-sectional study being performed in Shiraz southern Iran by Lankarani et al (2013) used random sampling of Iranian general population was diagnosed by transabdominal ultrasonography. 819 subjects were included in the study among which were 340 males (41.5%) and 479 females (58.5%) with the mean age of 43.1 The prevalence of NAFLD in this group of Iranian adult general population is 21.5%. NAFLD in Iranian population is associated with male gender, old age, obesity, and features of metabolic syndrome. (Lankarani et al., 2013)

Study conducted by Elkhader and Mahmoud. (2013), on which 500 participants from Khartoum- Sudan were enrolled to determine the prevalence of NAFLD in a population based sample. In this study the ultrasound scan was used as noninvasive

diagnostic tool. The result is that overall prevalence of NAFLD was 15%, 4.4% in males and 6.6% in females. The most significant factors as associated with the presence of NAFLD were weight category, elevated alanine aminotransferase (ALT) and increase Non high density lipoprotein (Non-HDL) cholesterol level. Obesity is a major risk. (Elkhader & Mahmoud, 2013)

Another study carried out in Sudan by Elmobarak et al (2014) to determine the prevalence of NAFLD and risk factors among 100 asymptomatic co-patients .NAFLD was diagnosed in 20 patients, giving prevalence of 20%. Males and females were nearly equally affected and the prevalence of NAFLD increased with age and BMI, making obesity a main risk factor. Due to small number of diabetic individuals and hypertension, these two conditions were not statistically significant when related to NAFLD. (Elmobarak et al., 2014)

A cross-sectional study conducted in Beijing, China by Li et al (2013), using questionnaires (including socio-demographic characteristics, semi-quantitative food-frequency questionnaire, eating habits and cooking styles), anthropometric measurement, biochemical test and liver ultrasonography. A total of 1,583 study subjects were enrolled in this study. The overall prevalence of non-alcoholic fatty liver disease was 18.1% (17.6% for males and 12.0% for females, respectively). High frequency of animal oil, high intake of oil and triglyceride were positively related to non-alcoholic fatty liver disease.

Study done by Zeb et al (2012) in USA includes 6,814 asymptomatic participants from a population based sample. The ratio of liver-to-spleen (L/S) Hounsfield units (HU) <1.0 and liver attenuation <40HU were utilized for diagnosing and assessing the severity of liver fat content. Participants with heavy alcohol intake were excluded. Final analysis was performed on participants where images of both liver and spleen were available on the scans. The result of this study is that the overall

prevalence of fatty liver (4,175 patients) was 17.2% the associated risk factors were dyslipidemia, hypertension and obesity.

Dassanayake et al.(2009) studied the prevalence and risk factors for NAFLD among adults in an urban Sri Lankan population.The study sample was consisted of 2985 participants, 35–64-year-old, selected by stratified random sampling. NAFLD was diagnosed on established ultrasound criteria for fatty liver. (32.6%) had NAFLD Females were more affected than males, with mean age 52.8 years .NAFLD strongly associated with constituent features of the metabolic syndrome.

Al-hamoudi et al. (2012) conducted a prospective study among patients referred for ultrasonography in King Khalid University Hospital in Riyadh, Saudi in which the NAFLD was defined as an appearance of fatty liver on routine abdominal ultrasound in the absence of coexisting liver disease and alcohol consumption. Patients were classified into normal and high ALT (ALT >60 U/L) level groups for analysis. The prevalence of NAFLD in the study was 16.6% (218/1312). Patients with normal ALT had the mean (SD) age of 45.9 (10.6) years and the mean body mass index of 34.5 (7.9) kg/m2. Forty percent of the 151 patients with normal ALT had diabetes, 66.2% were obese, and 29.1% had hypertension. Forty-three patients (23%) had high ALT levels. These patients had significantly lower age (P=.003) and fasting blood sugar (P=.03) than the normal ALT group. Non-diabetic patients (odds ratio 0.30, 95% CI 0.1-0.8), men (female OR 0.23, 95% CI 0.1-0.5), lower cholesterol (P=.001), high-density lipoprotein (P=.006), and low-density lipoprotein (P=.008) levels were more likely to be observed among patients with high ALT levels. In a multivariate analysis, younger age (OR 0.96, 95% CI 0.93-0.99), being male (OR 0.23, 95% CI 0.09-0.57), and a lower cholesterol level (OR 0.55, 95% CI 0.37-0.82) were significant predictors of high ALT levels.

Asabamak et al, (2016) made study in Nigeria, to determine the prevalence of non-alcoholic fatty liver disease (NAFLD) among a population of diabetic (DM)

subjects compared with non-diabetic subjects. One hundred and fifty subjects, mean age 56years (standard deviation = 9, range 20-80 yr) and gender ratio (F: M) of 83:67(55%:45%), were recruited. 106 were diabetics and 44 non-diabetics. The overall prevalence of NAFLD amongst all study subjects was 8.7%. The prevalence rate of NAFLD was higher in the DM cases than in the Control subjects but this difference was not statistically significant (9.5 *vs.* 4.5%, p = 0.2). Central obesity as measured by waist circumference (WC) and SGPT levels were significantly higher in people with fatty liver. The mean body mass index (BMI) of diabetic and non-diabetic patients was similar (31 *vs.* 30 kg/m2). The prevalence of the metabolic syndrome was higher in the subjects with NAFLD than in those without fatty liver disease but this difference was not statistically significant (p = 0.8).

Study conducted by Caballería et al, (2010) to determine the prevalence of nonalcoholic fatty liver disease (NAFLD) in Spain. Individuals between 15 and 85 years of age were randomly selected from 25 primary healthcare centers in the province of Barcelona, Spain. Clinical histories were reviewed, and anamnesis, physical examination, blood analysis and hepatic echography were performed. Individuals with an alcohol intake greater than 30 g/day in men and greater than 20 g/day in women or with known liver disease were excluded. Seven hundred and sixty-six individuals with a mean age of 53±14 years (range 17–83, 42.2% men) were included in the study. One hundred and ninety-eight individuals presented NAFLD with echographic criteria (prevalence 25.8, 33.4% men and 20.3% women *P*<0.001). The associated risk factors are: Male sex, age, metabolic syndrome, insulin resistance and alanine aminotransferase .

Table 2.1: Summarize the previous study include region, sample size, diagnostic tool, prevalence and risk factors

| **Reference,year** | **Region** | **Number** | **Diagnostic** | **NAFLD %** | **Risk factors** |
|---|---|---|---|---|---|
| Asabamak et al.,(2016) | Nigeria | 150 | U/S | 8.7 | Central obesity |
| Almobarak et al.,2014 | Khartoum Sudan | 100 | U/S | 20 | Age and obesity |
| Elkhader et al. ,2013 | Khartoum,sudan | 500 | U/S | 15 | increase alanine aminotransferase (ALT) and Non high density lipoprotein (Non-HDL) cholesterol level. Obesity |
| Lankarani et al., 2013 | South Iran | 819 | U/S | 21.5 | Male, old age, obesity, and of metabolic syndrome. |
| Li et al , 2013 | Beijing, China | 1,583 | U/S | 18.1 | High intake of oil and triglyceride |
| Al-hamoudi etal. ,2012 | Saudi | 1312 | U/S | 16.6 | None |
| Zeb et al ,2012 | USA | 6,814 | CT | 17,2 | Dyslipidemia , Hypertension and obesity . Diabetic patients |
| Caballería et al ,(2010) | Spain | 760 | U/S | 25.8 | Male, age, metabolic syndrome, insulin resistance and alanine aminotransferase a |
| Dassanayake et al.,2009 | Sri Lankan | 2985 | U/S | 32.6%) | Metabolic disorders |

# Chapter Three

## Materials and Methods

### 3.1. Materials

This study was conducted in Khartoum states (capital of Sudan), in two medical centers Antalya medical center and Nilein medical diagnostic center. Data were collected in the period from (December 2015) to (June 2018).

### 3.1.1 Study Population:

About 292 adult participants were enrolled in the study the participants were selected randomly from patients that scheduled to undergo a CT scan of the abdomen. Among them were 142 males (48.6%) and 150 females (51.4%) with the mean age of 48.08 ±15.56 (ranging from 18 to 88 years).Those who had a history of alcohol consumption, hepatic mass or liver cirrhosis and non Sudanese participants were excluded.

### 3.1.2 Machine Used:

#### 3.1.2.1 GE 8 slice MDCT scan:

Scanning parameters: 120-140 kV, 200 -220 mAs. X-ray tube specification: focal spot 0.6mm x 0.6mm and anode heat dissipation 400k uH/min, anode heat storage capacity4.0 MHU.

Gantry specification: Rotation speed 360º in 0.30, 1, 1.5 second, tilt +/-30 ºand aperture 70 cm. Detector specification :Scan type eight (option) ,spiral or axial, slice thickness 0.5,1.0,1.5, 3.0,5.0and 10 mm , scan mode 0.50:1/1.5:1.Algorithm (option)standard ,soft tissue ,bone and edge enhancement , matrix 512*512 and 20 cm field of view.

#### 3.1.2.2 Siemans Somatom Emotion Duo CT scanner :

-Dual multislice helical, 0.8 s rotation time, Multislice UFC™ (Ultra Fast Ceramic) Detector , 40 kW generator , patient table (200 kg/440 lbs table load)

-Gantry: Aperture 70 cm ,Scan field 50 cm ,Tilt ± 30°,Rotation time 0.8, 1.0, 1.5 s, Temporal resolution down to 400 ms

-Data acquisition system: Max. number of slices/rotation 2, Number of physical detector rows 2, Number of physical detector 672 channels/slice, Number of projections up to 1,500 (1/360°)

-Tube assembly : DURA 352 MVHigh performance CT X-ray tube ,Tube current range 30–240 mA ,Tube voltage 80, 110, 130 kV, Tube anode heat storage capacity 3.5 MHU,Focal Spot size 0.8 x 0.4 mm/8°.


Figure (3.1): Shows Nilien medical center CT scanner (Author source)

Figure (3.2): Antalya GE 8slice (Brightspeed) CT scanner. (Author source)

**3.2 Method:**

**3.2.1 Scanning Protocol:**

Scan was obtained with patient supine, feet first, patient centered and instructed to be hold his/her breath at end of inspiration. Patient instructed to elevate his/her hand over the head to avoid out of field artifact.

Scan ranged from the dome of diaphragm to the iliac crest, and slice thickness of 10mm (2*5mm) Rotation time was 1sec with pitch of 2 and kv of 120 with mA range 300-350 and FOV = 300mm

Window setting which used to display images was for evaluation of soft tissue, window width (ww) of 350-400 Hounsfield unit (HU) and window level (wl) of 35-50 HU.

**3.2.2 Data Collection:**

The following information was collected for each patient including sex, age, height, body weight (WT), BMI, Waist circumference, medical history and abdominal CT scan. Weight, standing height and waist circumference (WC) were

measured in a standardized fashion. WC measurement was made midway between the last rib and the iliac crest. The standing height and WC measurement were made at minimal inspiration to the nearest 0.1cm. Body mass index was calculated by dividing weight in kilograms by height in meters squared .Participants who reported current use of anti-hypertension or anti-diabetes medications were regarded as having hypertension or diabetes, respectively

### 3.2.3 Images Evaluation:

Unenhanced CT was performed for each case the CT Measurement was done by professional technologists (Figure 3.3) .The hepatic attenuation is measured by means of a random selection of circular regions of interest (ROIs) on both lobes (two measurement for each one). For each ROI, the largest possible ROI is selected by avoiding areas of visible hepatic vascular and biliary structures. The ROI values are averaged as a mean hepatic attenuation. To provide an internal control, the mean splenic attenuation is also calculated by random large ROI values of splenic attenuation measurement. The largest possible ROI is selected to represent splenic parenchymal attenuation. The liver spleen ratio (L/S) is derived by divided the mean hepatic attenuation over splenic attenuation. Calculated as the following equation:

Liver to spleen ratio = $mean\ hepatic\ attenuation / splenic\ attenuattion$

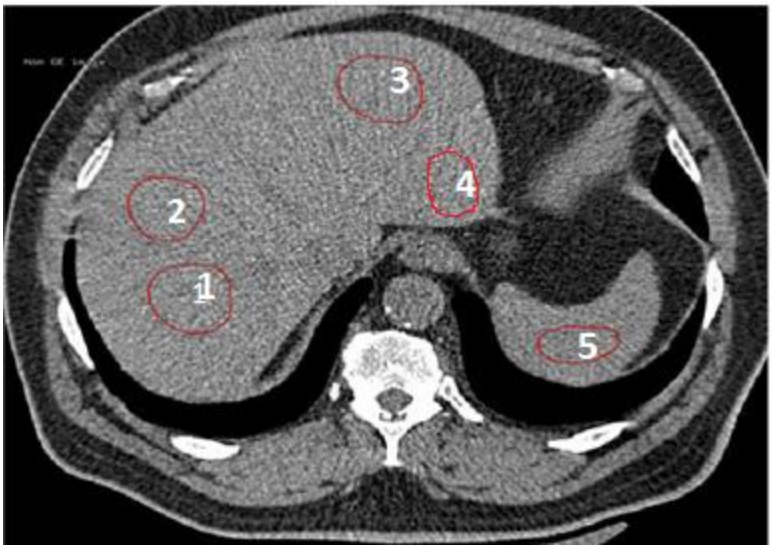



Figure (3.3): Axial slice CT image show 5 areas for measurement. (Author source)

### 3.2.4 Statistical Analyses:

Statistical analyses were performed using the Microsoft excel and Statistical Package for the Social Sciences (SPSS) software, version 20.0. The prevalence of NAFLD was calculated as a proportion of diagnosed patients to included subjects. The chi-square test was used to compare the proportions between those with NAFLD and normal populations. The independent t - test was used for comparing the non parametric data between the two categories. The results are expressed as mean± SD and proportions as appropriate. A two-tailed p-value less than 0.05 were considered statistically significant.

### 3.2.5 Ethical Considerations:

Special consideration was given to the right of the confidentiality and anonymity for all participants. Anonymity was achieved by using number for each participant to provide link between the collected information and the participants. Justice and human dignity was considered by teaching the selected participant equally when offering them an opportunity to participate in the research. Permission for conducting the study was obtained from head of the radiology department at the two medical centers.

# Chapter Four

## Results

Table (4.1) Shows distribution of Gender in the study sample represent as frequencies and percentages (%)

| Gender | Frequency | Percentages |
|---|---|---|
| Male | 142 | 48.6 |
| Female | 150 | 51.4 |
| Total | 292 | 100.0 |

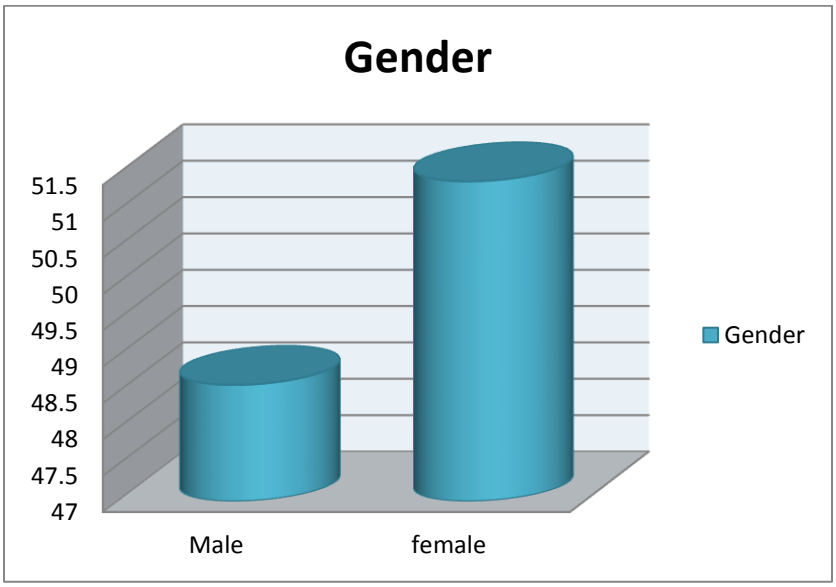



Figure (4.1): Percentage of participant's gender

Table (4. 2) Shows distribution of age in the study sample represented as frequencies and percentages (%).

| Age categories | Frequency | Percentage |
|---|---|---|
| 18 -27 | 32 | 11.0 |
| 28 - 37 | 41 | 14.0 |
| 38 - 47 | 68 | 23.3 |
| 48 - 57 | 67 | 22.9 |
| 58 - 67 | 51 | 17.5 |
| 68 -77 | 26 | 8.9 |
| 78 - 88 | 7 | 2.4 |
| Total | 292 | 100.0 |

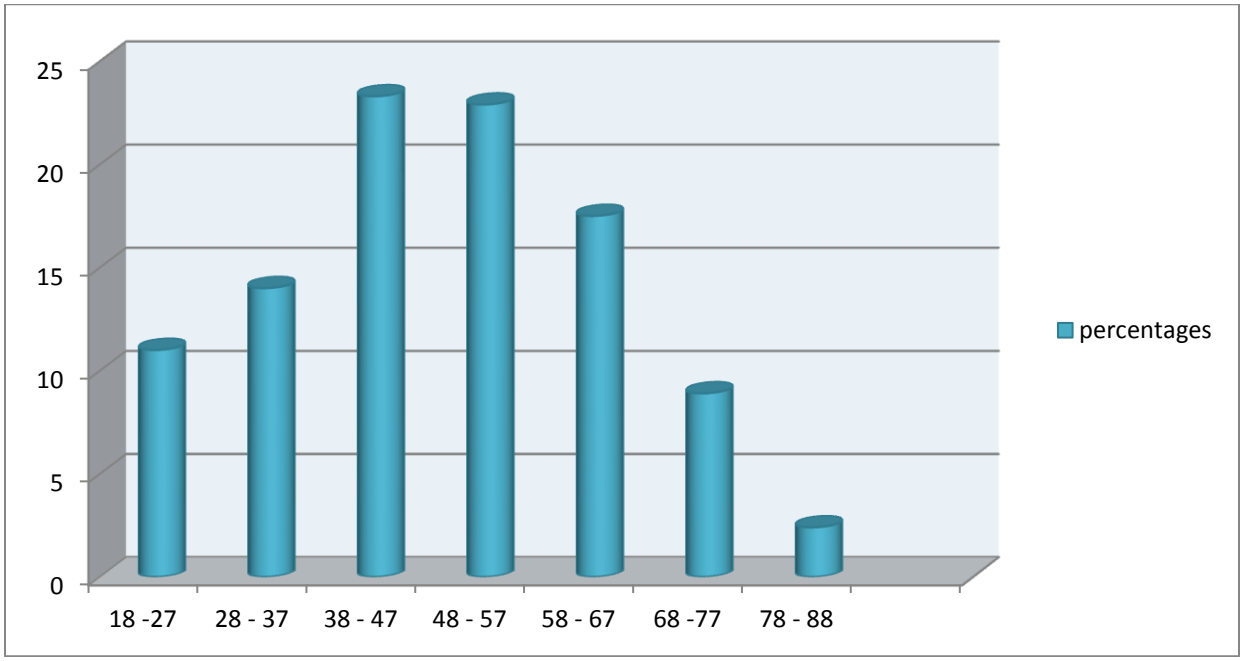



Figure (4.2): Percentage of participant's age

Table (4.3) Shows distribution of participants according to their location in Sudan represented as frequencies and percentages (%).

| location | Frequency | Percent |
|---|---|---|
| East | 25 | 8.6 |
| West | 82 | 28.1 |
| Center | 118 | 40.4 |
| North | 56 | 19.2 |
| South | 11 | 3.8 |
| Total | 292 | 100.0 |

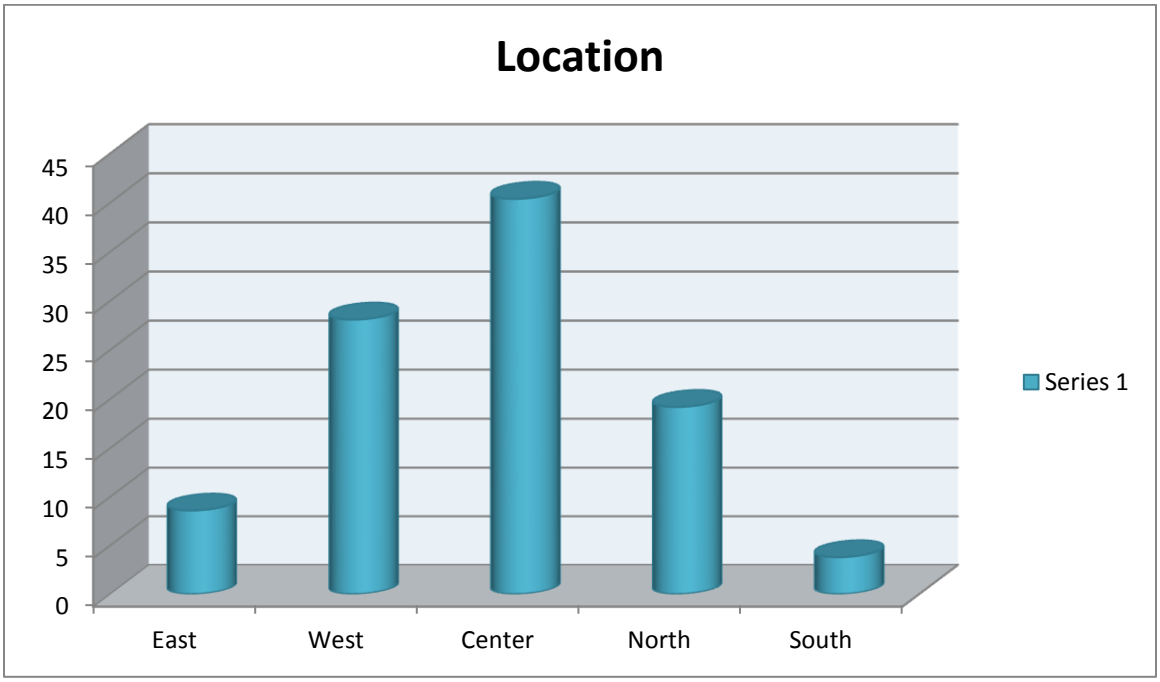



Figure (4.3): Percentage of participant's ethnicity.

Table (4.4) Shows distribution of participants according their BMI classes, represented as frequencies and percentages (%).

| BMI classes | Frequency | Percent |
|---|---|---|
| underweight | 6 | 2.1 |
| Normal | 123 | 42.1 |
| Over weight | 130 | 44.5 |
| Obese | 33 | 11.3 |
| Total | 292 | 100.0 |

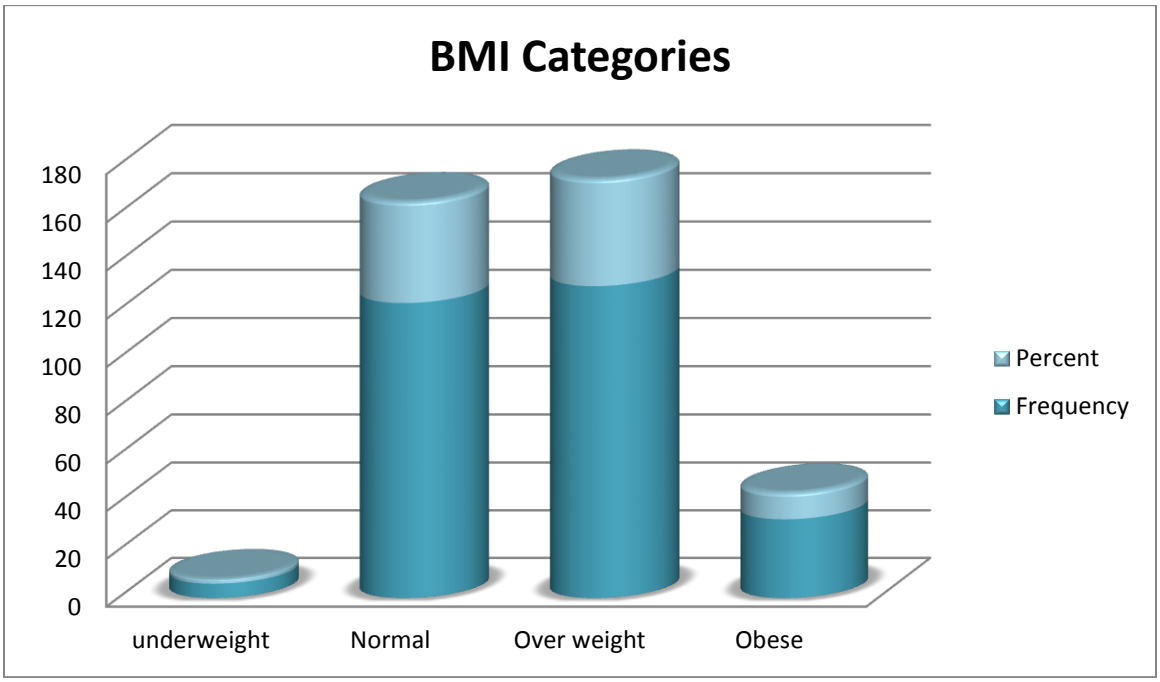



Figure (4.4): Percentage of participant's BMI

Table (4.5): Provides the general characteristics of the study population (n=292) based on baseline demographics, anthropometric and CT measurement, represented as Minimum, Maximum, Mean and Std. Deviation

| Variables | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|
| Age/ year | 18.00 | 88.00 | 48.07 | 15.56 |
| Weight/ kg | 37.50 | 130.00 | 68.17 | 13.34 |
| Height/m | 1.20 | 1.87 | 1.63 | .09 |
| BMI/kg/$m^2$ | 15.21 | 45.53 | 25.66 | 4.59 |
| WC/cm | 40.00 | 144.00 | 85.90 | 16.54 |
| Rt lobe/HU | 29.00 | 74.20 | 56.69 | 7.03 |
| Lt lobe/HU | 33.55 | 80.15 | 57.40 | 7.62 |
| LA/HU | 31.68 | 75.20 | 57.04 | 6.79 |
| Spleen/HU | 32.50 | 67.60 | 48.98 | 5.42 |
| L/S | .62 | 1.75 | 1.18 | .18 |

BMI =body mass index , WC= waist circumference , LA= liver attenuation

Table (4.6): Provides the general characteristics of the study population (n=292) based on baseline medical history and patient habits.

| Variables | Frequency | percentages |
|---|---|---|
| Diabetes mellitus, yes | 29 | 9.9 |
| Hypertension. yes | 49 | 16.8 |
| Physical activities, yes | 10 | 3.4 |
| Drink coffee, yes | 169 | 57.9 |
| Smoker, yes | 20 | 6.8 |

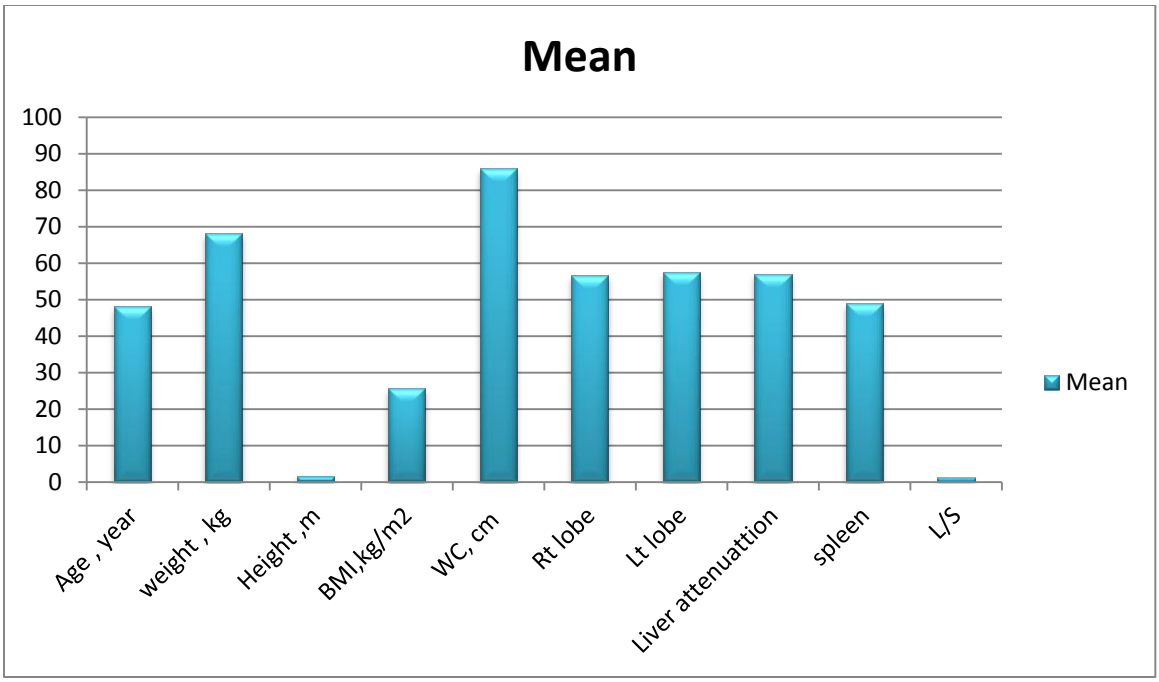



Figure (4.5): Characteristics of the study population based demographics, anthropometric and CT measurement

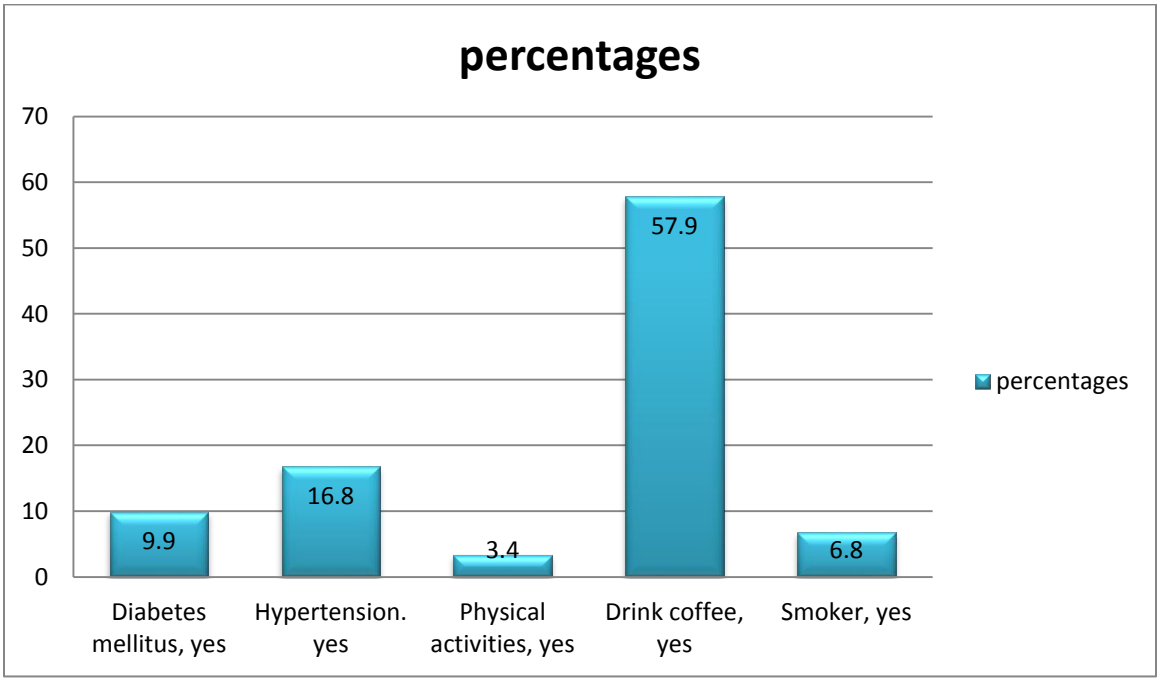



Figure (4.6): Characteristics of the study population based on medical history and patient habits

Table (4.7): Show the percentage of NAFLD in Sudanese population

| | Frequency | Percentage( % ) |
|---|---|---|
| NAFLD | 43 | 14.7 |
| Normal | 249 | 85.3 |
| Total | 292 | 100.0 |

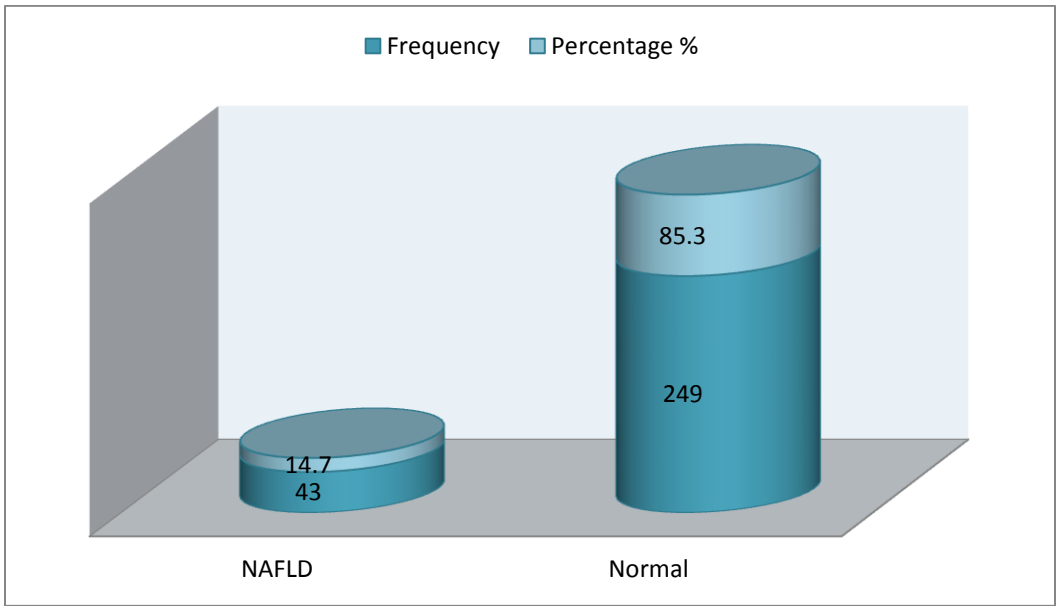



Figure (4.7): Show the percentage of NAFLD and normal subject.

Table (4.8): Comparison of the Socio-demographic, Anthropometric and liver attenuations between Those with NAFLD and Normal Subjects.

| Variables | Normal | NAFLD | P-value |
|---|---|---|---|
| Age/ year | 47.32±15.94 | 52.37 ±12.42 | .022* |
| weight / kg | 67.41±13.05 | 72.57± 14.33 | .031* |
| Height/m | 1.63±.09 | 1.65± .09 | .073 |
| BM/ kg/m$^2$ | 25.52±4.64 | 26.48±4.23 | .181 |
| WC/ cm | 85.41±16.74 | 88.61±15.29 | .241 |
| Rt lobe/ Hu | 58.23±5.78 | 47.74±6.99 | .000* |
| Lt lobe/ Hu | 58.95±6.57 | 48.42±7.10 | .000* |
| LA/ Hu | 58.59±5.59 | 48.08±6.20 | .000* |
| Spleen/Hu | 48.39±5.07 | 52.39±6.15 | .000* |
| L/S | 1.22±.15 | .92±.01 | .000* |

*Mean significant relation at p<0.05, body mass index, WC= waist circumference, LA= liver attenuation, L/S= Liver to spleen ratio

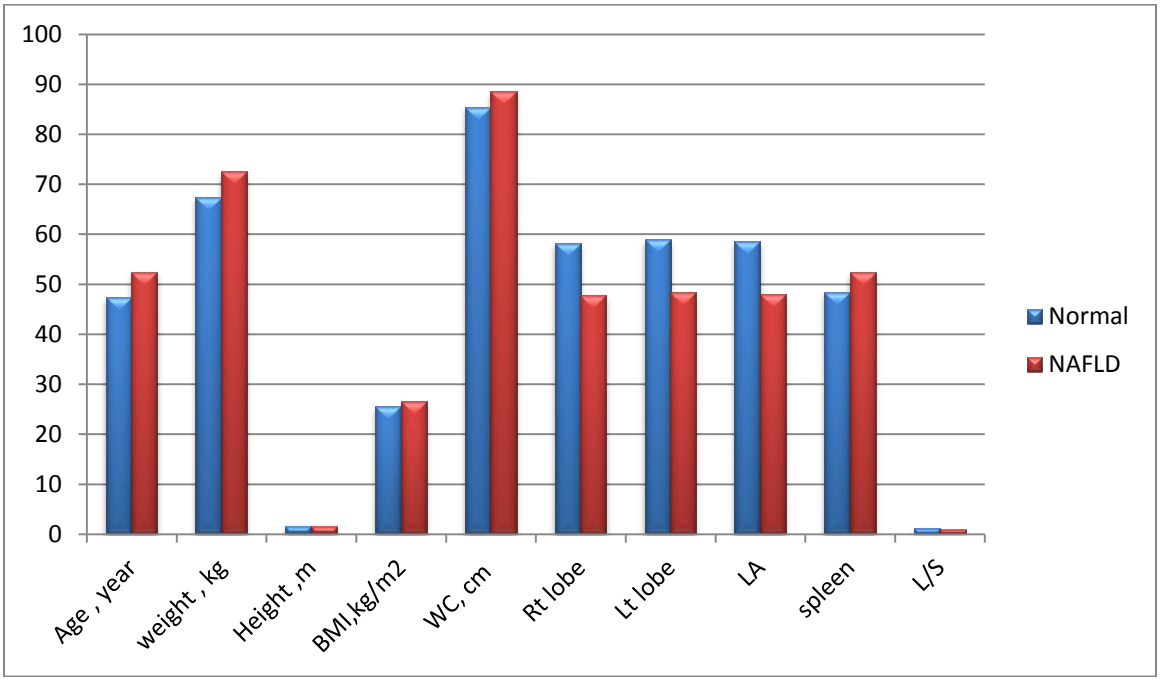



Figure (4.8): Show Comparing of the Socio-demographic, Anthropometric and liver attenuations between NAFLD and Non-NAFLD Subjects

Table (4.9): Comparing between subject with NAFLD and normal one based on medical history and patient habits.

| Variables | NAFLD | Normal subject | P- value |
|---|---|---|---|
| Male | (22)51.2% | (120)48.2% | .744 |
| Female | (21) 48.8% | (129) 51.8% | |
| Diabetes mellitus, yes | (3)10.3% | (26)89.7% | .592 |
| Hypertension. yes | (10)23.3% | (39)76.7% | .267 |
| Physical activities, yes | (1) 10% | (9) 90% | 1.00 |
| Drink coffee, yes | (24)55.8% | (145)58.2% | .867 |
| Smoker, yes | (2)10% | (18) 90% | .748 |

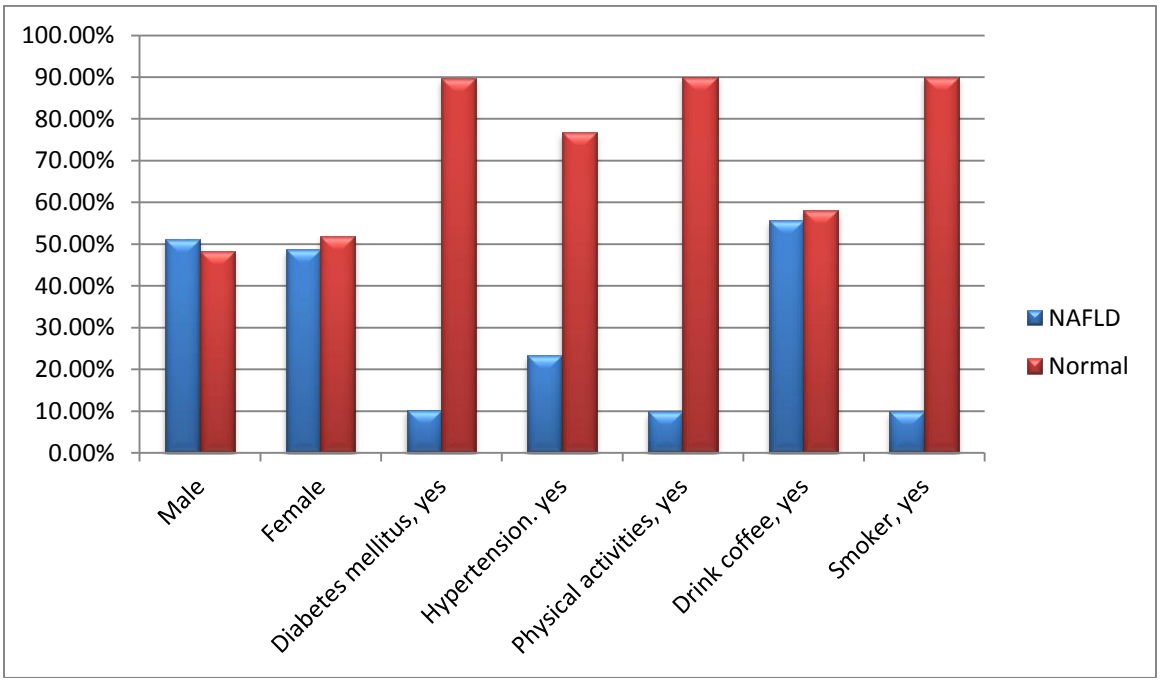



Figure (4.9): Show the Comparison between NAFLD and Normal subjects based on medical history and patient habits.

Table (4.10): percentage of NAFLD and normal subject according to age categories

| | | Age categories | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | | 18 -27 | 28 - 37 | 38 - 47 | 48 - 57 | 58 - 67 | 68 -77 | 78 - 88 | |
| NAFLD | Number | 0 | 5 | 11 | 11 | 12 | 3 | 1 | 43 |
| | Percentages | 0.0% | 11.6% | 25.6% | 25.6% | 27.9% | 7.0% | 2.3% | 100.0% |
| | Prevalence | 0.0% | 12.2% | 16.2% | 16.4% | 23.5% | 11.5% | 14.3% | 14.7% |
| | | | | | | | | | |
| Normal | Number | 32 | 36 | 57 | 56 | 39 | 23 | 6 | 249 |
| | Percentages | 12.9% | 14.5% | 22.9% | 22.5% | 15.7% | 9.2% | 2.4% | 100.0% |
| | Prevalence | 100.0% | 87.8% | 83.8% | 83.6% | 76.5% | 88.5% | 85.7% | 85.3% |
| | | | | | | | | | |
| Total | Number | 32 | 41 | 68 | 67 | 51 | 26 | 7 | 292 |
| | Percentages | 11.0% | 14.0% | 23.3% | 22.9% | 17.5% | 8.9% | 2.4% | 100.0% |
| | Prevalence | 100.0% | 100.0% | 100.0% | 100.% | 100.0% | 100.0% | 100% | 100.0% |
| | | | | | | | | | |

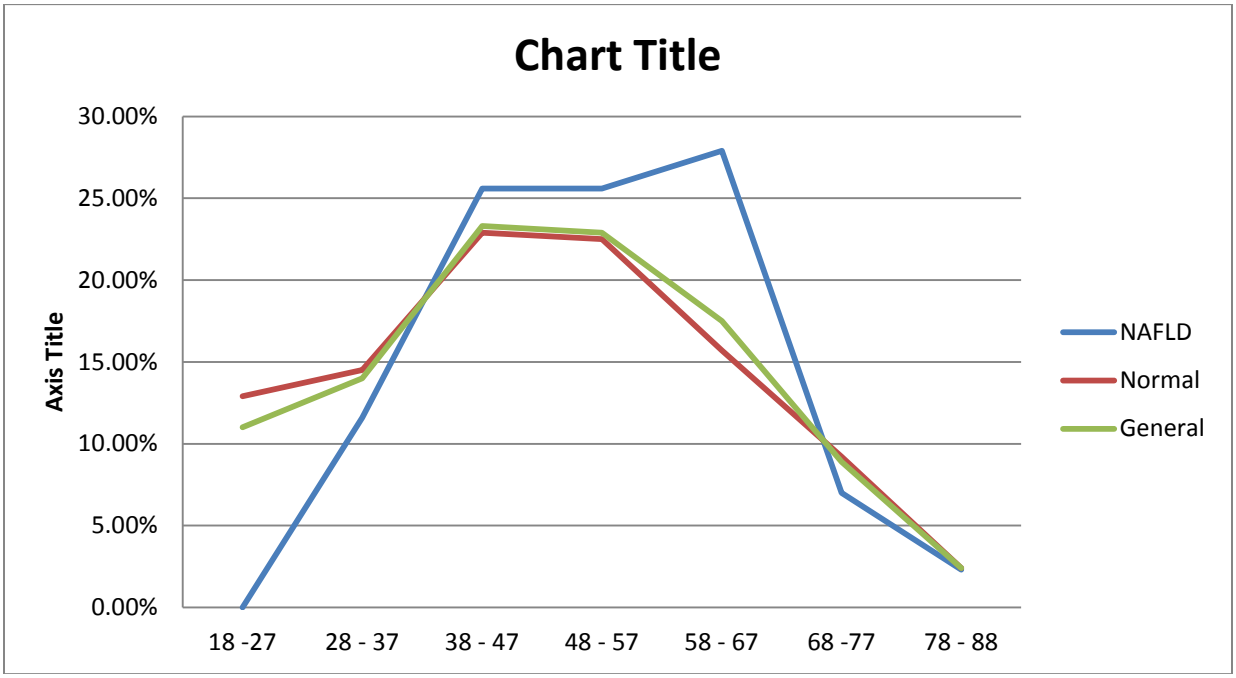



**Figure 4.10**: Prevalence and percentage of NAFLD and normal according to age categories.

**Table 4.11**: Distribution of NAFLD and normal according to ethnicity (location in Sudan)

| Location | General | NAFLD | Normal subject |
|---|---|---|---|
| East | (25) 8.6% | (3) 7.0% | (22) 8.8% |
| West | (82) 28.1% | (10) 23.3% | (72) 28.9% |
| Center | (118) 40.4% | (18) 41.9% | (100) 40.2% |
| North | (56) 19.2% | (11) 25.6% | (45) 18.1% |
| South | (11) 3.8% | (1) 2.3% | (10) 4.0% |
| Total | (292)100% | (43)100% | (249)100% |

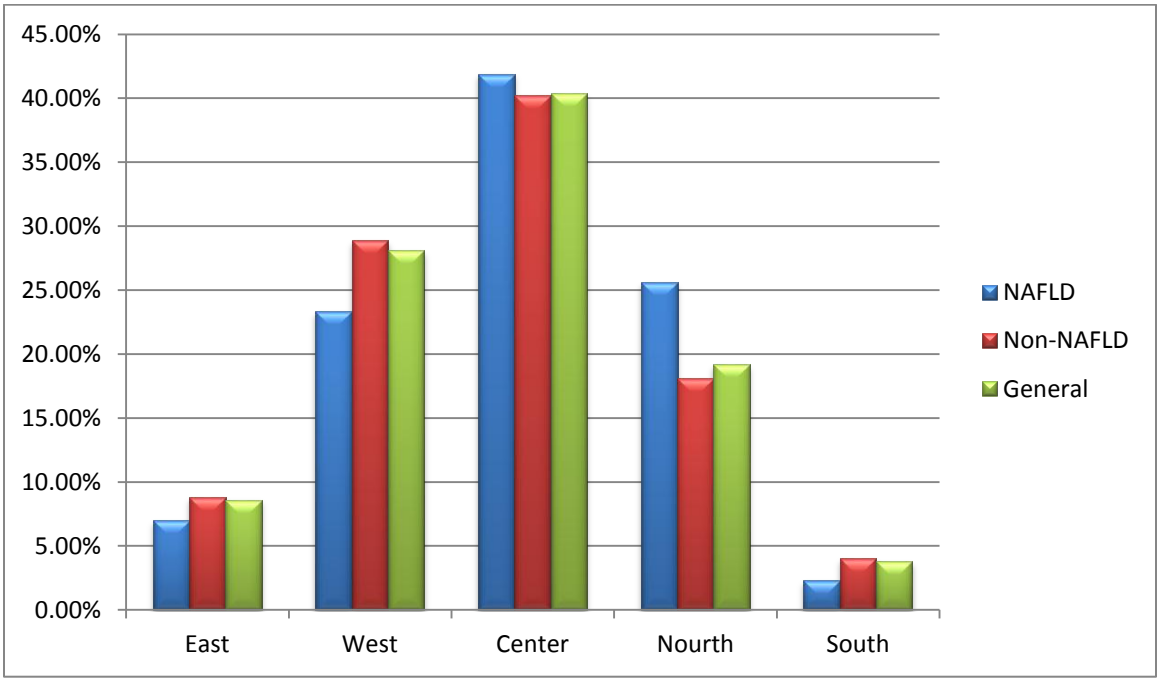



Figure 4.11: Show Distribution of NAFLD and Normal subject according to ethnicity (location in Sudan)

Table (4.12): Distribution of NAFLD and Normal subject related to BMI categories

| | | BMI Categories | | | | |
|---|---|---|---|---|---|---|
| | | Under weight | Normal | Over weight | Obese | Total |
| NAFLD | Number | 0 | 17 | 18 | 8 | 43 |
| | Percentages | 0.0% | 39.5% | 41.9% | 18.6% | 100.0% |
| | Prevalence | 0.0% | 13.8% | 13.8% | 24.2% | 14.7% |
| | | | | | | |
| Non-NAFLD | Number | 6 | 106 | 112 | 25 | 249 |
| | Percentages | 2.4% | 42.6% | 45.0% | 10.0% | 100.0% |
| | Prevalence | 100.0% | 86.2% | 86.2% | 75.8% | 85.3% |
| | | | | | | |
| Total | Number | 6 | 123 | 130 | 33 | 292 |
| | Percentages | 2.1% | 42.1% | 44.5% | 11.3% | 100.0% |
| | Prevalence | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |
| | | | | | | |

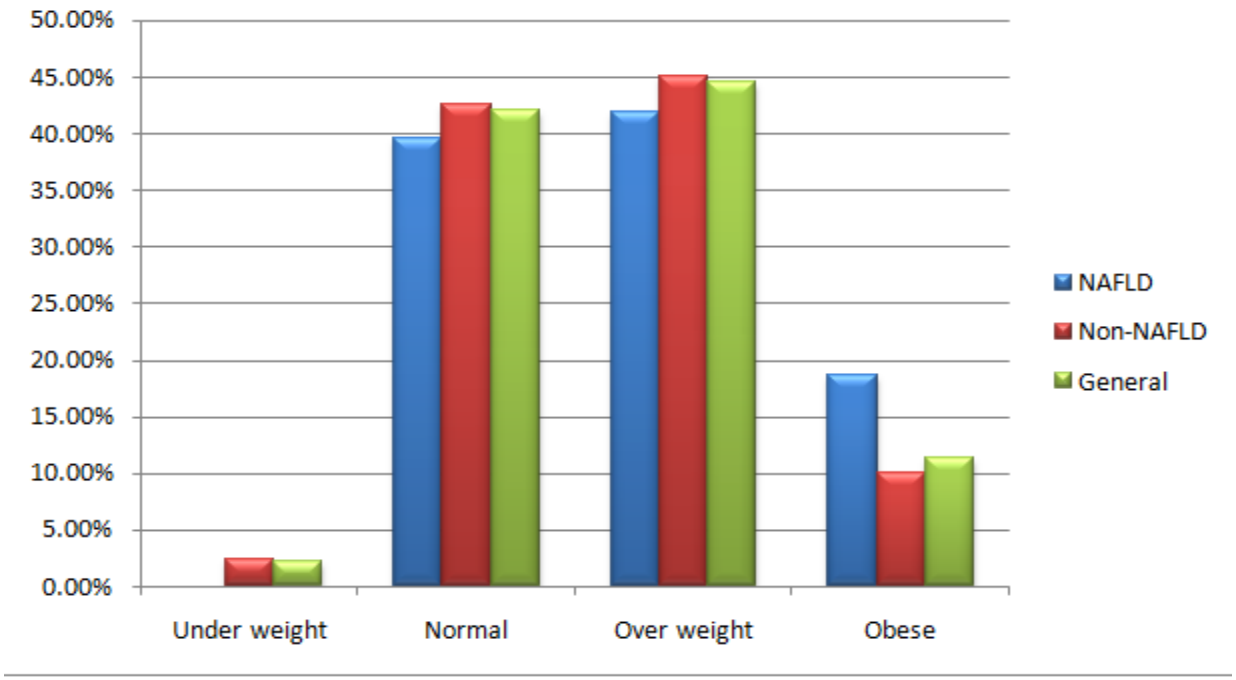



Figure (4.12): compared between general population , NAFLD and Normal subject according to the body mass index categories

Table (4.13)**:** Bivariate correlation to determine the associated risk factors of NAFLD in Sudanese

| | | Sex | Age | BW | BH | BMI | HT | DM | Smoker | PHA | DC |
|---|---|---|---|---|---|---|---|---|---|---|---|
| NAFLD | Correlation Coefficient | .021 | -.114 | -.142* | -.091 | -.100 | .072 | -.041 | -.036 | -.025 | -.017 |
| | Sig. (2-tailed) | .720 | .051 | .015 | .122 | .088 | .220 | .485 | .538 | .669 | .768 |
| | N | 292 | 292 | 292 | 292 | 292 | 292 | 292 | 292 | 292 | 292 |
| L/S | Correlation Coefficient | .086 | -.123* | -.107 | -.085 | -.071 | .038 | -.009 | -.004 | -.056 | 004 |
| | Sig. (2-tailed) | .144 | .036 | .067 | .145 | .229 | .518 | .874 | .948 | .338 | .950 |
| | N | 292 | 292 | 292 | 292 | 292 | 292 | 292 | 292 | 292 | 292 |

*Mean significant relation at p<0.05, BW= Body weight, BH= body height, HT= hypertension, DM=Diabetic mellitus, PHA=physical activities, DC= drink coffee, L/S=Liver to spleen ration

Table (4.14): Binary logistic regression use body weigh as independent variable.

**Variables in the Equation**

| | | B | S.E. | Wald | Df | Sig. | Exp(B) | 95% C.I.for EXP(B) | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Lower | Upper |
| Step 1[a] | weight | -.026 | .011 | 5.283 | 1 | .022 | .974 | .953 | .996 |
| | Constant | 3.583 | .830 | 18.642 | 1 | .000 | 35.990 | | |

a. Variable(s) entered on step 1: weight.

Table (4.15): linear regression use the age as independent variable

**Coefficients[a]**

| Model | | Unstandardized Coefficients | | Standardized Coefficients | T | Sig. | 95.0% Confidence Interval for B | |
|---|---|---|---|---|---|---|---|---|
| | | B | Std. Error | Beta | | | Lower Bound | Upper Bound |
| 1 | (Constant) | 1.240 | .033 | | 37.385 | .000 | 1.174 | 1.305 |
| | age | -.001 | .001 | -.117 | -2.005 | .046 | -.003 | .000 |

a. Dependent Variable: liver to spleen ratio

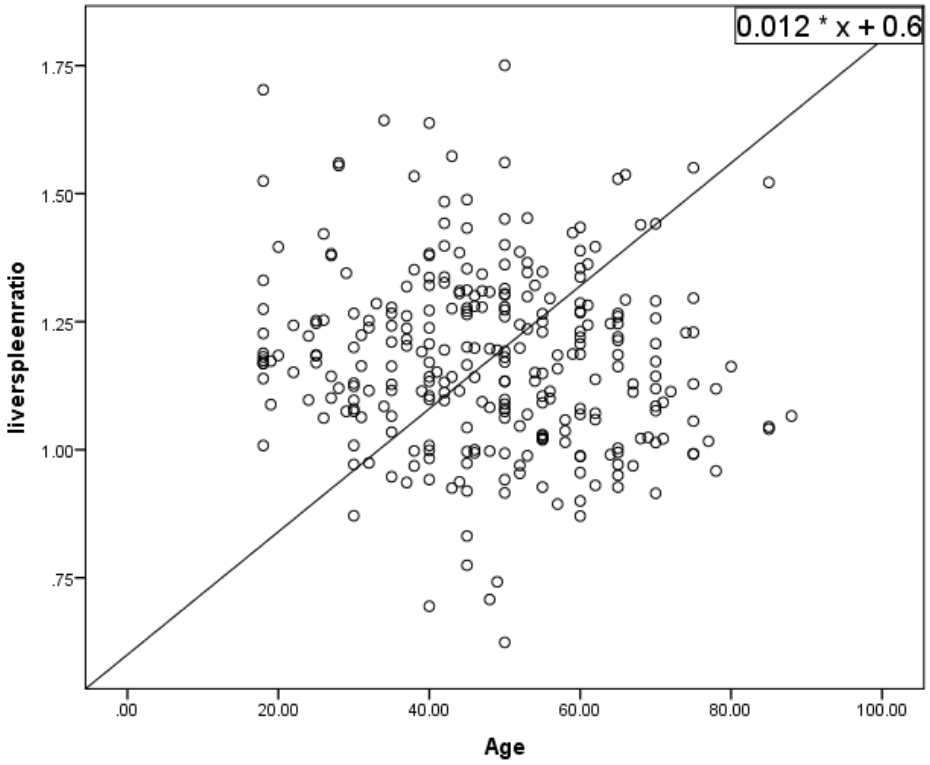



Figure (4.13): Show the scatter plot for the linear relation between age and liver to spleen ratio.

# Chapter Five

# Discussion, Conclusion and Recommendations

## 5.1 Discussion:

Non-alcoholic fatty liver disease (NAFLD), a clinical syndrome that is predicted to affect millions of people worldwide, will become the next global epidemic (Sherif et al., 2016) .The natural history of NAFLD ranges from asymptomatic indolent to the end stage liver disease.

The prevalence of NAFLD in industrial countries ranges from 20% to 60% (Bellentani et al.,2004) , Israel 30% (Zelber-Sagi el al., 2006) , Italy 23% (Bedogni et al., 2005), Saudi Arabia16.6% (Al-hamoudi et al.,2012) and Nigeria 8.7% (Asabamak et al., 2016) while the prevalence of NAFLD in this study was found to be 14.7% Table (4.7).The discrepancy between the studies across the world is probably due to the methods of sample selection, modalities used for diagnosis and diversity of lifestyles and dietary habits in different areas.

On the other hand, if we compare this figure with the previous studies among Sudanese population (15% to 20%) it appears to be within range. A study conducted by Almobarak et al in 2014 looked at the radiological prevalence of NAFLD in Khartoum -Sudan. In their study, a total of 100 subjects were included in the study. The Prevalence was 20%. Another study done by Elkhader et al (2013) among 500 Sudanese adults aged 15 to 80 years. Used the ultrasound as diagnostic tools, found that the prevalence of NAFLD was 15%, 4.4% in males and 6.6% in females. The difference in prevalence of NAFLD in our study compared to Al-mobarak and colleagues may be attributed to the sample size and the diagnostic tool. In our study, we used computed tomography to diagnose NAFLD while they

used the ultrasound. In addition Al-mobarak used a small sample size which may not reflect the actual characteristic of the study population.

NAFLD is a disease that can occur in all sexes, ages, and ethnic groups. According to the previous studies the Male sex is a predictor of incidence of fatty liver. The data of higher prevalence of NAFLD among men compared to women was supported from studies in Shanghi-China (Hu et al., 2012), Framingham (Speliotes et al., 2010) and, Spain (Caballería et al., 2010). Our study revealed that the prevalence of NAFLD was estimated to be 15.5% for men and 14% for women table 4.9. So the prevalence of NAFLD among Sudanese is higher in male than females but with no significant correlation, this is similar to what found in Al-moubarak study in which women had same prevalence rates as men 45% and 55% respectively. The theoretical explanation for this condition is related to role of endocrine. Consistent with a protective role of estrogens, during their fertile period, women tend to be spared from NAFLD compared to men. This is why the prevalence in men higher than in women (Bertolotti et al., 2014).

NAFLD was mostly found in the middle age and old groups (Karnikowski et al., 2007, Frith et al., 2009 & Yang et al., 2011). In the present study, Subjects with NAFLD was significantly older than Non-NAFLD subjects (52.37 ±12.42 Vs 47.32±15.94) as show in Table 4.8. The peak prevalence was in the (58–67) age groups; up to 23.5% of subjects had NAFLD in this is group Table 4.10. The prevalence is gradually increases in all age groups but declines in those subjects in their seventies figure 4.10. This pattern of prevalence is called "inverted U-Shaped" which found in many studies around the world as mention by Bertolotti et al., (2014). The decline which occurs in older subjects attributed to the progression of the disease in elderly subjects to liver fibrosis. Previous studies found that:older age was significantly associated with severe fibrosis. (Miyaaki et al., 2008)

The prevalence of NAFLD was differs by ethnicity and location in Sudan (Center: 41.9%; North: 25.6%; West: 23.3%, East: 7.0% and South: 2.3%) Table (4.11).Most of NAFLD subject were found at the center (khartom,Omdurman and Bahri) and this may attributed to the life style (sedentary life ) and eating habits which may include fast food and soft drinks lead to increase body weight which is the associated risk factor of NAFLD in Sudanese.

NAFLD was earlier reported to occur just among obese individuals (BMI $\geq$ 25). Thus, until recently, it was generally assumed that NAFLD occurs only in obese individuals. However, more recently, it is being recognized that NAFLD may also occur in non-obese subjects (i.e., those with normal body mass index [BMI $\leq$ 25]) (Younossi et al., 2012, Kim et al., 2011 &Das et al 2010). In our study the NAFLD show different prevalence with in different BMI categories (obese 24.2%, overweight 13.8%, Normal 13.8% and underweight 0.0%) Table (4.12). So the highest prevalence occurs in obese group and there is direct proportion between the NAFLD and the BMI but with no significant relation.

Nonalcoholic fatty liver disease is more prevalent in cohorts of patients with preexisting metabolic conditions than the general population. Specifically, type II diabetes mellitus and NAFLD have a particularly close relationship. A study of patients with type II diabetes mellitus reported a 69% prevalence of ultrasonographic NAFLD (Leite, 2009). In this study the prevalence among diabetic patient is 10%, which is lower than the prevalence of NAFLD in the general population as show in Table (4.9). And also the result found there is no significant relation between diabetic mellitus and NAFLD in Sudanese. This attributed to the low number of diabetic patients and the small sample size in this study.

The major risk factors of NAFLD are: obesity, hyperlipidemia, diabetes mellitus (DM) and metabolic syndrome (insulin resistance syndrome) which represent the

strongest risk factor, but it varies with different communities (Farrell & Larter, 2006). In this study: the body weight and age were found to be the associated risk factor of NAFLD in Sudanese  table 4.13.This match what found by Elkhader et al (2013).

The prevalence of non-alcoholic fatty liver disease may be higher than the result found in this study and this is due to the use of CT scan to diagnose the disease. CT scan can identify cases of moderate and severe fatty liver, but do not recognize the cases of mild liver fat. Therefore, there are cases not recognized which makes the prevalence more than what is mentioned in the study

## 5.2 Conclusion:

- The prevalence of NAFLD in Sudanese is 14.7% in general, which is Low in compare with reported figure in western countries and Asia.
- Age and body weight are the major associated risk factors of NAFLD in Sudanese population.
- Female had same prevalence of NAFLD as male in Sudanese population.
- Obese subject had the highest prevalence but NAFLD also affect nonobese subject in Sudanese.
- NAFLD subjects were older and had higher body weight than normal subject.
- There is no significant relation between the sex, hypertension, diabetes mellitus and NAFLD in Sudanese population.
- NAFLD is more common at the center of Sudan((khartom,Omdurman and Bahri) in compare with the other location

## 5.3 Recommendations:

- Unenhanced CT scan can be used as screening and diagnostic tools for NAFLD .And the disadvantage of the high radiation dose of the CT can be avoided by making a Single slice, low dose CT scan.
- The importance of body weight control, not only in the obese but also in nonobese subjects, for reducing the risk of or preventing NAFLD.
- As NAFLD has the possibility of progression toward end-stage liver Disease, appropriate action should be undertaken in our region for screening and control of this disease. Epidemiological survey must be conducted by the government to find out the characteristic and severity of NAFLD in Sudan.
- Awareness of NAFLD epidemiology, natural history and methods of management allows prompt recognition of the disease and the management of complications.
- There is an idea that must be applied and put into practice. Measurement of CT numbers of both liver and spleen should be taken in all a bdomen CT scan to facilitate the detection of cases of fatty liver.
- Future studies should focus on studying the relationship between NAFLD and diabetes to determine the characteristics of NAFLD in diabetic patients and non-diabetics.
- Future studies should focus on studying the prevalence of NASH and liver fibrosis in Sudanese because it is still a blind area.

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# Appendices (1)
# Images

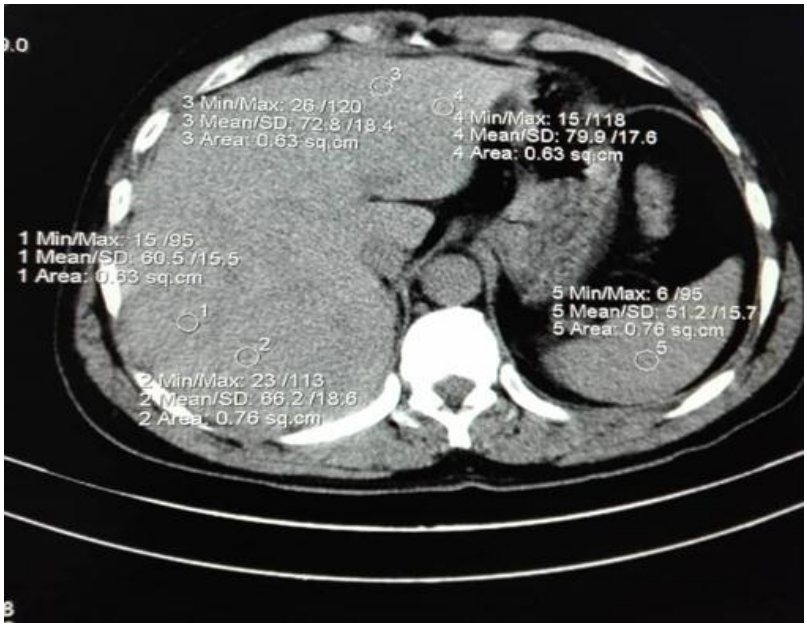


Image No (1) : Male , 36 years old ,1 Rt lobe =66.2 HU, 2 Rt lobe 60.5 HU, 1Lt lobe = 72.8, 2Lt lobe =79.9,spleen attenuation = 51.2

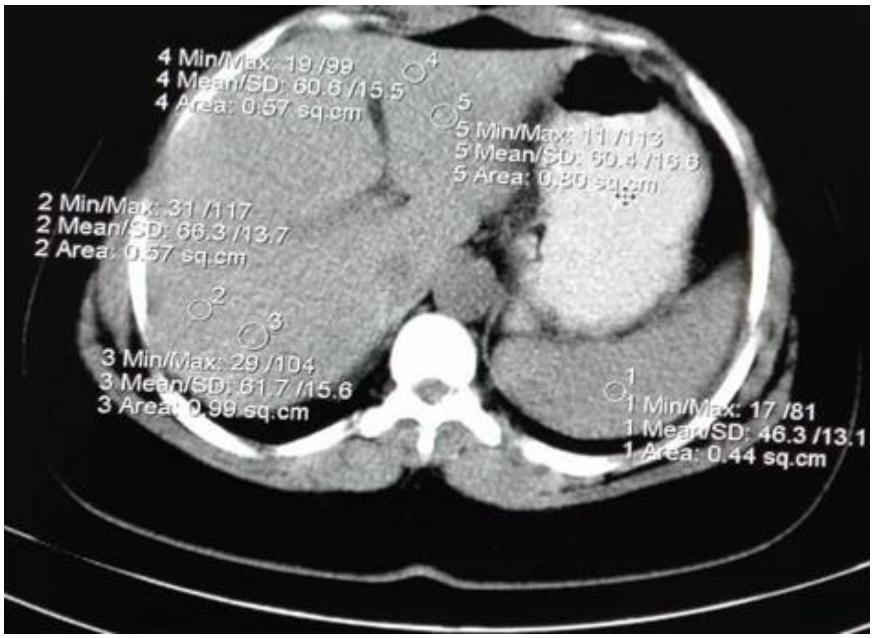

Image No (2) : Female , 35 years old ,1 Rt lobe =61.7 HU, 2 Rt lobe 66.3 HU, 1Lt lobe = 60.6, 2Lt lobe =60.4,spleen attenuation = 46.3

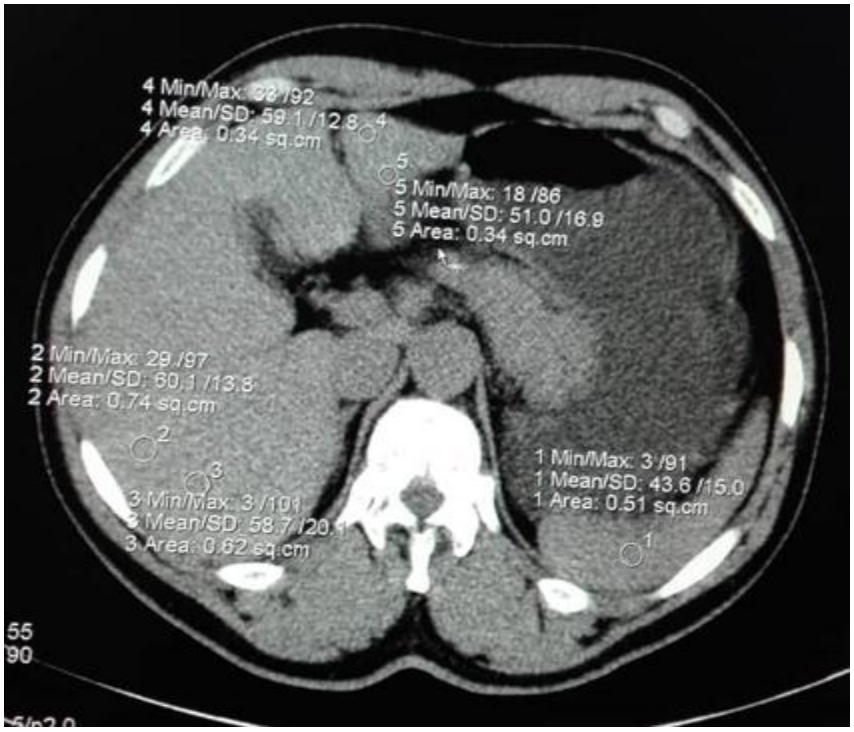


Image No (3) : Male , 52years old ,1 Rt lobe =58.7 HU, 2 Rt lobe 60.1 HU, 1Lt lobe = 59.1, 2Lt lobe =51 ,spleen attenuation = 43.6

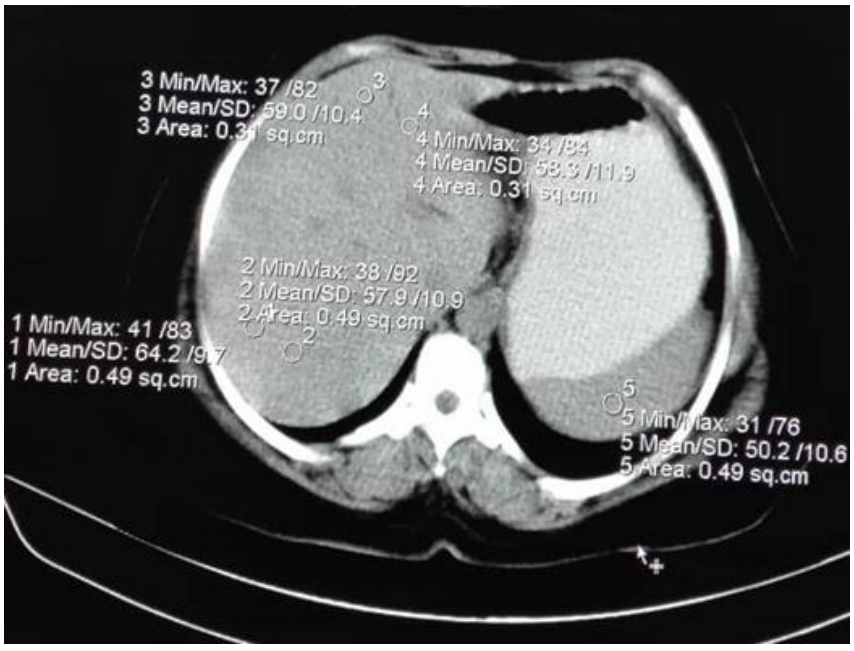

Image No (4) : Female , 43years old ,1 Rt lobe =57.9 HU, 2 Rt lobe 64.2 HU, 1Lt lobe = 59, 2Lt lobe =58.3,spleen attenuation = 50.2

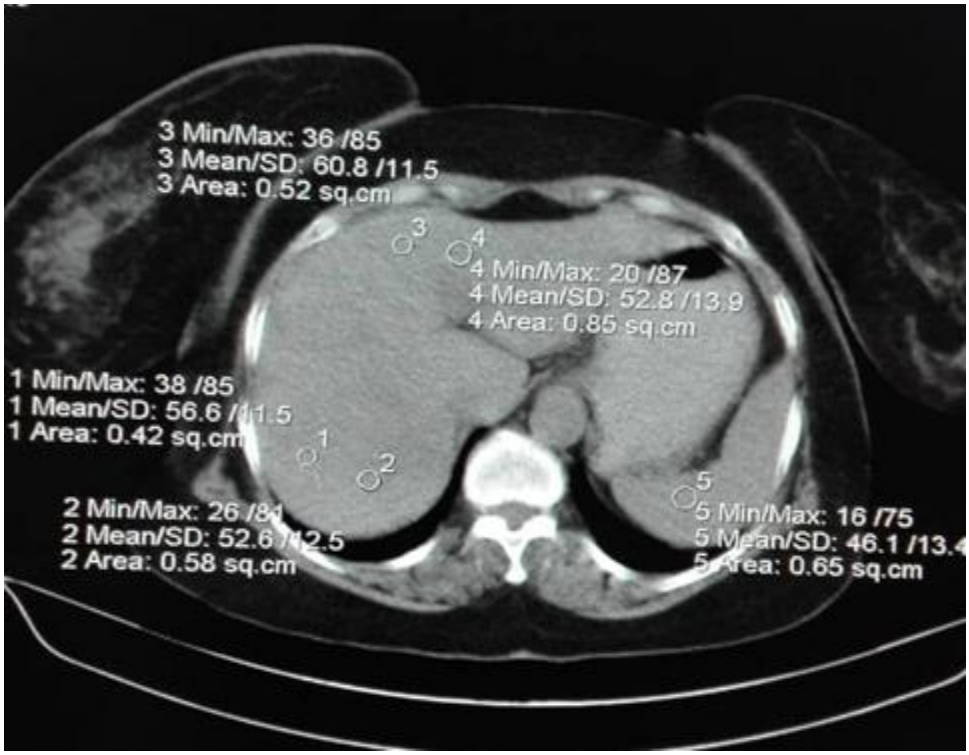


Image No (5) : Female , 65 years old ,1 Rt lobe =52.6 HU, 2 Rt lobe 56.6 HU, 1Lt lobe = 52.8 , 2Lt lobe =60.8 ,spleen attenuation = 46.1

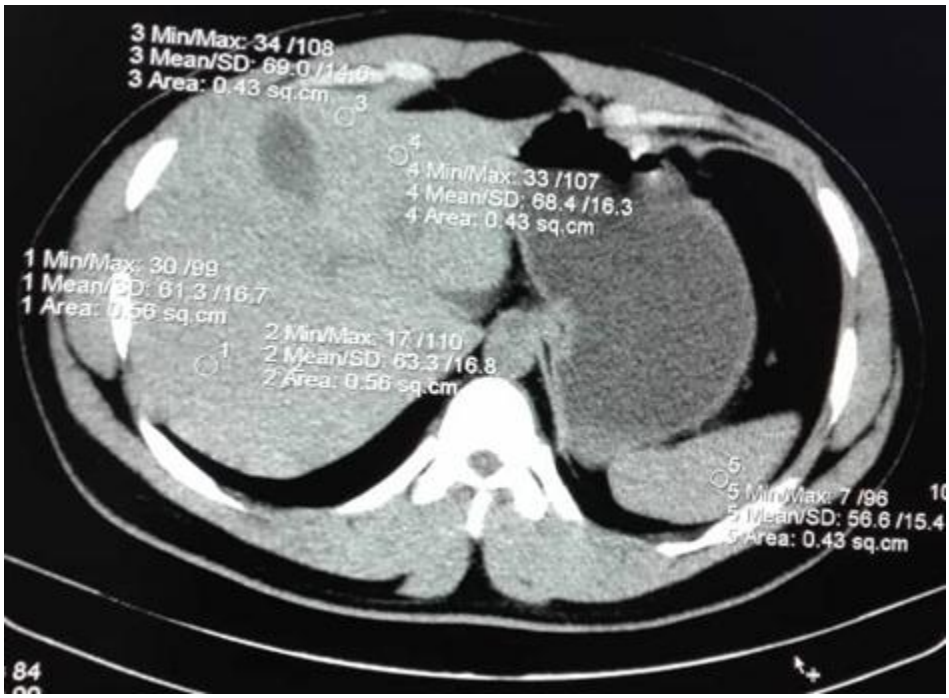

Image No (6) : Male , 33 years old ,1 Rt lobe =63.3 HU, 2 Rt lobe 61.3 HU, 1Lt lobe = 68.4 , 2Lt lobe =69 ,spleen attenuation = 56.6

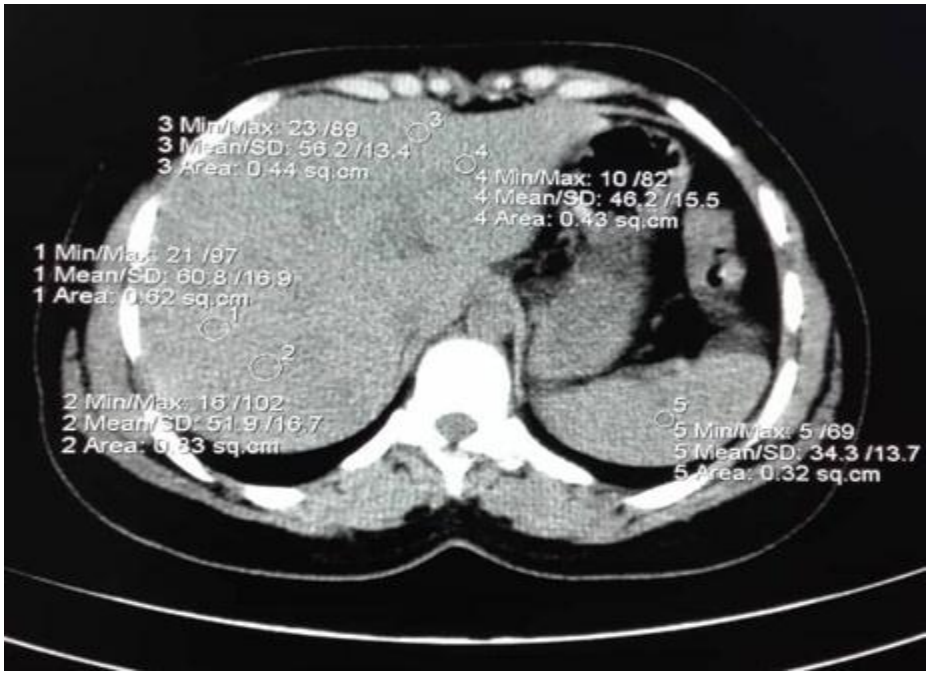


Image No (7) : Female , 30 years old ,1 Rt lobe =51.9 HU, 2 Rt lobe 60.8 HU, 1Lt lobe = 56.2 , 2Lt lobe =46.2 ,spleen attenuation = 34.3

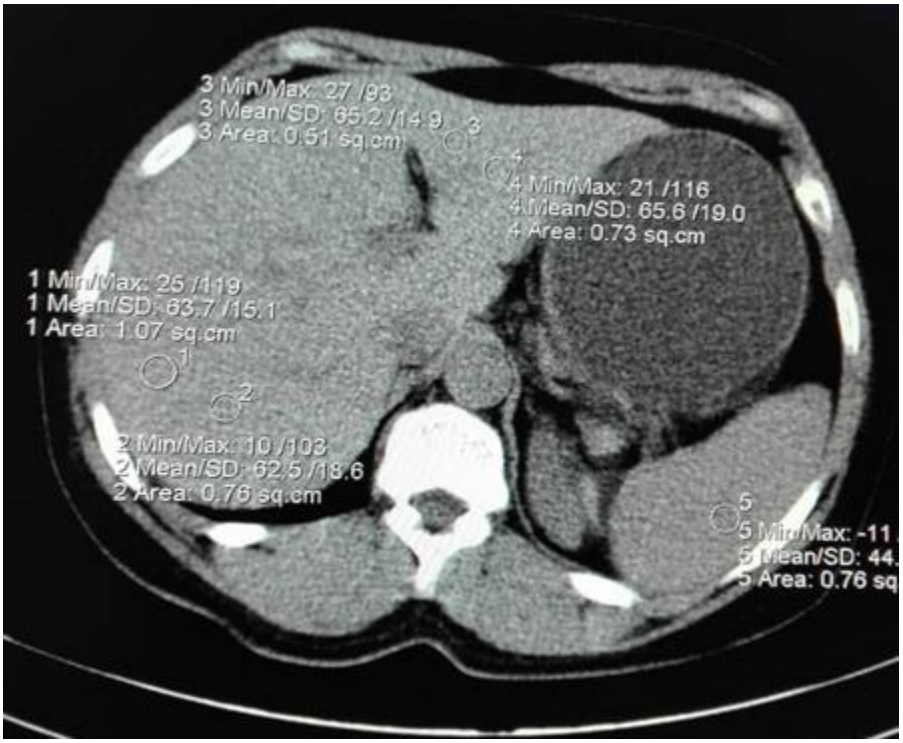

Image No (8) : Female , 50 years old ,1 Rt lobe =62.5 HU, 2 Rt lobe= 63.7 HU, 1Lt lobe = 65.2 , 2Lt lobe =65.6 ,spleen attenuation = 44

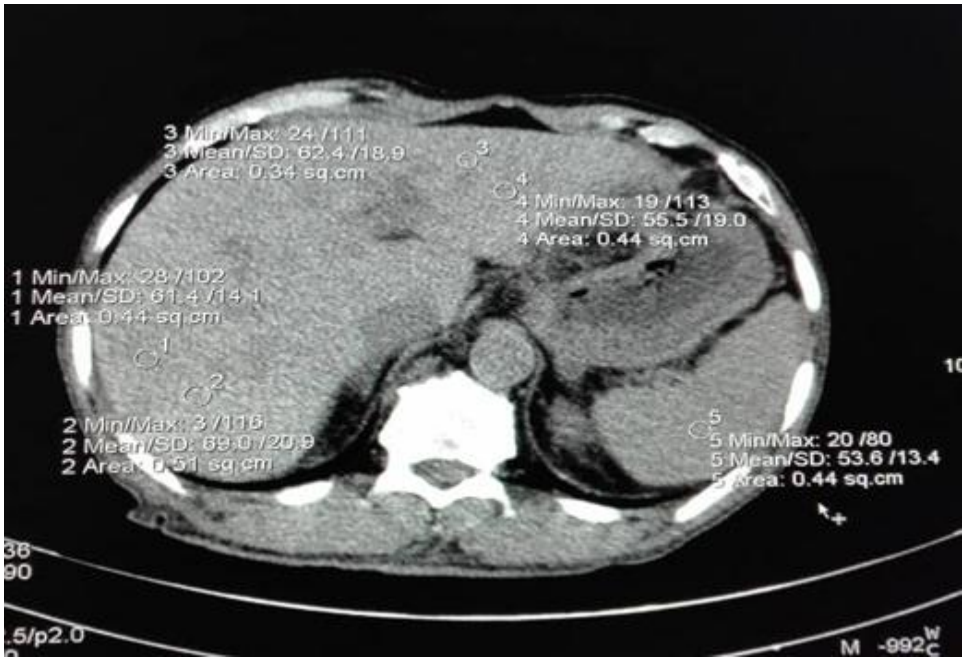


Image No (9) : Male , 80 years old ,1 Rt lobe =69 HU, 2 Rt lobe= 61.4 HU, 1Lt lobe = 62.4 , 2Lt lobe =55.5 ,spleen attenuation = 53.6

# Appendices (2)

## Data collection sheet

| patient demographics | | | | | |
|---|---|---|---|---|---|
| I.D: | | Age: | | ☐ female ☐ male | |
| Ethnic: | East: | West | Middle | North | South |

| Anthropometric measurement | | | |
|---|---|---|---|
| Weight: | Height: | BMI: | Waist circumference: |

| Medical history | | | |
|---|---|---|---|
| **Does the patient have:** | | | |
| Hypertension | ☐ yes | ☐ No | |
| Type 2 diabetes | ☐ yes | ☐ No | |

| Patient habits | | | | |
|---|---|---|---|---|
| **Does the patient:** | | | | |
| Have smoking habits | ☐ yes | ☐ No | ☐ EX | |
| Alcohol consumption | ☐ yes | ☐ No | ☐ EX | If yes how much per day |
| Making exercise | ☐ yes | ☐ No | | |
| Drink coffee | ☐ yes | ☐ No | | |
| Take medication | ☐ yes | ☐ No | | Type of drug |

| CT Measurement | | |
|---|---|---|
| CT number of liver Rt lobe | CT number of liver Lt lobe : | CT number of spleen |
| **1** | 1 | |
| 2 | 2 | |