الآيه

قال تعالى:

(أَلَمْ تَرَ أَنَّ اللَّهَ أَنْزَلَ مِنَ السَّمَاءِ مَاءً فَأَخْرَجْنَا بِهِ ثَمَرَاتٍ مُخْتَلِفاً أَلْوَانُهَا وَمِنَ الْجِبَالِ جُدَدٌ بِيضٌ وَحُمْرٌ مُخْتَلِفٌ أَلْوَانُهَا وَغَرَابِيبُ سُودٌ * وَمِنَ النَّاسِ وَالدَّوَابِّ وَالْأَنْعَامِ مُخْتَلِفٌ أَلْوَانُهُ كَذَلِكَ إِنَّمَا يَخْشَى اللَّهَ مِنْ عِبَادِهِ الْعُلَمَاءُ إِنَّ اللَّهَ عَزِيزٌ غَفُورٌ)

صدق الله العظيم

سورة فاطر (27-28)

Dedication

To the candles lighting my life … my mother, father.

To the soul of my grandmother who sacrificed her life for all of us.

To My brother and sisters who are always keeping me in their prayers, believing in me and supporting my decisions.

To My kids for taking me in and providing the love, support and comfort that can only come from family

To my friends, colleagues and teachers for helping me to perform this work.

To all whom I love;

I dedicate this work

HUDA

Acknowledgements

Praise and thanks to Allah for his countless blessing.

I would like to express my gratitude sincerely to my supervisor Dr. Afraa sidig for her continuous support, patience, motivation, enthusiasm, and immense knowledge. Her guidance helped me during all the term of this work .

I wish to express my grateful and sincere thanks to Dr. Hanady Elias Al-Ghad International Colleges for Applied Medical Sciences, department of medical imaging technology, Saudi Arabia, for her continued support throughout this study.

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Furthermore, I wish to thank all who made this work possible with their support, advice, time and to all others with great love and many thanks for their insights and unlimited support.

Abstract

This study was a descriptive - case-control study done in Kingdome of Saudi Arabia –Jeddah city at "International Medical Centre" in the period from January 2018 to October 2020.

Group of 196 subjects 100 of them have had type II diabetic Mellitus patients and 96 non-diabetic patients as a control group aged from 31 to 85 years, 54% were males and 46% females.

Over time high blood glucose levels cause damage to most body organs, the aim of this study will be to understand affecting of diabetes on the liver, spleen, and pancreas and evaluate liver function among diabetes patients.

The objectives of this study to measure the CT number of liver, spleen, and pancreas also the size of liver and spleen in diabetic & non-diabetic groups, and to evaluate the spleen to liver size ratio in diabetic & non-diabetic groups. And to correlate after measuring the attenuation and size of liver, spleen, and pancreas by CT with age, body mass index, type of diabetes, and duration of diabetes.

The data were collected using a data collecting sheet to record age, gender, BMI, liver attenuation (HIU) spleen and pancreas attenuation, liver and spleen size, diabetic duration clinical finding and HbA1c All data obtained in the study were documented and analyzed using the SPSS program to test the significance of differences, the p-value of less than 0.05 was considered to be statistically significant.

The study found that there was a significant difference in liver attenuation in diabetic and control group $p < 0.01$, the left liver lobe (segment3) attenuation in DM patients was 44.62±9.93 HU and in non-diabetic was 56.2±10.69 HU, the right liver lobe (segment 5) attenuation for diabetic patients was 43.46±9.77 HU and in non-diabetic was 56.02±10.65 HU, the right liver lobe (segment 6) attenuation for diabetic patients was 44.62±9.93 HU and non-

diabetic was 56.2±10.69 HU, there was a negative moderate significant correlation between duration of diabetes and attenuation (HU) of the liver, $P< 0.01$

It's concluded that a strong relationship exists between BMI and duration of disease and liver size measurement changes and Hounsfield units on CT scan.

ملخص الدراسة

كانت هذه الدراسة وصفية - دراسة الحالات والشواهد التي أجريت في المملكة العربية السعودية - مدينة جدة في "المركز الطبي الدولي" في الفترة من يناير 2018 إلى أكتوبر 2020.

مجموعة من 196 شخصًا ، 100 منهم لديهم مرضى السكري من النوع الثاني و 96 مريضًا غير مصاب بالسكري كمجموعة ضابطة تتراوح أعمارهم بين 31 إلى 85 عامًا ، 54 ٪ منهم من الذكور و 46 ٪ من الإناث.

مع مرور الوقت ، يتسبب ارتفاع مستويات الجلوكوز في الدم في تلف معظم أعضاء الجسم ، والهدف من هذه الدراسة هو فهم تأثير مرض السكري على الكبد والطحال والبنكرياس وتقييم وظائف الكبد بين مرضى السكري.

تهدف هذه الدراسة إلى قياس عدد الأشعة المقطعية للكبد والطحال والبنكرياس وكذلك حجم الكبد والطحال في المجموعات المصابة بالسكري وغير المصابة بالسكري ، وتقييم نسبة الطحال إلى حجم الكبد في مجموعات مرضى السكر وغير المصابين. والربط بعد قياس توهين وحجم الكبد والطحال والبنكرياس بالأشعة المقطعية مع العمر ومؤشر كتلة الجسم ونوع مرض السكري ومدة مرض السكري.

تم جمع البيانات باستخدام ورقة جمع البيانات لتسجيل العمر والجنس ومؤشر كتلة الجسم وتوهين الكبد وتوهين الطحال والبنكرياس وحجم الكبد والطحال ومدة السكري والكشف السريري وتحليل مستوى السكر التراكمي تم توثيق جميع البيانات التي تم الحصول عليها في الدراسة وتحليلها باستخدام برنامج SPSS لاختبار دلالة الفروق ، واعتبرت قيمة الاحتمالية الأقل من 0.05 ذات دلالة إحصائية.

وجدت الدراسة أن هناك فرقًا معنويًا في توهين الكبد في مرضى السكري والمجموعة الضابطة

$p < 0.01$ ، وكان توهين فص الكبد الأيسر (الجزء 3) لدى مرضى 44.62 ± 9.93 HU السكر وفي غير المصابين بالسكري كان 56.2 ± 10.69 HU ، الجانب الأيمن كان توهين شحمة الكبد (الجزء 5) لمرضى السكري 43.46 ± 9.77 HU وفي غير مرضى السكري كان 56.02 ± 10.65 HU ، وكان توهين فص الكبد الأيمن (الجزء 6) لمرضى السكري 44.62 ± 9.93 HU وكان غير مرضى السكري 56.2 ± 10.69 في HU ، كان هناك ارتباط معتدل سلبي معتدل بين مدة مرض السكري وتوهين الكبد (HU) ، $P < 0.01$

وخلص إلى وجود علاقة قوية بين مؤشر كتلة الجسم ومدة المرض وتغيرات قياس حجم الكبد ووحدات قياس التوهين على الأشعة المقطعية.

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List of Abbreviations

ALP	Alkaline phosphatase
ALT	Alanine transaminase
AST	Aspartate transaminase
CLDs	Chronic liver diseases
CT	Computed tomography
DM	Diabetes mellitus
HbA1C	Glycated hemoglobin
HDL	High-density lipoprotein
HU	Hounsfield units
IVC	Inferior vena cava
L/S	Liver-to-spleen ratio
MRI	Magnetic resonance imaging
NAFLD	Nonalcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
PACS	Picture archiving and communication system
PDFF	Proton density fat fraction
UGT	Uridine diphosphate glucurony l transferase
T2DM	Type -2 diabetes mellitus
US	Ultrasonography
VLDL	Very low-density lipoprotein

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CHAPTER ONE

INTRODUCTION

1.1. Introduction

Diabetes mellitus is one of the major non-communicable diseases and the prevalence is rising globally. Type 2 diabetes is the most common form, accounting for 90% of all cases [Amos AF, McCarty DJ.2010].

The prevalence of diabetes worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of diabetes is projected to increase from 171 million in 2000 to 366 million in 2030. Diabetes is more prevalent in men than women [Wild S, Roglic G, King H.2030].

Diabetes mellitus is a long-term metabolic disorder that is characterized by high blood sugar, insulin resistance, and relative lack of insulin. Common symptoms include increased thirst, frequent urination, and unexplained weight loss. Symptoms may also include increased hunger, feeling tired, and sores that do not heal. Often symptoms come on slowly. Long-term complications from high blood sugar include heart disease, strokes, diabetic retinopathy which can result in blindness, kidney failure, and poor blood flow in the limbs which may lead to amputations. (Retrieved 10 February 2016)

In addition, it has recently been estimated that people born in the year 2000 have a 33–38% lifetime risk of developing diabetes.

There exists an association between diabetes and liver disease. Liver plays a major role in the regulation of carbohydrate homeostasis. Hepatocellular glycogen accumulation leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients. (Retrieved 10 February 2016)

Type 2 diabetes is partly preventable by staying a normal weight, exercising regularly, and eating properly. Treatment involves exercise and dietary changes. If

blood sugar levels are not adequately lowered, the medication metformin is typically recommended. Many people may eventually also require insulin injections. (Retrieved 10 February 2016)

To evaluate hepatic abnormalities there are many radiographic modalities one of them is ultrasound, US is probably currently the most widely used imaging method for detecting hepatic steatosis but its low accuracy in detecting mild steatosis and does not provide reliable quantitative information, also its operator dependency. there for US may not be an adequate tool for monitoring NAFLD patients. (Tarantino G, Finelli 2013)

Also there is the computerized tomography, CT allows for a more quantitative assessment with measurement of liver attenuation in Hounsfield units (HUs). It appears that non-contrast CT scanning is more useful for detecting steatosis than contrast-enhanced scans. Several techniques for determining the appropriate CT values include measurement of hepatic attenuation only and normalization of hepatic attenuation by splenic attenuation, reporting the difference in attenuation between the liver and spleen and the ratio of these values. The attenuation of the spleen is approximately 8–10 HUs less than the liver in normal subjects. With unenhanced CT, an attenuation of the liver is less than 40 HUS, or a liver-to-spleen attenuation difference greater than −10 HUs is highly predictive of hepatosteatosis. In addition, a liver-to-spleen ratio of less than 1 is sometimes used to diagnose fatty liver. CT has been demonstrated to be useful for diagnosing >30% steatosis by the use of liver: spleen attenuation ratios; the method has a sensitivity of 73%–100% and a specificity of 95%–100% (Lawrence DA, Oliva IB, Israel GM 2012).

Unlike CT and US, which evaluate hepatic steatosis through proxy parameters (echogenicity and attenuation, respectively), MRI and MRS can more directly

measure the quantity of hepatic fat. MRI and MRS both measure proton density fat fraction (PDFF), defined as the amount of protons bound to fat divided by the amount of all protons in the liver, including those bound to fat and water. The basic magnetic resonance (MR) physics used in both techniques to differentiate protons in fat from those in water is the chemical-shift phenomenon, i.e., the difference in MR frequency between the protons in fat and water (Hamilton G, Middleton MS 2009).

Therefore, CT measurements of fat in liver useful modality for patients at risk of metabolic syndrome such as Diabetes Mellitus. CT allows more quantitative assessment (with measurement of liver attenuation in Hounsfield units) which is the dividing line to compare liver function analysis and hepatic tissue texture (Gholam PM, Flancbaum L, Machan JT 2007).

1.2 The problem of the study

Diabetes reduces lifetime by about 6 years, compared with that of subjects without diabetes, because it increases the risks of death from all causes, including chronic liver diseases (CLDs). It's one of the major non-communicable diseases and the prevalence is rising globally and There exists an association between diabetes and liver disease. Also, liver can be affected by steatosis or accumulation of fat, a condition known as non-alcoholic fatty liver disease (NAFLD). It is a well-recognized complication of diabetes with frequency of 40–70% [Gavin N. Levinthal, MD, and Anthony S. Tavil 1999].

There for this study will be a long standing for diabetes over liver disease. It will focus on understanding diseases affecting the liver and evaluate the liver function among diabetes patients in Jeddah KSA.

1.3. Objectives of the study

1.3.1. General

Evaluation of impact of diabetes on liver, spleen and pancreas using computed tomography scan.

1.3.2. Specific

- To measure CT number of liver, spleen and pancreas in diabetic & non-diabetic groups
- To measure the size of liver and spleen in diabetic & non-diabetic groups.
- To evaluate the spleen to liver size ratio in diabetic & non-diabetic groups.
- To correlate after measuring the attenuation of liver, spleen and pancreas by CT with Age, body mass index, type of diabetes and duration of diabetes.
- To correlate after measuring the size of liver and spleen by CT with Age, body mass index, type of diabetes and duration of diabetes.

CHAPTER TWO

LITERATURE REVIEW

2.1. Anatomy of the liver

2.1.1. General anatomy

The liver is the largest organ, accounting for approximately 2% to 3% of average body weight. The liver has 2 lobes typically described in two ways, by morphologic anatomy and by functional anatomy (figure 2.1) located in the right upper quad- rant of the abdominal cavity beneath the right hemi diaphragm, it is protected by the rib cage and maintains its position through peritoneal reflections, referred to as ligamentous attachments (figure 2.2). (Abdel-Misih and Bloomston, 2010).

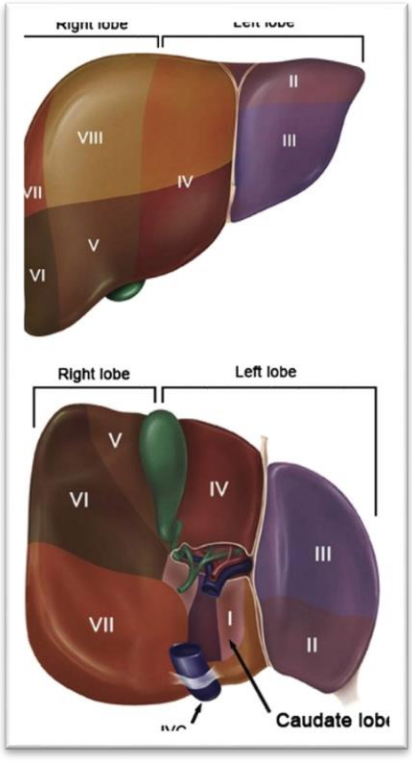


Fig. 2.1 Anterior and posterior surfaces of liver illustrating functional division of the liver into left and right hepatic lobes with Couinaud's segmental classification based on functional anatomy.(Brunicardi and Schwartz, 2005)

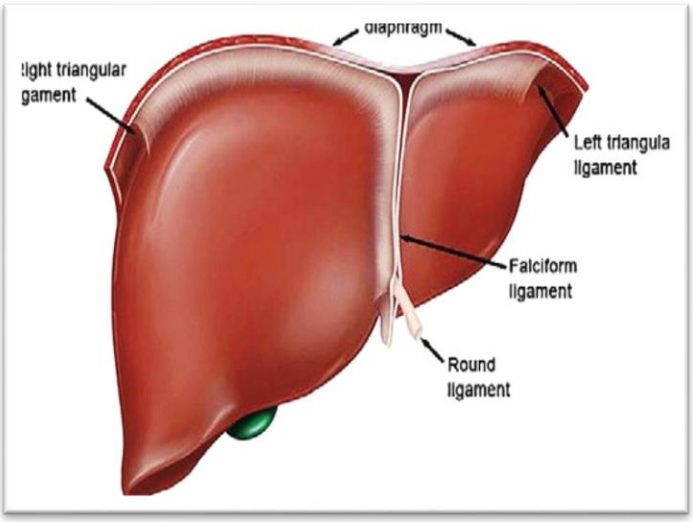


Fig. 2.2 Ligamentous attachments of the liver. (Brunicardi and Schwartz, 2005)

2.1.2. Per hepatic organs

The gastrointestinal tract has several associations with the liver (illustrated in figure 2.3). The stomach is related to the left hepatic lobe by way of the gastro hepatic ligament or superior aspect of the lesser omentum. Additionally, the duodenum and portal structures are in direct association with the liver through the hepatoduodenal ligament (inferior aspect of the lesser omentum) and porta hepatis. (Abdel-Misih and Bloomston, 2010).

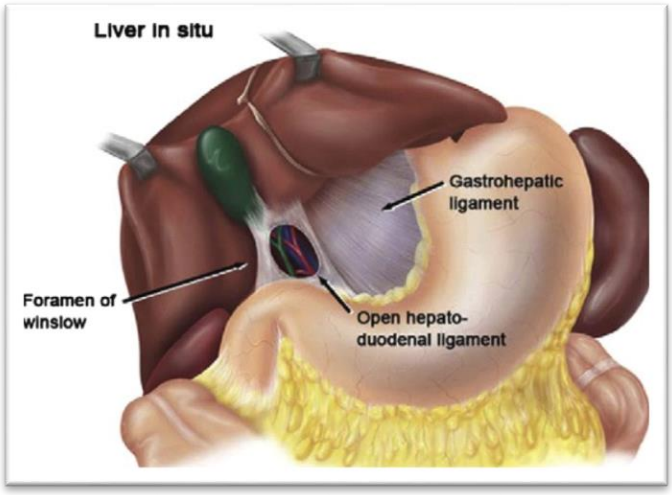


Fig. 2.3 Association of stomach, porta hepatis, and hepatic flexure to the liver. (Brunicardi and Schwartz, 2005)

2.1.3. Hepatic vasculature

The liver is a very vascular organ and at rest receives up to 25% of total cardiac output, more than any other organ. Its dual blood supply is uniquely divided between the hepatic artery, which contributes 25% to 30% of the blood supply, and the portal vein, which is responsible for the remaining 70% to 75%. (Abdel-Misih and Bloomston, 2010).

2.1.3.1. Arterial vasculature

Although the arterial vasculature of the liver is variable, as illustrated in (figure 2.4) in the most common arterial configuration, the common hepatic artery originates from the celiac axis along with the left gastric and splenic arteries. The common hepatic artery proceeds laterally and branches into the proper hepatic artery and the gastroduodenal artery. (Abdel-Misih and Bloomston, 2010).

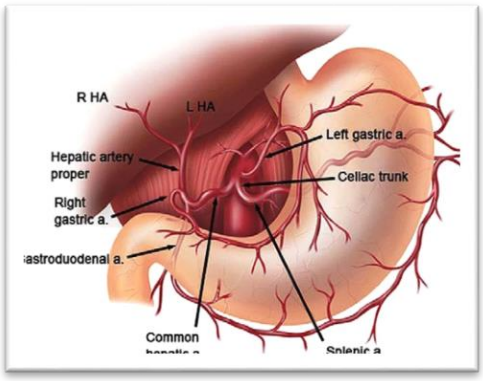


Fig. 2.4 Common hepatic arterial configuration. HA, hepatic artery. (Brunicardi and Schwartz, 2005)

The liver to divide into left and right hepatic arteries to feed the respective hepatic lobes. Additionally, the right gastric artery has a variable origin arising from the hepatic artery as it courses laterally. The cystic artery to the gallbladder commonly arises from the right hepatic artery. In (figure 2.5) common arterial variants are illustrated. (Abdel-Misih and Bloomston, 2010).

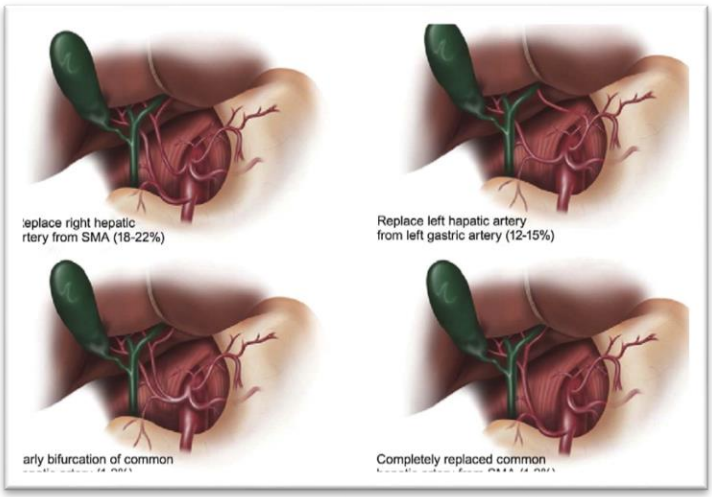


Fig. 2.5 Common variations of hepatic vasculature. (Brunicardi and Schwartz, 2005)

2.1.3.2. Venous vasculature

The portal vein provides the bulk of the nutritive blood supply to the liver. As illustrated in (figure 2.6) the portal vein forms from the confluence of the superior mesenteric vein and splenic vein behind the neck of the pancreas. (Wang et al., 2017).

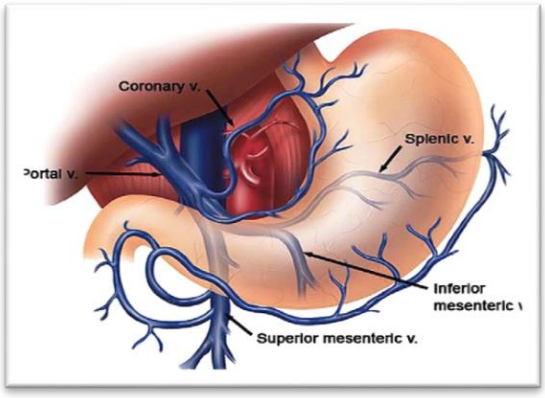


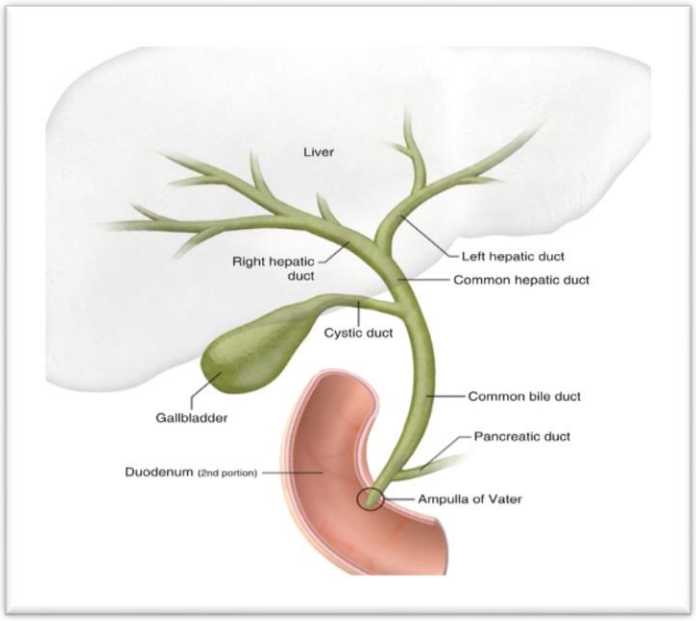
Fig. 2.6 Portal vein and the hepatic venous vasculature inflow. (Brunicardi and Schwartz, 2005)

The venous drainage of the liver is through the intrahepatic veins that ultimately coalesce into three hepatic veins that drain into the IVC superiorly. The left and middle hepatic veins may drain directly into the IVC but more commonly form a short common trunk before draining into the IVC. The right hepatic vein is typically larger, with a short extrahepatic course and drains directly into the IVC. (Wang et al., 2017).

2.1.3.3. Biliary tree

The intrahepatic biliary tree is comprised of multiple ducts that are responsible for the formation and transport of bile from the liver to the duodenum and typically follows the portal venous system. (Abdel-Misih and Bloomston, 2010)

At (figure2.7) biliary anatomy parallels the portal venous supply of the liver. The right hepatic duct drains the entire right lobe of the liver. It is formed by the union of the anterior right hepatic duct.(Wagner-Bartak et al., 2015)



At (Fig 2.7) Normally, the right and left hepatic ducts converge to form the common hepatic duct at the porta hepatis. The common hepatic duct is joined by the cystic duct from the gallbladder to form the common bile duct (CBD). (Wagner-Bartak et al., 2015)

2.2. Liver physiology

2.2.1. Function

2.2.1.1. Bile production

Bile is an important fluid as it helps excrete material not excreted by the kidneys and aids in the absorption and digestion of lipids via secretion of bile salts and acids. Bile is produced by hepatocytes and is mainly composed of water, electrolytes, bile salts, bile acids, cholesterol, bile pigment, bilirubin, and phospholipids in addition to other substances. Bile is secreted from hepatocytes into the bile canaliculi where it travels from smaller ducts to the larger ducts eventually ending up in the duodenum or being stored in the gallbladder for storage and concentration.(Kalra and Tuma, 2018)

2.2.1.2. Fat-soluble vitamin storage and/or metabolism

Most fat-soluble vitamins reach the liver via intestinal absorption in the form of chylomicrons or VLDL. The liver stores and/or metabolizes fat-soluble vitamins. The liver receives vitamin E in its alpha and gamma tocopherol forms. Alpha-tocopherol is integrated with VLDL or HDL in the liver and is then secreted back into circulation while the liver metabolizes the gamma-tocopherol form for excretion.(Kalra and Tuma, 2018)

2.2.1.3. Drug metabolism

Another critical function of the liver is metabolism and/or detoxification of xenobiotics. Other organs, such as the kidney and gut can aid in drug metabolism. Multiple factors such as age, gender, drug-drug interactions, diabetes, pregnancy, liver or kidney disease, inflammation, or genetics to name a few, affect drug metabolism.(Kalra and Tuma, 2018)

2.2.1.4. Bilirubin metabolism

The liver plays a significant role in the breakdown of heme. Hemolysis takes place in multiple locations throughout the body, including the liver, spleen, and bone marrow. Heme is broken down into biliverdin, which is then reduced to unconjugated bilirubin. The liver receives unconjugated bilirubin bound to albumin from the circulation. The unconjugated bilirubin then undergoes conjugation via by the uridine diphosphate glucuronyl transferase (UGT) system, a phase II process, to become hydrophilic (Kalra and Tuma, 2018).

2.2.2. Pathophysiology of the liver

Cirrhosis is a result of continuous liver injury, inflammation, fibrosis, and necrosis. Alcoholism and chronic hepatitis B and C commonly cause cirrhosis. Hepatitis C is the most damaging. The fibrosis present in cirrhosis occurs from the secretion of TGF-beta from the Ito cells in the space of Disse. (Kalra and Tuma, 2018).

Jaundice, the yellowing of the skin, can be seen in altered bilirubin metabolism. The first sign of jaundice is often yellowing under the tongue, followed by scleral icterus (yellowing of the sclera). The result of the fractionated bilirubin can help identify the etiology of the cholestasis into pre hepatic and intrahepatic or extrahepatic causes. (Kalra and Tuma, 2018).

2.2.3. Clinical significance of the liver

A variety of viruses can lead to liver damage. Hepatitis viruses A and E lead to acute hepatitis without resulting in chronic hepatitis, although hepatitis E can lead to fulminant hepatitis in pregnant patients. Hepatitis A and E are typically seen in travelers and from contaminated water or seafood sources.(Kalra and Tuma, 2018)

Besides malignant lesions, there are a variety of benign liver lesions. The four most commonly discussed are hemangiomas, which are the most common, focal nodular hyperplasia (FNH), hepatocellular adenomas, and hepatic cysts. The liver is susceptible to malignancy. Most cases of malignancy involving the liver are a result of metastasis to the liver due to it receiving blood from so much of the body. The most common primary malignancy of the liver is hepatocellular carcinoma HCC can arise from hepatocellular adenomas, but can also arise from cirrhosis, which occurs for a variety of reasons, such as primary biliary cirrhosis, alcoholism, NAFLD, chronic hepatitis B or C and more. (Kalra and Tuma, 2018).

Non-alcoholic, fatty liver disease (NAFLD) is a spectrum of liver disease ranging from benign steatosis to cirrhosis requiring liver transplant. It is one of the most common chronic liver conditions necessitating a liver transplant. There are a variety of causes of NAFLD, ranging from metabolic syndrome, pregnancy, nutrition, drugs, toxins, and more. It is most commonly seen in diabetics and obese patients. It can also present in asymptomatic patients receiving workup for other reasons. It can sometimes present with right upper quadrant pain and/or discomfort. Liver enzymes can be elevated, classically with an elevated ALT: AST ratio. (Kalra and Tuma, 2018).

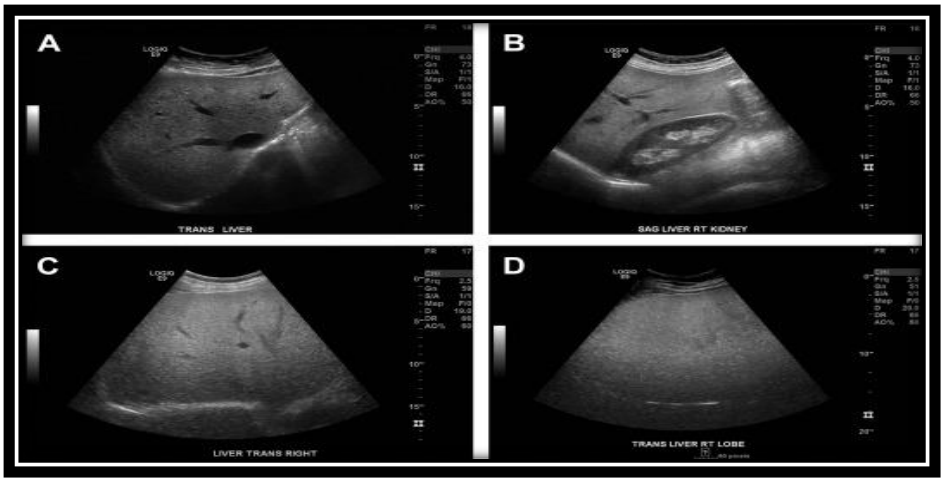
2.3. Medical imaging for liver diagnosis

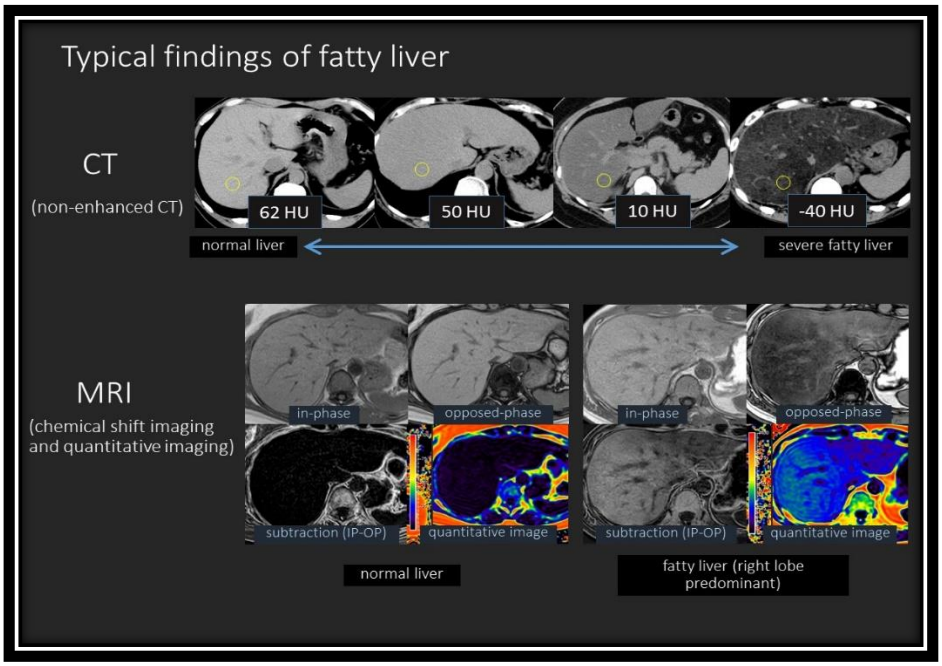
Computed tomography (CT or CAT scan) is a noninvasive diagnostic imaging procedure that uses a combination of X-rays and computer technology to produce horizontal, or axial, images (often called slices) of the body. A CT scan shows detailed images of any part of the body, including the bones, muscles, fat, and organs. CT scans are more detailed than standard X-rays. In standard X-rays, a beam of energy is aimed at the body part being studied. A plate behind the body part captures the variations of the energy beam after it passes through skin, bone, muscle, and other tissue. While much information can be obtained from a standard X-ray, a lot of detail about internal organs and other structures is not available. In computed tomography, the X-ray beam moves in a circle around the body. This allows many different views of the same organ or structure. The X-ray information is sent to a computer that interprets the X-ray data and displays it in a two-dimensional (2D) form on a monitor. CT scans may be done with or without "contrast." Contrast refers to a substance taken by mouth and/or injected into an intravenous (IV) line that causes the particular organ or tissue under study to be seen more clearly. Contrast examinations may require fasting for a certain period of time before the procedure. (Abu Elenin and Gerasimchuk, 2014)

The liver is the largest internal organ in the body. This dark reddish brown organ is located in the upper right-hand portion of the abdominal cavity, beneath the diaphragm, and on top of the right kidney and intestines. The wedge-shaped liver consists of 2 main lobes, both of which are made up of thousands of lobules. These lobules are connected to small ducts that connect with larger ducts to ultimately form the hepatic duct. The hepatic duct transports the bile produced by the liver cells to the gallbladder and duodenum (the first part of the small intestine). (Abu Elenin and Gerasimchuk, 2014)

CT scans of the liver and biliary tract (the liver, gallbladder, and bile ducts) can provide more detailed information about the liver, gallbladder, and related structures than standard X-rays of the abdomen, thus providing more information related to injuries and/or diseases of the liver and biliary tract. CT scans of the liver and biliary tract may also be used to visualize placement of needles during biopsies of the liver or during aspiration (withdrawal) of fluid from the area of the liver and/or biliary tract. CT scans of the liver are useful in the diagnosis of specific types of jaundice (yellowing of the skin and eyes as a result of certain conditions of the liver). (Abu Elenin and Gerasimchuk, 2014).

Reasons for the procedure. A CT scan of the liver and biliary tract may be performed to assess the liver and/or gallbladder and their related structures for tumors and other lesions, injuries, bleeding, infections, abscesses, unexplained abdominal pain, obstructions, or other conditions, particularly when another type of examination, such as X-rays, physical examination, and ultra sound is not conclusive. A CT scan of the liver may be used to distinguish between obstructive and non-obstructive jaundice. Another use of CT scans of the liver and biliary tract is to provide guidance for biopsies and/or aspiration of tissue from the liver or gallbladder. (Abu Elenin and Gerasimchuk, 2014).





(Figure 2.8) CT,MRI and US findings for fatty liver (Miyaji et al., 2019)

2.4. Diabetic

2.4.1. Normal physiology

When we consume food, it is digested and absorbed from the intestinal tract into the bloodstream. We usually consume more food at each feeding than is needed at that point. Some of it is used immediately but most of it is stored for later use. This is especially true of carbohydrates and fat. The fat is stored in fat cells for future use as fuel. The carbohydrate is stored as glycogen in the liver and muscle cells, also for future use as fuel, especially for the brain that is completely dependent on glucose for its function. Insulin is necessary for the transport of glucose into the cells for use as fuel or for storage. It also facilitates fatty acid uptake and storage by the fat cells and amino acid uptake by all cells. Insulin deficiency then results in a reversal of these processes and in essence creates a state equivalent to starvation. Insulin is produced by the β cells of the islets of Langerhans of the pancreas under the influence of the blood glucose level. Insulin is a protein hormone secreted by the β cells and is deposited into the intracellular space. It then passes into the bloodstream and proceeds through the circulation to the cells of the body. At the cellular level, insulin interacts with a protein on the cell surface called an insulin receptor. This interaction stimulates a cascade of intracellular reactions, each catalyzed by a different enzyme, which ultimately results in the production of another protein, called a glucose transporter (GLUT4 in muscle cells). GLUT4 passes or migrates to the cell surface facilitating the entrance of larger molecular nutrients such as glucose and protein. One of the key enzymes in this process is PPAR-γ (peroxisome proliferator activated receptor-γ). This is an enzyme in the cell nucleus that has many functions but here it causes the production of messenger RNA (ribonucleic acid) that then forms the glucose transporter protein, (GLUT 1–5). It is this enzyme that is activated by the oral agents' rosiglitazone and pioglitazone.3 PPAR-γ has also been

shown to be involved in protecting vascular tissue from the damage caused by high blood glucose levels. This effect is unrelated to its effect on blood glucose control or on insulin resistance. Insulin has a number of functions in different cells. It facilitates not only the uptake of food components into the cells but also their storage. Insulin stimulates the enzymes that make glycogen and fat and suppresses the enzymes that break down glycogen and fat. This breakdown of storage substances is a normal process and is vital to the metabolic process. In the absence of insulin, the process is too rapid. The system cannot utilize the metabolites produced and a catabolic state is created. The liver can also produce new glucose (gluconeogenesis) from protein and to a lesser extent from the glycerol produced in fat breakdown. Glucose production by the liver is one of the most important processes resulting in the hyperglycemia of diabetes, whether from insulin deficiency or from insulin resistance. (Guthrie and Guthrie, 2004).

2.4.2. Types of diabetes mellitus

2.4.2.1. Type 1 diabetes mellitus

In type 1 diabetes mellitus, there is a lack of insulin product due to autoimmune pancreatic beta-cell destruction. This may be triggered by environmental factors in people who are genetically susceptible. Destruction of the beta-cells continues over months or years, until their masses have decreased to a point in which insulin concentration can no longer control plasma glucose levels. (Moini, 2019)

2.4.2.2. Type 2 diabetes mellitus

Type 2 diabetes mellitus involves inadequate secretion of insulin. Early in the disease, insulin levels are often very high, and this situation may continue later in disease development. However, peripheral insulin resistance as well as increased

production of glucose by the liver cause insulin levels to be inadequate to normalize levels of plasma glucose. Then, insulin production becomes reduced, and hyperglycemia worsens. Type 2 diabetes usually develops in adults, becoming more common with aging. Plasma glucose levels reach higher levels following meals in older than in younger adults. This is especially true following high-carbohydrate loads. The levels require more time to return to normal, partly due to increased accumulation of visceral and abdominal fat, along with decreased muscle mass. Today, type 2 diabetes is more common than ever among children, with childhood obesity becoming an epidemic. In children, 40%50% of new-onset diabetes is type 2. More than 90% of adults with diabetes have this form. Clear genetic factors exist, influencing prevalence of type 2 diabetes in Hispanics, American-Indians, and Asians as well as other ethnic groups, and in relatives of patients. Several genetic polymorphisms have been identified, but there has been no single causative gene identified. (Moini, 2019)

2.4.2.3. Gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is a form that develops during pregnancy. It is characterized by an impaired ability to metabolize carbohydrates, usually due to a deficiency of insulin, or insulin resistance. The condition disappears after delivery of the infant. However, in a significant number of cases, it returns years later as type 2 diabetes mellitus. There is evidence suggesting that placental lactogen and considerable destruction of insulin by the placenta play roles in precipitating GDM. In most cases, pregnant women are regularly screened for GDM between 24 and 28 weeks of gestation, using a 50 g, 1-hour glucose tolerance test. If the patient has risk factors for gestational diabetes, she will be screened during the first trimester. Risk factors include a previous pregnancy that involved gestational diabetes or a neonate weighing more than 4500 g at birth, unexplained loss of a fetus, family history of

diabetes in close relatives, history of persistent glycosuria, and a body mass index .30 kg/m2. With gestational diabetes, the most accurate results are obtained via a glucose tolerance test. When the result is 140199 mg/dL, a full glucose tolerance test is performed. If glucose is 200 mg/dL or higher, insulin is administered. If two or more test results are abnormal, the patient is treated for the remainder of the pregnancy with diet. If necessary, insulin or oral hypoglycemics are given. Adequate control of plasma glucose during pregnancy nearly eliminates the risks of adverse outcomes. Pregnancy aggravates the preexisting type 1 and type 2 diabetes, but does not appear to worsen diabetic retinopathy, nephropathy, or neuropathy. Gestational diabetes begins during pregnancy, often in women who are overweight, hyperinsulinemic, and insulin-resistant. However, it can develop in thin women who are relatively insulin-deficient. Gestational diabetes occurs in 1%3% of all pregnancies, but can be significantly higher in Mexican-Americans, American-Indians, Asians, Indians, and Pacific Islanders. During pregnancy, diabetes increases fetal and maternal morbidity as well as mortality. The neonate is at risk for respiratory distress, hypoglycemia, hypocalcemia, hyperbilirubinemia, hyperviscosity, and polycythemia. Inadequate control of preexisting or gestational diabetes during organogenesis, up to approximately 10 weeks of gestation, increases the risk of serious congenital malformations, and for spontaneous abortion. Later in pregnancy, poor diabetic control increases risks for fetal macrosomia, preeclampsia, and spontaneous abortion. Fetal macrosomia is usually defined as fetal weight above 4000 g, but often over 4500 g at birth. Gestational diabetes can sometimes cause fetal macrosomia even when blood glucose is nearly normal. To minimize risks to the fetus and mother, a diabetes team of physicians, nurses, nutritionists, social workers, and pediatricians should be involved in treatment. Any complications of pregnancy, regardless of seriousness, must be quickly diagnosed and treated. There should be a delivery plan, with an experienced pediatrician present. Neonatal

intensive care must be available if needed. Insulin is used for some women with gestational diabetes, with human insulin preferred because it reduces antibody formation. Areas of treatment should involve self-monitoring of blood glucose, administration of insulin, increased physical activity, a carbohydrate-controlled meal plan, and adequate intake of calcium and iron. (Moini, 2019)

2.4.3. Diagnosis of diabetes

2.4.3.1. Diagnostic tests for diabetes

Diabetes may be diagnosed based on the plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-h plasma glucose (2-h PG) value after a 75-g oral glucose tolerance test (OGTT) or the A1C criteria (1,3) the same tests are used to screen for and diagnose diabetes and to detect individuals with prediabetes. Diabetes may be identified anywhere along the spectrum of clinical scenarios: in seemingly low-risk individuals who happen to have glucose testing, in individuals tested based on diabetes risk assessment, and in symptomatic patients.

Fasting and 2-Hour Plasma Glucose the FPG and 2-hPG may be used to diagnose diabetes. The concordance between the FPG and 2-h PG tests is imperfect, as is the concordance between A1C and either glucose-based test. Numerous studies have confirmed that, compared with FPG cut points and A1C, the2-hPG value diagnoses more people with diabetes.

A1C The A1C test should be performed using a method that is certified by the NGSP (www.ngsp.org) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. Although point-of-care A1C assays may be NGSP certified, proficiency testing is not mandated for performing the test, souse of point-of-care assays for diagnostic purposes is not recommended. The A1C

has several advantages compared with the FPG and OGTT, including greater convenience (fasting not required), greater pre analytical stability, and less day-to-day perturbations during stress and illness. However, these advantages may be offset by the lower sensitivity of A1C at the designated cut point, greater cost, limited availability of A1C testing in certain regions of the developing world, and the imperfect correlation between A1C and average glucose in certain individuals. National Health and Nutrition Examination Survey (NHANES) data indicate that an A1C cut point of 6.5% (48 m mol/mol) identifies one third fewer cases of undiagnosed diabetes than a fasting glucose cut point of 126 mg/dL (7.0 mmol/L) (4). It is important to take age, race/ ethnicity, and anemia/hemoglobin pathies into consideration when using the A1C to diagnose diabetes. (Association, 2016)

2.4.3.2. Type 2 diabetes

Recommendations c Testing to detect type 2 diabetes in asymptomatic people should be considered in adults of any age who are overweight or obese (BMI 25 kg/m2 or 23kg/m2inAsianAmericans) and who have one or more additional risk factors for diabetes. B c for all patients, testing should begin at age 45 years. B c If tests are normal, repeat testing carriedoutataminimumof3-year intervals is reasonable. C c to test for type 2 diabetes, fasting plasma glucose, 2-h plasma glucose after 75-g oral glucose tolerance test, and A1C are equally appropriate. B c in patients with diabetes, identify and, if appropriate, treat other cardiovascular disease risk factors. B c Testing to detect type 2 diabetes should be considered in children and adolescents who are overweight or obese and who have two or more additional risk factors for diabetes. (Association, 2016)

2.4.4 Pathophysiology of diabetic liver

A link between diabetes and liver Glutamic Acid Decarboxylase Autoantibody (GADA), one of the disease has been suggested for a very long time. Diabetes was main islet cell antigens, this could lead to an autoimmune found to be an important cause of liver disease, where patient's reaction and Beta-cell (B-cell) destruction. However, with diabetes were found to have a spectrum of liver diseases, hepatitis C is mainly linked to T2DM rather than T1DM ranging from abnormal liver enzymes, nonalcoholic fatty liver making the autoimmune hypothesis unlikely in addition to disease, cirrhosis, hepatocellular carcinoma, and acute liver the fact that most HCV-positive diabetic patients do not failure, all associated with the increased prevalence of hepatic express anti-islet or anti-GAD antibodies. Only one study complications including liver cirrhosis and portal hypertension. by Hieronimus et al. found a positive case of GADA among 47. On the other hand, liver disease was considered to be an HCV-infected patient. However, other studies did not find important cause of death in T2DM, where in one prospective any significant differences in the frequency of islet-cell cohort study, cirrhosis accounted for 12.5% of all death causes. Antibodies among diabetic patients with or without HCV Another population-based observational study, the Verona infection.

Diabetes study, followed up 7,148 people with T2DM for 5 years Since patients with HCV infection have decreased first and noted an increased risk of death from gastrointestinal phase insulin release, this raised the possibility of early diseases, particularly from chronic liver cirrhosis and hepato- B-cell dysfunction that was at first attributed to direct cellular carcinoma compared with the general nondiabetic infection of the pancreatic beta cell. Laskus et al. showed population. The presence of HCV-RNA in the pancreatic acinar cells and within the epithelial cells of the pancreatic duct. (Sangiorgio et al., 2000)

2.5. Epidemiology of NAFLD

the global prevalence of NAFLD among patients with T2DM is 55.5%, with the lowest prevalence reported from Africa (30.4%) and similarly high rates from the rest of the world. In fact, these rates for the prevalence of NAFLD are almost twice the prevalence rates that had previously been reported for the general population from the same regions. (Mahady and Adams, 2018, Dai et al., 2017)

Diabetics with NAFLD experienced an overall mortality rate as high as 585 per 100,000 people. In fact, this rate is substantially higher compared to overall mortality rates of some other common chronic liver diseases, including chronic viral hepatitis. (Kubo et al., 2019, Wright et al., 2018)

In this context, the overall mortality rate for hepatitis C patients in the United States ranges between 4.7 per 100,000 (2010) and 5.0 per 100,000 populations (2014), while the overall mortality for hepatitis B patients is reported to be 0.5 per 100,000. (Zibbell et al., 2018).

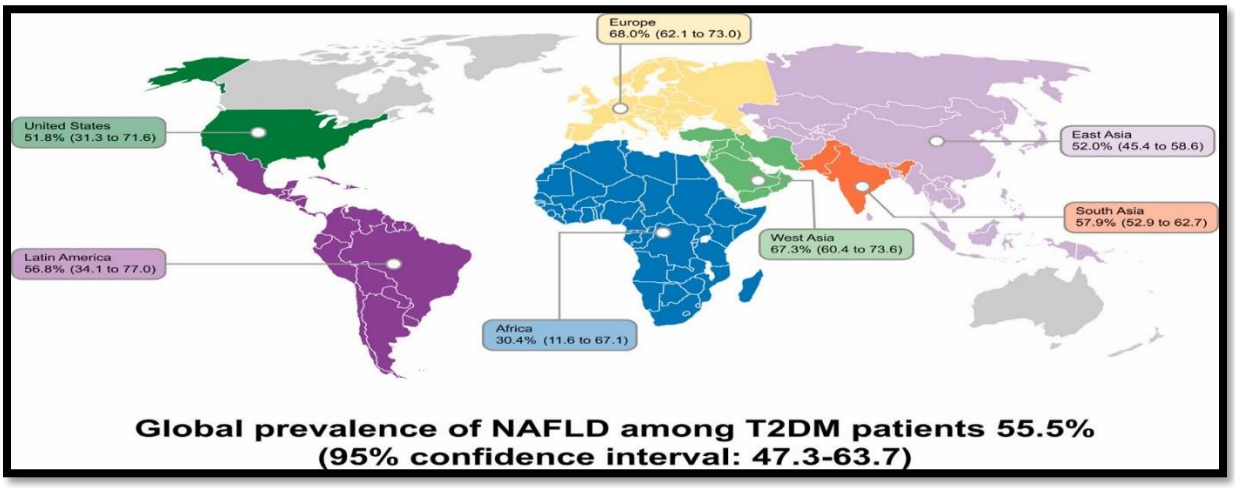


Fig. 2.9 Global and regional prevalence of NAFLD among patients with T2DM. H-MRS, proton magnetic resonance spectroscopy; NAFLD, non-alcoholic fatty liver

disease; T2DM, type 2 diabetes mellitus. NAFLD diagnosed by ultrasound or H-MRS. Data are displayed as prevalence (95% CI). (Zibbell et al., 2018)

2.6. Treatment

Treatment of NALFD life style modification lifestyle modification is the cornerstone of treatment of NAFLD. These interventions are not only effective in improving NAFLD but also associated conditions such as metabolic syndrome, T2DM, and the related risk of cardiovascular disease. Weight reduction plays an important role in the treatment of NASH. Weight loss has been shown to decrease hepatic steatosis and improve abnormal aminotransferase levels (Palmer and Schaffner, 1990).

Weight loss can be an effective treatment to improve the histology of NASH if patients can attain sufficient weight reduction. In a study by Harrison et al., subjects with biopsy-proven NASH who lost 5% of body weight had improvement in insulin sensitivity and hepatic steatosis compared with those who lost less than 5% of their body weight.100 However, it was only in subjects who achieved at least 9% weight reduction that there was significant improvement in inflammation, ballooning, and NAS. A randomized controlled trial (RCT) involving patients with biopsy-proven NASH by Promrat et al. examined the efficacy of lifestyle intervention using a combination of diet, exercise, and behavior modification compared to the control group that received structured education (Promrat et al., 2010). Percent weight reduction correlated significantly with improvement in NAS. Weight loss has been shown to prevent progression of fibrosis in NASH (Wong et al., 2010). However, very rapid weight loss may lead to increased portal inflammation and fibrosis. In a small study of severely obese patients with NAFLD who were placed on a very low calorie formula diet resulting in a median weight loss of 34 kg over an 8-weekperiod,24% of patients developed mild portal inflammation or portal fibrosis

(Andersen et al., 1991). Therefore, one should be cautious in recommending very low calorie diets for individuals with NAFLD.

Weight reduction surgery because NAFLD is present in the majority of patients who undergo bariatric surgery, there has been an interest in foregut bariatric surgery as a potential treatment option for NASH.

2.7. Previous study

Sakitani et al. (2017) had found that fatty liver was significantly associated with DM characteristics and the patients with fatty liver diagnosed by CT in the same manner. In females, although younger age was associated with increased fatty liver, longer duration of diabetes mellitus was a risk factor for fatty liver. A total of 970 patients (717 male and 253 female) between January 2008 and March 2014 were examined. The median age and BMI in male and female patients with diabetes mellitus was 65 and 67 years and 23.9 and 24.5kg/m2, respectively. Of these, 175 male (24.4%) and 60 female (23.7%) patients with diabetes mellitus were diagnosed with fatty liver by the L/S ratio calculated using CT Age, duration of diabetes mellitus, waist circumference, SAT, and ALP levels were significantly higher in female patients with fatty liver than in male patients with fatty liver. The study was at the Institute for Adult Diseases, Asahi Life Foundation, Tokyo, Japan This study was elucidated the clinical characteristics of patients with diabetes mellitus that were diagnosed with fatty liver by L/S ratio using CT results indicated that, in patients with type 2 diabetes mellitus, younger age, high VAT, and albumin, ALT, and triglyceride levels in males and younger age and high bilirubin levels in females were associated with fatty liver. The prevalence of fatty liver diagnosed by CT in patients with diabetes mellitus was 24.4% (175/717) in males and 23.7% (60/252) in females.

Masuoka, H.C, (2013) this study was affiliated to the division of gastroenterology and hepatology, department of medicine, Indiana university school of medicine, Indianapolis. In this study they had discussed and explained the relationship of non-alcoholic fatty liver disease (NAFLD) to obesity and diabetes (variables) BMI obesity and dyslipidemia were well-established risk factors for NAFLD, individuals with obesity and T2DM are at significantly higher risk for NAFLD. The incidence of NAFLD is rapidly increasing throughout the world due to the increasing frequency of obesity andT2DM. The NAFLD is a spectrum of chronic liver diseases ranging from simple steatosis, which is relatively benign from a liver standpoint, to NASH, which can progress to cirrhosis and liver failure. The diagnosis of NAFLD requires imaging evidence of hepatic steatosis while excluding competing etiologies, such as significant alcohol consumption, viral hepatitis, and hemochromatosis. Liver biopsy remains the gold standard for diagnosing NASH and for assessing fibrosis. Recent advances in laboratory testing and non-invasive imaging have shown promise for identifying steatohepatitis and advanced fibrosis in individuals with NAFLD. Weight loss of at least 5% is required to improve steatosis, whereas weight loss in the range of 7–10% may be needed to improve steatohepatitis. A number of pharmacologic therapies have been evaluated in NASH, and agents such as vitamin E and TZDs have shown some promise. Ongoing studies hold promise for developing more effective diagnostic tests and therapies

Vernon, G., Baranova, A. and Younossi, Z.M., (2011) this study had clarified that nonalcoholic fatty liver disease is the most common cause of elevated liver enzymes. Within the NAFLD spectrum, only NASH progresses to cirrhosis and hepatocellular carcinoma. With the growing epidemic of obesity, the prevalence and impact of NAFLD continues to increase, making NASH potentially the most common cause of advanced liver disease in coming decades.

The study was based on a PubMed search (1980-August 2010) for ‘non-alcoholic fatty liver disease’ OR ‘nonalcoholic steatohepatitis’ OR ‘fatty liver’ OR ‘steatosis’ AND ‘incidence’ [MeSH Terms] OR ‘prevalence’ [MeSH Terms] OR ‘natural history’. Studies of paediatric cohorts were excluded. Case studies, review articles and studies of paediatric populations were excluded. The remaining articles were categorised by topic and summarised, noting generalisations concerning their content.

Results Four study categories included NAFLD incidence, prevalence, risk factors and natural history. Studies related to NAFLD prevalence and incidence indicate that the diagnosis is heterogeneous and relies on a variety of assessment tools, including liver biopsy, radiological tests such as ultrasonography, and blood testing such as liver enzymes. The prevalence of NAFLD is highest in populations with preexisting metabolic conditions such as obesity and type II diabetes. Many studies investigating the natural history of NAFLD verify the progression from NASH to advanced fibrosis and hepatocellular carcinoma.

Ricci et al., (1997) had study the average CT value (HU) of normal liver was assessed by scanning 20 healthy volunteers without a past history of liver disease. Volunteers (11 males and 9 females) were recruited from medical students and University personnel with an age range of 20-39 years.

They found a linear correlation ($r=0.99$, $p<0.001$) linked CTD and the increasing percentage of fat equivalent material. A CTD calibration curve was derived as a reference for the in viva determinations. In 29 consecutive patients with steatosis diagnosed by histology, CTD was linearly correlated ($r=0.83$, $p< 0.001$) with the hepatic fat content (HFC) expressed as percent of the whole liver, obtained by a computerized histomorphometric analysis. Based on the calibration curve obtained

in 29 subjects who underwent liver biopsy, 38 additional consecutive steatotic patients were examined and the degree of hepatic fat content was calculated. The HFC was linearly correlated ($r= -0.86$, $p<0.001$) with the liver-to-spleen ratio

They had suggested calibrated CT may be useful in the assessment of the degree of liver steatosis. The test object employed is simple and easy to manipulate. The use of calibrated, "test object assisted" CT may provide quantitative rather than qualitative information on the degree of steatosis, and may be useful to evaluate the natural course of this frequent disorder and the changes induced by treatment aimed at reducing fatty infiltration

Stefano bonapace et al, (2012) had study the data on cardiac function in patients with nonalcoholic fatty liver disease (NAFLD) he was assessed whether NAFLD is associated with abnormalities in cardiac function in patients with type 2 diabetes.

studied 50 consecutive type 2 diabetic individuals without a history of ischemic heart disease, hepatic diseases, or excessive alcohol consumption, in whom NAFLD was diagnosed by ultrasonography. A tissue Doppler echocardiography with myocardial strain measurement was performed in all patients.

Thirty-two patients (64%) had NAFLD, and when compared with the other 18 patients, age, sex, BMI, waist circumference, hypertension, smoking, diabetes duration, microvascular complication status, and medication use were not significantly different. In addition, the left ventricular (LV) mass and volumes, ejection fraction, systemic vascular resistance, arterial elasticity, and compliance were also not different. NAFLD patients had lower e9 (8.2 6 1.5 vs. 9.9 6 1.9 cm/s, P 0.005) tissue velocity, higher E-to-e9 ratio (7.90 6 1.3 vs. 5.59 6 1.1, P , 0.0001), a higher time constant of isovolumic relaxation (43.1 6 10.1 vs. 33.2 6 12.9 ms, P , 0.01), higher LV–end diastolic pressure (EDP) (16.5 6 1.1 vs. 15.1 6 1.0 mmHg, P ,

0.0001), and higher LV EDP/end diastolic volume (0.20 6 0.03 vs. 0.18 6 0.02 mmHg, P 0.05) than those without steatosis. Among the measurements of LV global longitudinal strain and strain rate, those with NAFLD also had higher E/global longitudinal diastolic strain rate during the early phase of diastole (E/SRE). All of these differences remained significant after adjustment for hypertension and other cardio metabolic risk factors. Data showed that in patients with type 2 diabetes and NAFLD, even if the LV morphology and systolic function are preserved, early features of LV diastolic dysfunction may be detected.

Iwasaki et al., (2004) had study the hepatic steatosis affected graft function as well as postoperative recovery of donors in living donor liver transplantation. Liver macrovesicular steatosis in living donors was assessed using quantitative X-ray computed tomography (CT) analysis and histological examination of intraoperative liver biopsy.

A total of 266 living donors with completed pre transplant CT data and intraoperative "time 0" biopsy was included in the study. Liver biopsy specimen obtained during donor operation was examined for macrovesicular steatosis and was classified as none; mild (30%); moderate (30%–60%); or severe (60%). Liver-to-spleen CT attenuation values ratio (L/S ratio) on noncontrast-CT was evaluated for its usefulness as an index of hepatic steatosis in comparison with other parameters including body mass index (BMI) and serum liver function tests (gammaglutamyl transpeptidase, alanine aminotransferase, aspartate aminotransferase, cholinesterase, and total cholesterol) used receiver operating characteristic (ROC) analysis.

Histological grade of macrovesicular steatosis was none in 198 patients (74.4%), mild in 50 (18.8%), moderate in 15 (5.7%), and severe in 3 (1.1%). The median L/S ratios for the respective histological grades were 1.20 (range: 1.00-1.46), 1.12 (0.83-

1.37), 1.01 (0.74-1.21), and 0.90 (0.70-0.99) (P<0.0001). The ROC curve for L/S ratio was located closest to the upper left corner, and the area under the curve of L/S ratio was significantly larger than that of any other preoperative variables.

L/S ratio calculated from preoperative CT can be a useful tool to discriminate hepatic macrovesicular steatosis. Based on the present results, the optimal cut-off value for L/S ratio to exclude more than moderate steatosis

Matteoni et al., (1999) this study compared clinical characteristics and outcomes of patients with different types of nonalcoholic fatty liver. All liver biopsy specimens from 1979 to 1987 with fat accumulation were assessed for inflammation, ballooning degeneration, Mallory hyaline, and fibrosis. Biopsy specimens were also assessed for histological iron and hepatitis C RNA. Outcomes were cirrhosis, mortality, and liver-related mortality. Of 772 liver biopsy specimens, complete data were available in 132 patients. Fatty liver (type 1) did not differ from the other three types combined with respect to gender, race, age, or obesity. Cirrhosis was more common in the other types combined (22%) than fatty liver alone (4%; P I 0.001). Overall mortality, histological iron, and hepatitis C did not differ between groups. Most of the liver-related deaths were in type 4. Conclusions: The outcome of cirrhosis and liver-related death is not uniform across the spectrum of nonalcoholic fatty liver. These poor outcomes are more frequent in patients in whom biopsies show ballooning degeneration and Mallory hyaline or fibrosis.

772 liver biopsy specimens were identified with fatty liver from computerized pathology registry. 43%; abnormal liver test results, 29%; suspicion of liver disease or cirrhosis, 16%; and hepatomegaly, 12%. There were 49 patients (37%) with type 1, 10 (8%) with type 2, 19 (14%) with type 3, and 54 (41%) with type 4 NAFLD. For all patients combined, median values were normal for PT, total bilirubin, AST,

albumin, and glucose. Based on chart review, State of Ohio death registry, 36% (48 of 132) of the patients died. There were 9 liver-related deaths (coded as cirrhosis, nonalcoholic) and 36 other causes of death series of patients with NAFLD, with up to 18 years of follow-up, showed that fatty liver alone seems to be a relatively benign disease, but the necrotic forms of NAFLD may have an aggressive course leading to cirrhosis and liver-related death.

(Osawa and Mori, 1996) this study had clarified that diagnosis of fatty liver using ultrasonography was attempted based on the difference between the echo intensities of the liver and kidney determined from ultrasonic histograms. Livers were then classified as having fatty infiltration, normal histology, or intermediate histology based on CT ratios established previously in earlier work comparing non-contrast-enhanced liver and spleen.

The hepato renal difference was significantly greater in the fatty liver group than in the normal liver group (8.9 * 2.0 dB vs 2.5 * 4.5 dB, $p < 0.001$). When a hepato renal difference of 37.0 dB was taken as the criterion, this method had a sensitivity of 91.3%, a specificity of 83.8%, and an accuracy of 86.7% for the diagnosis of fatty liver. Thus, quantitative ultrasonic diagnosis of fatty liver can be performed using echo intensity histograms. Between December 1991 and March 1993, 70 patients (33 men and 37 women; mean age: 39.2 years) among 351 who underwent abdominal CT scanning were enrolled in this prospective study. Thirty-one patients had a suspected diagnosis of fatty liver on the basis of ultrasonic imaging and subsequently underwent abdominal CT scanning. Thirty-nine patients were investigated for various abdominal diseases, and a diagnosis of normal liver or fatty liver was made by CT, after which abdominal ultrasonography was performed.

It had been reported that the CT number of normal liver ranges widely from 40 to 70 Hounsfield units (HU), and that it is 7 to 8 HU higher than the CT number of the spleen.' As fat accumulates in the liver, the x-ray absorption of the tissues decreases, leading to a decrease in the CT number. Achieved high sensitivity (91.3%), specificity (83.8%), accuracy (86.7%), positive predictive value (77.8%), and negative predictive value (93.9%) with respect to CT diagnosis when a hepatorenal difference 37.0 dB was taken to indicate fatty liver. It is generally considered that ultrasound is inferior to CT for making a diagnosis of fatty liver. CT and liver biopsy are very useful for making an objective and quantitative diagnosis.

Lim et al., (2014) had study pancreatic volume and fat content might be associated with b-cell function or insulin resistance (IR). They investigated the difference in pancreatic volume and fat content between age- and body mass index (BMI)-matched normal subjects and patients with having different durations of type 2 diabetes (T2D). study was compared pancreatic volume and fat parameters between 50 age- and BMI-matched normal subjects, 51 subjects with newly diagnosed type 2 diabetes (T2D-new), 53 subjects with T2D \5 years (T2D\5Y), and 52 subjects with T2D C5 years (T2DC5Y). Age and BMI were matched to range of ±2 years and ±0.5 kg/m2.

For this study, we recruited 50 nondiabetic subjects (Normal group), 51 subjects with newly diagnosed type 2 diabetes (T2D-new group), 53 subjects with T2D \5 years (T2D\5Y group), and 51 subjects with T2D C5 years (T2DC5Y group) by age and BMI matching (a range of ±2 years in age and ±0.5 kg/m2 of BMI). These were all selected from individuals who visited Seoul National University Bundang Hospital (SNUBH), Seongnam, Korea.

This study found that patients with T2D had smaller pancreatic volume and greater pancreatic fat content than normoglycemic subjects. Within patients with T2D, as duration of diabetes increased, pancreatic volume decreased and pancreatic fat content increased, resulting in an increased fat percentage in the pancreatic parenchyma. Pancreatic fat density assessed by HU values based on unenhanced MDCT images also decreased according to the duration of diabetes.

Jeong et al., (2018) had investigated the relationship between pancreatic steatosis and diabetic retinopathy (DR) in patients with type 2 diabetes mellitus (T2DM) In this study, pancreatic steatosis was significantly associated with DR in non-obese patients with T2DM. Further studies are necessary to clarify the causal relationship between pancreatic steatosis and the development of DR. The attenuation of three pancreatic regions (head, body, and tail) and the spleen (S) in 186 patients with T2DM was measured using non-enhanced computed tomography imaging. They found that pancreatic steatosis parameters were associated with DR in T2DM patients, especially in the non-obese group.

Ahbab et al., (2019) had detected a relationship between adipose tissue accumulation, prediabetes and diabetes. Study was conducted from January 2016 to January 2017 in Haseki Training and Research Hospital University of Health Sciences in I˙stanbul. Haseki Training included 110 patients. Three groups were classified as controls, patients with prediabetes and patients with type 2 diabetes. The abdominal computed tomography (CT) attenuation measurement results of the pancreas were evaluated independently by two experienced radiologists. CT measurements and biochemical parameters were compared between study groups. A p-value less than 0.05 was considered statistically significant. The presence of prediabetes and type 2 diabetes was correlated with a decrease in the mean Hounsfield Unit (HU) value of the pancreas (p=0.002). Age was determined to be

an independent risk factor and was correlated with NAFPD (p=0.0001). When compared to the controls (p=0.041), 71% of patients with prediabetes and 67% of patients with type 2 diabetes were observed to have an increased incidence of NAFPD. Decreased serum amylase was found to be correlated with the mean HU value of the pancreas (p=0.043).

NAFPD was independently correlated with both prediabetes and type 2 diabetes adjusted for age (p=0.0001) in this study. Additionally, age was determined to be an independent risk factor and was correlated with NAFPD.

CHAPTER THREE

MATERIALS AND METHODS

3.1. Area and duration

This study was descriptive - case control study done in Kingdome of Saudi Arabia - Jeddah during the period from January 2018 to October 2020 at "INTERNATIONAL MEDICAL CENTER".

3.2. Materials

3.2.1. Patients

Subjects for this study were both males and females who had undergone abdominal CT examinations A total of 196 patients were selected using a convenient sampling method. Among them,100 subjects had T2DM regarded as cases, and 96 were non-diabetics as controls aged from 31 to 85 years some of them were admitted to "INTERNATIONAL MEDICAL CENTER" hospital and others are attending its referral clinic for routine follow up.

3.2.2. Machine

The study was simultaneously conducted in Department of Diagnostic Radiology in CT department. The abdominal CT examinations were done using (TOSHPA) CT Machine, at 120 kVp, 50mA-100mA (AP&LAT), 5-mm slice thickness (1 mm for Axial -1 mm for Coronal). Collimation was 0.5 x 80, pitch of 0.8.

3.2.3. Inclusion criteria

All subjects who had type II diabetes mellitus and Non-DM who underwent to medical imaging department for Abdomen CT scan for routine follow up or with an appointment.

3.2.4. Exclusion criteria

Factors leads to sample discrepancies (affecting the CT image attenuation) such as:

1) Subjects who recent undergo to contrast material studies (48 hours)

2) Subjects who underwent transplantation of liver or liver donors

3) Subjects who toke Medications (steroid, tamoxifen)

4) Subjects who recorded with neoplasm

3.2.5. Ethical clearance

All data collected after approval letter (Appendix)

3.3. Methods

3.3.1. CT abdomen protocol

Every patient was examined in supine positioning, typically feet first, scanning from above the diaphragm (top of the liver) to the level of the iliac crests. The patients were told to hold his/her breath at the end of inspiration. Slice thickness 5mm/slice, the reconstruction algorithm takes 2.5mm.

3.3.2. Technique

Patient position is supine position feet first, the longitudinal alignment line with the patient mid line and the transverse line at the Xiphoid process. The scan begins from Xiphoid process to symphysis pubis.

3.3.3. Method of image interpretation

The data were collected using the following variables: age, gender, BMI, liver attenuation (HIU) spleen and pancreas attenuation, liver and spleen size, diabetic duration clinical finding and HbA1c

- The attenuation measurements were obtained for each ROI, which include a larger area of the liver and spleen. Regions excluded were of non-uniform parenchymal attenuation, including apparent hepatic vessels

- Three regions of interest (ROIs) within the liver were delineated: left liver lobe (segment 3), right liver lobe (segment 5), right liver lobe (segment 6), this is the CT number of liver founded on an image and were measured by HU

- One region of interest (ROI) within the spleen was delineated: middle of the spleen, this is the CT number of spleen founded on an image and were measured by HU

- One region of interest (ROI) within the pancreas was delineated: the body of the pancreas, this is the CT number of pancreas founded on an image and were measured by HU

- The size for the liver and spleen in two dimensions' axial and coronal were obtained and measure by (mm)

- Diabetic duration and HbA1c to evaluate the effect of these variables on liver

- Clinical finding associated with patients who had type 2 diabetes

3-3-4 Statistical analysis

The collected data was analyzed using SPSS version 23. Frequency and percentage are taken to describe qualitative data. The descriptive statistics were done to estimate

the mean values of the quantitative data. The independent sample t-test was applied to compare the CT attenuation values of the liver, pancreas, and spleen in cases and controls. Pearson correlation was used to find a correlation between duration of T2DM and the CT mean attenuation values of liver, spleen, and pancreas. P-value was considered significant if less than 0.05.

CHAPTER FOUR

RESULT

Table (4.1) frequency distribution of age \ years

Age \years	Frequency	Percent	Valid Percent	Cumulative Percent
31-40	7	7.0	7.0	7.0
41-50	16	16.0	16.0	23.0
51-60	33	33.0	33.0	56.0
61-70	32	32.0	32.0	88.0
71-85	12	12.0	12.0	100.0
Total	100	100.0	100.0	

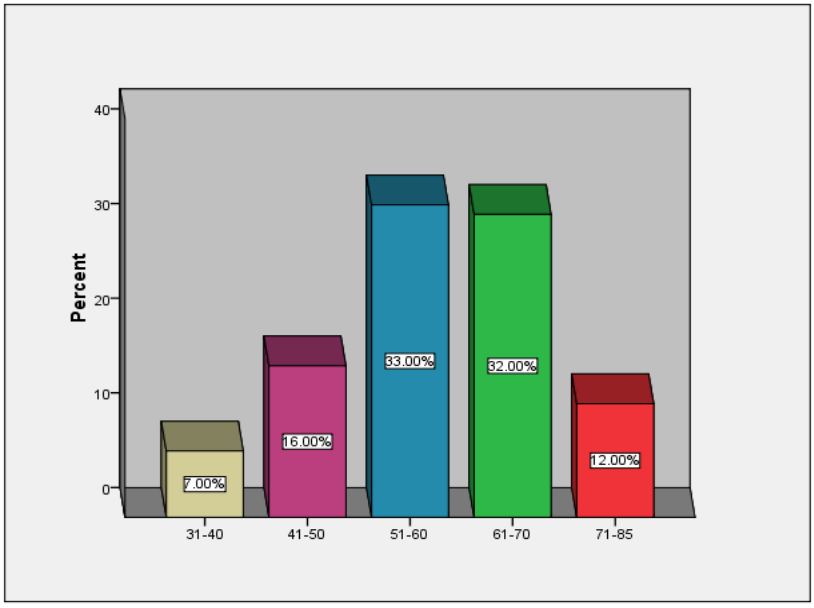


Figure (4.1) frequency distribution of age \ year

Table (4.2) frequency distribution of gender

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	46	46.0	46.0	46.0
Male	54	54.0	54.0	100.0
Total	100	100.0	100.0	

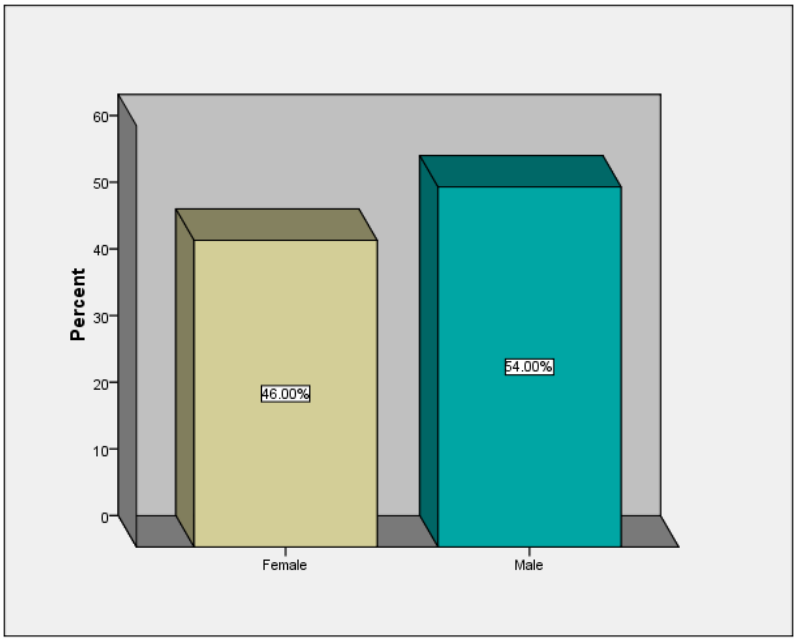


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Figure (4.2) frequency distribution of gender

Table (4.3) frequency distribution of duration

Duration	Frequency	Percent	Valid Percent	Cumulative Percent
4-10	33	33.0	33.0	33.0
11-17	33	33.0	33.0	66.0
18-24	24	24.0	24.0	90.0
25-31	7	7.0	7.0	97.0
32-36	3	3.0	3.0	100.0
Total	100	100.0	100.0	

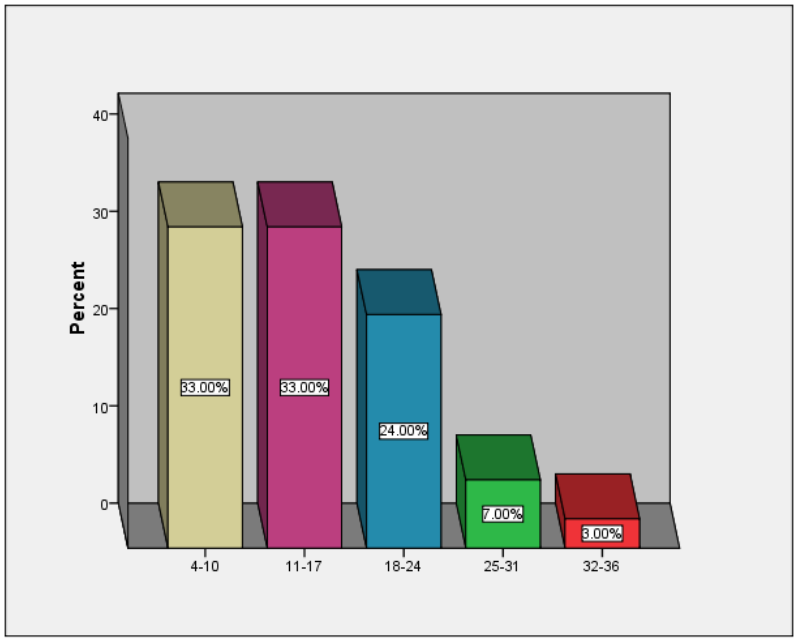

Figure (4.3) frequency distribution of duration

Table (4.4) descriptive statistic of age, BMI, duration, HbA1c, liver spleen, pancreas HU and Indexes (min, max, mean ± Std. Deviation)

	N	Minimum	Maximum	Mean	Std. Deviation
Age	100	31	85	58.91	11.101
Duration	100	4	36	14.62	7.191
BMI	100	17	48	30.74	7.252
HbA1c	75	4.0	12.0	7.476	1.9119
Left Liver Lobe HU (segment 3)	100	21	69	44.62	9.935
Right Liver Lobe HU (segment 5)	100	23	69	43.46	9.774
Right Liver Lobe HU (segment 6)	100	20	66	41.29	9.630
Liver Index (Axial 1)	100	151	261	203.08	22.923
Liver Index (Axial 2)	100	80	160	117.15	14.624
Liver Index (coronal)	100	86	230	165.85	28.753
Spleen HU(middle)	100	30	77	51.88	9.137
Spleen Index (Axial 1)	100	40	138	96.32	17.507
Spleen Index (Axial 2)	100	27	75	42.76	9.719
Spleen Index (coronal)	100	35	183	87.84	20.724
Pancreas HU (body)	100	16	55	34.58	8.748

Table (4.5) compare mean duration and means HU for liver, spleen, pancreas

Duration		Lt liver lobe HU(s3)	Rt liver lobe HU(s5)	Rt liver lobe HU(s6)	Spleen HU (middle)	Pancreas HU (middle)	P value
4-10	Mean	46.88	46.58	44.00	54.48	39.86	<0.001
	Std. Dev.	10.845	9.868	9.776	7.425	7.715	
11-17	Mean	48.03	46.79	44.73	54.58	35.45	
	Std. Dev.	9.736	9.707	9.412	8.074	6.364	
18-24	Mean	39.67	37.67	35.79	47.79	29.12	
	Std. Dev.	6.190	6.105	6.776	10.052	8.699	
25-31	Mean	38.14	35.71	34.14	45.43	30.29	
	Std. Dev.	4.880	5.251	4.220	4.467	5.187	
32-36	Mean	37.00	37.00	34.33	41.33	20.67	
	Std. Dev.	13.077	11.533	11.504	15.503	7.234	
Total	Mean	44.62	43.46	41.29	51.88	34.58	
	Std. Dev.	9.935	9.774	9.630	9.137	8.748	

Table (4.6) compare mean duration and means indexex for liver, spleen

Duration		Liver Index (Axial 1)	Liver Index (Axial 2)	Liver Index (coronal)	Spleen Index (Axial 1)	Spleen Index (coronal)	P value
4-10	Mean	201.64	115.97	162.30	96.85	88.00	> 0.05
	Std. Dev.	25.722	16.573	32.116	19.985	15.802	
11-17	Mean	208.03	120.36	167.03	98.88	92.94	
	Std. Dev.	21.356	13.299	26.952	15.167	15.698	
18-24	Mean	198.67	113.96	166.25	94.71	80.50	
	Std. Dev.	24.216	13.560	26.019	13.550	21.036	
25-31	Mean	203.29	122.14	168.43	92.29	85.86	
	Std. Dev.	11.557	14.960	36.235	15.903	17.170	
32-36	Mean	199.33	108.67	182.67	84.67	93.33	
	Std. Dev.	17.010	8.083	19.858	42.724	78.818	
Total	Mean	203.08	117.15	165.85	96.32	87.84	
	Std. Dev.	22.923	14.624	28.753	17.507	20.724	

Table (4.7) correlation age, duration, HbA1c means HU for liver, spleen, pancreas

		Lt liver lobe HU(s3)	Rt liver lobe HU(s5)	Rt liver lobe HU(s6)	Spleen HU (middle)	Pancreas HU(middle)
Age	Pearson Correlation	-.369**	-.422**	-.422**	-.421**	-.640**
	Sig. (2-tailed)	.000	.000	.000	.000	.000
	N	100	100	100	100	100
Duration	Pearson Correlation	-.375**	-.430**	-.415**	-.411**	-.574**
	Sig. (2-tailed)	.000	.000	.000	.000	.000
	N	100	100	100	100	100
HbA1c	Pearson Correlation	-.402**	-.484**	-.505**	-.459**	-.453**
	Sig. (2-tailed)	.000	.000	.000	.000	.000
	N	75	75	75	75	75

Table (4.8) correlation age, duration, HbA1c and means indexes for liver, spleen

**Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

		Age	Duration	HbA1c
Liver Index (Axial 1)	Pearson Correlation	-.157-	-.049-	.302**
	Sig. (2-tailed)	.119	.631	.009
Liver Index (Axial 2)	Pearson Correlation	-.156-	-.037-	.213
	Sig. (2-tailed)	.122	.713	.066
Liver Index (coronal)	Pearson Correlation	.037	.102	.150
	Sig. (2-tailed)	.718	.313	.200
Spleen Index (Axial 1)	Pearson Correlation	-.133-	-.136-	-.065-
	Sig. (2-tailed)	.186	.178	.582
Spleen Index (Axial 2)	Pearson Correlation	-.159-	-.157-	-.086-
	Sig. (2-tailed)	.114	.120	.464
Spleen Index (coronal)	Pearson Correlation	-.015-	-.116-	.035
	Sig. (2-tailed)	.881	.251	.767
	N	100	100	75

Table (4.9) frequency distribution of other associated clinical findings

Other	Frequency	Percent	Valid Percent	Cumulative Percent
Only Fatty liver	53	53.0	53.0	53.0
acute pancreatitis, fatty liver	1	1.0	1.0	54.0
anemia , calcium metabolism , lymphadenitis, fatty liver	1	1.0	1.0	55.0
anemia , hypertension, fatty liver	1	1.0	1.0	56.0
chronic renal failure ,stroke, fatty liver	1	1.0	1.0	57.0
diffuse steatosis, fatty liver	1	1.0	1.0	58.0
disorder of adrenal , obesity , glucose impairment, fatty liver	1	1.0	1.0	59.0
dyslipidemia	1	1.0	1.0	60.0
heart diseases, fatty liver	9	9.0	9.0	69.0
hypertension, atherosclerosis, fatty liver	1	1.0	1.0	70.0
hyperlipedemia, disorder of Urine, fatty liver	1	1.0	1.0	71.0
hyperlipedemia, fatty liver	1	1.0	1.0	72.0
fatty liver , hypertension	16	16.0	16.0	88.0
hypertension ,atherosclerosis, fatty liver	1	1.0	1.0	89.0
hypertension ,dyslipedemia	1	1.0	1.0	90.0

hypertension , hyperlipedemia, fatty liver	5	5.0	5.0	95.0
IHD, hypertension, fatty liver	1	1.0	1.0	96.0
malignant liver diseases , cirrhosis	1	1.0	1.0	97.0
Malignant neoplasm of ovary\abdominal mass.	1	1.0	1.0	98.0
obesity, hypertension, fatty liver	1	1.0	1.0	99.0
primary hypertension	1	1.0	1.0	100.0
Total	100	100.0	100.0	

Table (4.10) frequency distribution of age of control

Age \years	Frequency	Percent	Valid Percent	Cumulative Percent
31-40	20	20.8	20.8	20.8
41-50	23	24.0	24.0	44.8
51-60	30	31.2	31.2	76.0
61-70	5	5.2	5.2	81.2
71-85	3	3.1	3.1	84.4
less than 20	1	1.0	1.0	85.4
20-30	14	14.6	14.6	100.0
Total	96	100.0	100.0	

Table (4.11) frequency distribution of age of gender

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	41	42.7	42.7	42.7
Male	55	57.3	57.3	100.0
Total	96	100.0	100.0	

Table (4.12) descriptive statistic for control

	N	Minimum	Maximum	Mean	Std. Deviation
BMI	96	16	42	27.59	5.900
Left liver lobe HU (segment 3)	96	29	79	56.20	10.695
Right liver lobe HU (segment 5)	96	28	77	56.02	10.654
Right liver lobe HU (segment 6)	96	23	77	55.84	11.083
Liver Index (Axial 1)	96	154	243	201.95	20.460
Liver Index (Axial 2)	96	79	229	114.35	20.033
Liver Index (coronal)	96	82	227	159.44	29.557
Spleen HU(middle)	96	20	68	47.15	8.845
Spleen Index (Axial 1)	96	40	144	95.20	15.748
Spleen Index (Axial 2)	96	25	68	42.98	8.554
Spleen Index (coronal)	96	60	155	89.19	16.997
Pancreas HU(middle)	96	18	65	45.91	9.443
Age	96	18	81	45.96	13.409
Valid N (listwise)	96				

Table (4.13) independent sample t-test to compare means indices for liver, spleen, pancreas in DM and none DM means.

a. means

	Status	N	Mean	Std. Dev.	Std. Error Mean
Liver Index (Axial 1)	DM	100	203.08	22.923	2.292
	none DM	96	201.95	20.460	2.088
Liver Index (Axial 2)	DM	100	117.15	14.624	1.462
	none DM	96	114.35	20.033	2.045
Liver Index (coronal)	DM	100	165.85	28.753	2.875
	none DM	96	159.44	29.557	3.017
Spleen Index (Axial 1)	DM	100	96.32	17.507	1.751
	none DM	96	95.20	15.748	1.607
Spleen Index (Axial 2)	DM	100	42.76	9.719	.972
	none DM	96	42.98	8.554	.873
Spleen Index (coronal)	DM	100	87.84	20.724	2.072
	none DM	96	89.19	16.997	1.735

b. t.test

	t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	99% Confidence Interval of the Difference	
						Lower	Upper
Liver Index (Axial 1)	.362	194	.718	1.126	3.108	-6.959-	9.211
	.363	192.989	.717	1.126	3.101	-6.941-	9.193
Liver Index (Axial 2)	1.119	194	.264	2.796	2.498	-3.703-	9.295
	1.112	173.491	.268	2.796	2.514	-3.751-	9.343
Liver Index (coronal)	1.539	194	.125	6.411	4.165	-4.424-	17.247
	1.538	193.092	.126	6.411	4.167	-4.430-	17.253
Spleen Index (Axial 1)	.469	194	.640	1.117	2.382	-5.079-	7.313
	.470	193.192	.639	1.117	2.377	-5.066-	7.300
Spleen Index (Axial 2)	-.170-	194	.865	-.222-	1.310	-3.630-	3.185
	-.170-	192.566	.865	-.222-	1.306	-3.621-	3.177
Spleen Index (coronal)	-.496-	194	.621	-1.345-	2.713	-8.404-	5.713
	-.498-	189.425	.619	-1.345-	2.703	-8.378-	5.687

Table (4.14) independent sample t-test to compare means indexes for liver, spleen in DM and control

a. means

		N	Mean	Std. Deviation	Std. Error Mean
BMI	DM	100	30.74	7.252	.725
	none DM	96	27.59	5.900	.602
Age	DM	100	58.91	11.101	1.110
	none DM	96	45.96	13.409	1.369
Left liver lobe HU (segment 3)	DM	100	44.62	9.935	.993
	none DM	96	56.20	10.695	1.092
Right liver lobe HU (segment 5)	DM	100	43.46	9.774	.977
	none DM	96	56.02	10.654	1.087
Right liver lobe HU (segment 6)	DM	100	41.29	9.630	.963
	none DM	96	55.84	11.083	1.131
Spleen HU (middle)	DM	100	51.88	9.137	.914
	none DM	96	47.15	8.845	.903
Pancreases HU (middle)	DM	100	34.58	8.748	.875
	none DM	96	45.91	9.443	.964

b. t.test

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	99% Confidence Interval of the Difference	
						Lower	Upper
BMI	3.328	194	.001	3.150	.946	.688	5.612
	3.342	188.965	.001	3.150	.943	.697	5.602
Age	7.378	194	.000	12.952	1.755	8.385	17.518
	7.350	184.495	.000	12.952	1.762	8.365	17.538
Left liver lobe HU (segment 3)	-7.855-	194	.000	-11.577-	1.474	-15.411-	-7.743-
	-7.843-	191.489	.000	-11.577-	1.476	-15.417-	-7.737-
Right liver lobe HU (segment 5)	-8.607-	194	.000	-12.561-	1.459	-16.357-	-8.764-
	-8.591-	190.927	.000	-12.561-	1.462	-16.365-	-8.757-
Right liver lobe HU (segment 6)	-9.823-	194	.000	-14.551-	1.481	-18.404-	-10.697-
	-9.795-	187.894	.000	-14.551-	1.486	-18.416-	-10.685-
Spleen HU (middle)	3.677	194	.000	4.726	1.285	1.382	8.069
	3.679	193.986	.000	4.726	1.284	1.384	8.067
Pancreases HU (middle)	-8.714-	194	.000	-11.324-	1.300	-14.705-	-7.944-
	-8.700-	191.369	.000	-11.324-	1.302	-14.711-	-7.938-

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1. Discussion

There are many imaging techniques to evaluate the liver. Several previous studies recommended unenhanced computed tomography because of measurements of fat in the useful liver modality for patients at risk of metabolic syndrome such as Diabetes Mellitus. CT allows quantitative assessment (with measurement of liver attenuation in Hounsfield units). In this study, we used CT since it is useful in diagnosing the presence and assessing the severity of liver fat safely.

The present study revealed that fatty infiltrated liver was significantly correlated with T2DM. The prevalence of NAFLD is highest in populations with metabolic conditions such as obesity and T2DM. Specifically, T2DM and NAFLD closely related. A study of patients with T2DM found that fatty liver is significantly associated with DM characteristics, even at younger ages (Sakitani et al., 2017).

The sample of this research consisted of 100 patients with type 2 DM. Table (4.1) shows age distribution among a sample of the study, an elderly patient age between 51-60 years old were 33% of the total sample while younger (31-40 years) is low affected by this type 2 DM were 7%. Compare this result with Masuoka, H.C, 2013 who discussed the relationship of non-alcoholic fatty liver disease (NAFLD) to obesity and diabetes (variables) BMI obesity and dyslipidemia are well-established risk factors for NAFLD, though, in the multivariate analysis, only obesity, hypertriglyceridemia, and hypertension remained predictive. Similarly, a Korean study of living donors found obesity, and older age were independent risk factors for fatty liver and DM Type 2. (Masuoka, H.C. and Chalasani, N., 2013)

Table (4.2) shows that the males were more than women, 54% of the sample were males while 46% of the sample were females. Table (4-3) shows the duration of

diseases whom patients with DM from 4-10 years and 11-17 years were respectively high percentage more than whom duration of disease was 32-36 years.

At table (4.4) presented statistic of age, BMI, duration, HbA1c, liver spleen, pancreas HU and Indexes with the mean age were 58 years also the duration were 14 years, result showed mean BMI were 30.74 kg/cm2 similar study by Vernon G et al, 2011 who concluded, Obesity is a reported risk factor for NAFLD (DM Type 2). In patients with morbid obesity, the prevalence of non-alcoholic fatty liver disease (DM Type 2) can be more than 90% and up to 5% of patients may have liver cirrhosis (Vernon, G., Baranova, A. and Younossi, Z.M., 2011) Also, there is a significant correlation between the increase in BMI and the presence of NAFLD (56.1% of studied patients had overweight, whereas 49.1% were obese) however, no significant differences between the different BMI categories (P=0.360). Although the majority of participants (54% of study patients) had reported a longer duration of diabetes (10 years or more).

In Table (4.5) show Mean between duration and means HU for liver and spleen, we found that left liver lobe (segment 3) was 48.03 in patient duration disease was 11-17 years, right liver lobe HU (segment 5) in the same duration was 46.79 in right liver lobe HU (segment 6) was 44.73 which is excited in spleen HU measurement was 54.58 for the same duration.

In 32-36 duration the left liver lobe HU (segment 3) was 37.00, right liver lobe HU (segment 5) in the same duration was 37.00, in right liver lobe HU (segment 6),

was 34.33 which is excited in spleen HU measurement was 41.33 for the same duration. Similar results with Ricci C et al, 1997 who found that the CT method employed realizes that the lower the mean liver attenuation or CT number in Hounsfield units (HU), the lower the tissue density and hence the greater the fat

content. Therefore, liver density (attenuation in HUs) is inversely related to liver fat and thus is a surrogate for it. (Ricci et al., 1997)

A comparison between mean duration and means sizes for liver, spleen showed significant correlation with P value > 0.05 this was presented in table (4.6)

we found correlation at 11-17 duration was 208.03 for liver size axial 1 while 120.36 respectively for liver size axial 2. compare same previous duration (11-17) for spleen size in diabetic pts were 98.88 for axial 1 while 92.94 and spleen size coronal. At 32-36 duration was low respectively for liver and spleen size which were 199.33 for liver index axial 1,108.67 for liver index axial 2, in spleen size at the same duration 32-36 was 84.67and 93.33 axial 1 and coronal, these findings were presented in table (4.6).

At tables (4.7 and 4.8) presented the correlation between age and means HU for liver, spleen, and pancreas and we found correlation was significant at the 0.01 level (2-tailed), measurement at left liver lobe (segment 3) was -.369 which is low than the 0.001 level, and right liver lobe HU (segment 5&6) -.422, -.421 spleen HU middle and -.640 for body of the pancreas HU and correlate theses value by 0.01 level was significant .Also we measure the correlation between age and means size for liver and spleen in axial 1, axial 2 and coronal, our results were there was no significant at the 0.01 level (2-tailed) duration in the liver size and spleen size in the diabetic patient as we see in the table we take mean and stander deviation for liver size axial 1 and axial 2 and coronal compare that with means and stander deviation for spleen size coronal at correlation by p-value > 0.05 is significant.

Table (4.9) discuss the frequency distribution of other associated clinical findings with fatty liver diabetic type 2 patients the result was 53% of all patient had only fatty liver disease, pts who had fatty liver with Hypertension (high blood pressure)

was 22% which is relatively high percentage and whom those with heart disease was 9%, Hyperlipidemia, Hypertension, and fatty liver was 5%. Compare with the result of Stefano bonapace et al,2012 who resulted in Thirty-two patients (64%) had fatty liver, and when compared with the other 18 patients, age, sex, BMI, waist circumference, hypertension, smoking, diabetes duration, microvascular complication status, and medication use were not significantly and concluded (NAFLD) are limited and conflicting. He assessed whether NAFLD is associated with abnormalities in cardiac function in patients with type 2 diabetes and he said all of these differences remained significant after adjustment for hypertension and other cardio metabolic risk factors. (Bonapace et al., 2012)

There are other studies performed to observe the relation of fatty liver with diabetes done by. Tilg H, Moschen AR, and Roden M (2016) who concluded there was A suggestive correlation between marked increases of lipids (Hyperlipidemia) and hepatomegaly was seen among the diabetes patients with our study in table (4.9) mentioned Hyperlipidemia was 5% associated with fatty liver DM Type2 patients.

The principal risk factors for developing NAFLD are obesity and insulin resistance. Any metabolic syndrome such as type 2 diabetes, dyslipidemia, and hypertension (increased blood pressure) are linked to the development of NAFLD, and approximately 85% of patients with NAFLD have at least one metabolic syndrome. (Tilg et al., 2017)

The results at tables (4.10 and 4.11) showed the mean age for non-diabetic individuals were 51-60 years old and the male were highest frequent than female with 57%.

At table (4.12) showed descriptive statistic for non-diabetic individuals for BMI, attenuation and size for liver, spleen and pancreas.

In the present study, it was found that the CT attenuation values of the liver were significantly decreased in T2DM more than non-diabetic ones in agreement with previous studies (Iwasaki et al., 2004) . This decrease in attenuation value of the liver is attributed to the fact that the attenuation value of fat, usually about -100 HU, is much lower than that of soft tissue, ranging in 30-40 HU. Therefore, the attenuation value of liver parenchyma decreases as the steatosis develops and progresses. This finding indicates that CT assessment of liver parenchyma on an unenhanced CT scan is accurate since a strong correlation was reported between CT and histopathological analysis regarding the diagnosis of hepatic steatosis (Matteoni et al., 1999)

It was found that the liver-spleen (L/S) ratio was 0.83 in T2DM patients. This finding is in agreement with previous studies, which approximately reported similar results (Sakitani et al., 2017) On unenhanced CT scan, the normal liver parenchyma is slightly higher than that of the spleen. As fatty hepatic infiltration progresses, the attenuation value of liver parenchyma decreases, and therefore attenuation of the liver to spleen decreased. (Osawa and Mori, 1996) (Matteoni et al., 1999). Therefore, the L/S ratio is a significant indicator of a CT assessment of NAFLD this was presented in tables (4.13and 4.14).

In this study, it was found that a negative correlation existed between the duration of DM and attenuation values of the pancreas, liver, and spleen. As the duration of the DM increased, the attenuation of the liver, pancreas, and spleen decreased significantly (p-value < 0.001) presented at (table 4.5) It was found that the most affected organ is the pancreas, which showed a strong significant negative

correlation. Pancreatic fat density decreased accordingly as the duration of the disease increased (Lim et al., 2014). Similarly, Lim et al. stated that patients with T2DM had excessive pancreatic fat content than normoglycemic subjects (Jeong et al., 2018). Ahbab et al., 2019. reported that DM correlated with a decrease in the mean HU values of the pancreas (p=0.002). These decreased attenuation values were attributed to the fact that pancreatic fat content increased in T2DM, resulting in increased fat content in the pancreatic tissue. The negative correlations suggested that the values of these factors increase as the degree of pancreatic fatty infiltration increases. In general, these findings indicate that the duration of T2DM was a strong influencing factor affecting the CT attenuation of the pancreas, liver, and spleen.

5.2. Conclusion

This study concludes that elderly patients age between 51-60 years old were 33% most affected age. Male in our sample were more than female by fatty liver DM Type2.

Fatty liver is largely present in type 2 diabetes and correlates with a worse metabolic profile and with organ damage. When fatty liver is present in type2 diabetes co-morbidities and complications of diabetes mainly effect (hepatic, renal, and cardiovascular). In this study, we were able to confirm the above-mentioned association between the fatty liver, hypertension, and heart disease in a population of patients with type 2 diabetes. the associations were independent of age, sex, systolic blood pressure, and BMI.

From the finding of these studies, it's concluded that a strong relationship exists between BMI and duration of disease and liver size measurement changes and Hounsfield units on CT scan.

Although computerized tomography is an invasive technique it gives the accurate and reliable measurement to assess and characterize liver and spleen in fatty liver DM type 2 patients.

5.3. Recommendations

- Magnetic resonance imaging technique is good modality to asses' fatty liver disease, need to compare it with computerized tomography in the future.
- It is necessary to integrate imaging with clinical and laboratory findings to allow more definitive diagnosis.
- One of conclusion of our study confirmed the relation between fatty liver, hypertension, and heart disease in a population of patients with type 2 diabetes so need more studies to correlate if there is another clinical finding.
- Our study has some limitations: our sample were for elder population so we recommended to other researcher to take younger age samples to reach to finial diagnosis.

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Data collection request

Sudan University of Science & Technology

College of Graduate Studies and Scientific Research

Registrar's Office

بسم الله الرحمن الرحيم

جامعة السودان للعلوم والتكنولوجيا

كلية الدراسات العليا والبحث العلمي

مكتب المسجل

النمرة: ج س ع ت / ك د ع/ د.خ/ 2019/11/26

الى / المركز الطبي الدولي – المملكة العربية السعودية - جده

السلام عليكم ورحمة الله تعالى وبركاته،،،

الموضوع: تيسير أمر الباحثة / هدى اسامة عبد الرحمن سليمان

الجنسية/ سودانية

بالإشارة للموضوع أعلاه نفيدكم علماً أن الدارسة المذكوره أعلاه مسجلة لدينا لنيل درجة الماجستير بالبحث في تكنولوجيا الاشعة التشخصية بكلية علوم الاشعة الطبية ، بتاريخ 2017/12/24م تحت اشراف مشرف رئيس د. عفراء صديق حسين عمر والمشرف المعاون د. محمد ابراهيم الطاهر

Evaluation of Diabetic Impact on Liver Using CT Scan

نرجو التكرم بالسماح لها بالحصول على المعلومات والعينات المطلوبة .

ولكم منا خالص الشكر والتقدير،،،

جامعة السودان للعلوم والتكنولوجيا
كلية الدراسات العليا
أ.اماني السر محمد طه
م. مسجل الكلية

Data collection request

بسم الله الرحمن الرحيم

كلية الغد الدولية للعلوم الطبية التطبيقية
بجـــــــدة
تحت إشراف
وزارة التعـلـيـم

مكتب عميد الكلية

سعادة رئيس قسم المختبر بالمركز الطبي الدولي - بجدة حفظه الله

السلام عليكم ورحمة الله وبركاته،،،

انطلاقاً من حرص إدارة كلية الغد في تهيئة و تشجيع طلابها و منسوبيها فيما يخص عملية البحث العلمي نتقدم لسعادتكم بطلب التعاون معهم لجمع عينات لبحث علمي لمرضى السكر وعلاقته بأمراض الكبد لما ستساهم هذه المساهمة الكريمة من جانبكم لرفع المستوى العلمي و المهني لطلاب و منسوبي كلية الغد – جدة.

ولكم جزيل الشكر والتقدير،،،

عميد كلية الغد الدولية للعلوم

الطبية التطبيقية بجدة:

د. أحمد ناصر الجربوع

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المركز الطبي الدولي

Ethical Approval

International Medical Center

MBDICAL IMAGING DEPARTMENT

2019 / 11 /27

الى / مسجل كلية الدراسات العليا والبحث العلمي
جامعة السودان للعلوم والتكنولوجيا

السلام عليكم ورحمة الله وبركاته ،،،

اشارة الى خطابكم بالرقم : ج س ع ت / ك د ع/ د. خ / بتاريخ : 2019/11/26م والخاص بموضوع: تيسير أمر الباحثة : هدى أسامة عبد الرحمن سليمان ، سودانية الجنسية والسماح لها باجراء البحث الخاص بها داخل قسم الأشعة بالمركز الطبي الدولي.
نفيكم بأنه لا مانع لدينا من اجراء الباحثة لبحثها داخل القسم لدينا والحصول على كل المعلومات المطلوبة،

وتفضلوا بقبـول وافر الشكر والتقدير ،،،

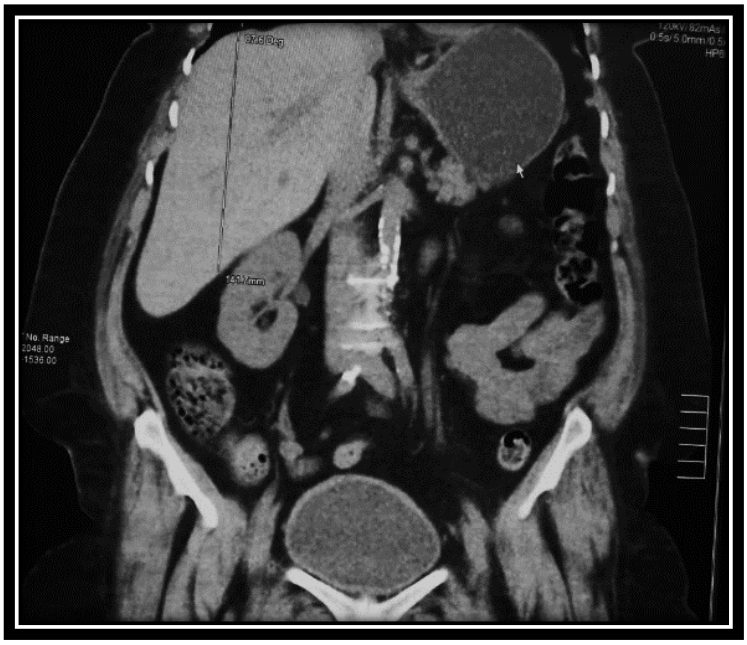
Abdulhafeez Khalid Widatalla
Medical Imaging Supervis
ID # 417

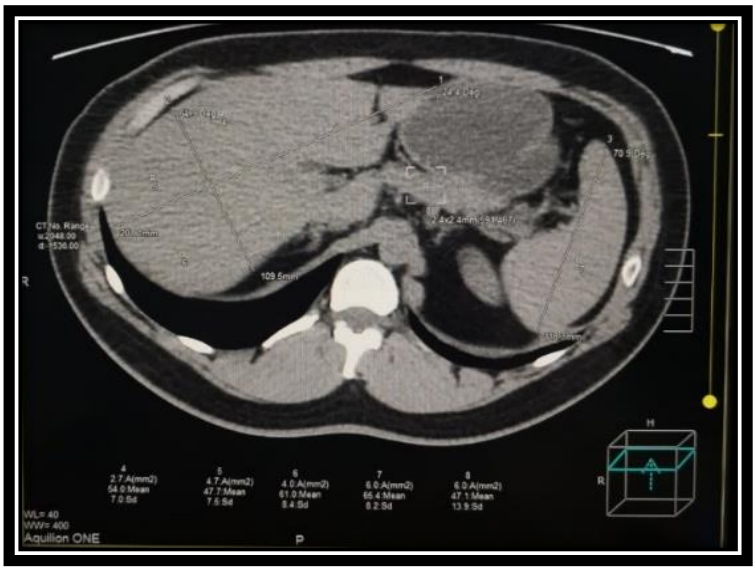
عبـد الحفيظ خـالد
مشـرف قسـم الأشعة

Data Collection Sheet

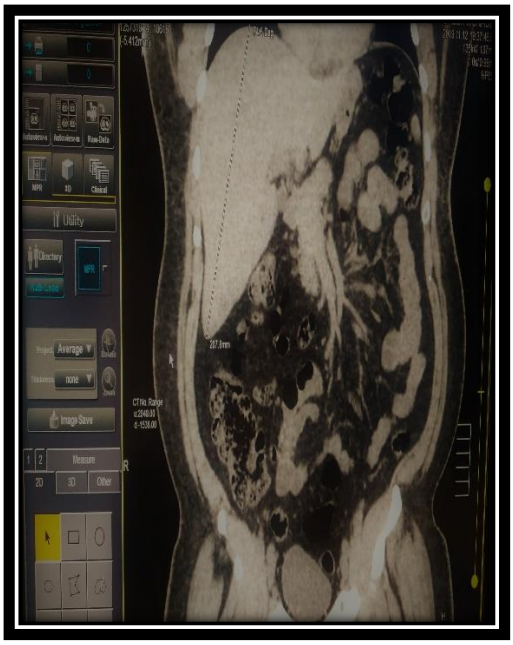
Patient NO.				
BMI				
Liver S3 - HU				
Liver S5- HU				
Liver S6- HU				
Liver -axial 1				
Liver -axial 2				
Liver-coronal				
Spleen-HU				
Spleen-axial 1				
Spleen-axial 2				
Spleen-coronal				
Pancreas-HU				
Gender				
Age				
HbA1c				
Associated disease				
Duration of DM				

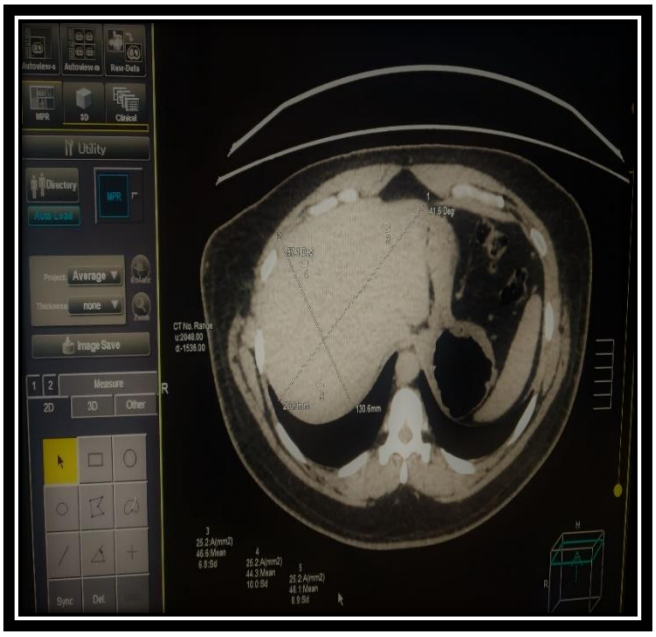
CT Abdomen Images



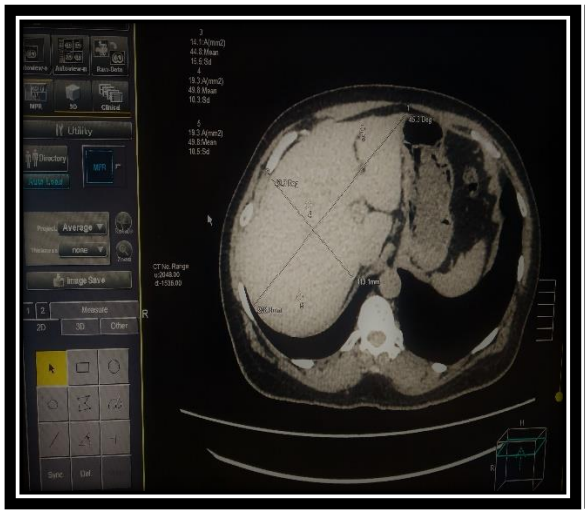


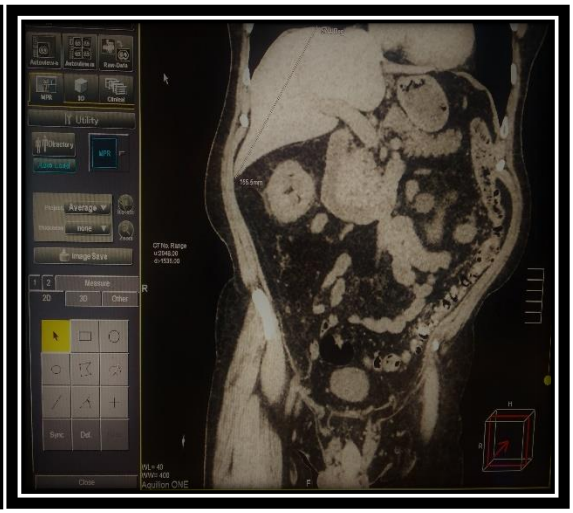
- 58 years female diabetic , the liver 54 HU the spleen 65 HU with Hepatomegaly.





- 48 years old male diabetic with hypertension , the liver index 207 mm in coronal and 200*130 mm in axial with attenuation 45 HU .





- 59 years old male diabetic with hypertension and BMI 27 , the liver index 155 mm in coronal and 208*113 mm in axial with attenuation 48 HU .

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