Sudan University of Science and Technology Collage of Graduate Studies

Characterization of Liver in Correlation with Liver Function Results using Computed Tomography

توصيف الكبد وإرتباطها مع نتائج وظائف الكبد بإستخدام الأشعة المقطعية المحوسبة

A Thesis Submitted for the Award PhD Degree in Diagnostic Radiologic Technology

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Aug 2018

الآية

بسم الله الرحمن الرحيم

﴿الرحمن * علم القرآن * خلق الإنسان * علمه البيان﴾

صدق الله العظيم

سورة الرحمن الآيات(1-4)

Dedication

To soul of my mother

To my father and husband for his continues inspiration and support

To my sons

To my daughter

To my brothers and sisters

To my friends

To whom I love much, I convey this work.

Acknowledgement

I would like to thank **Dr. Caroline Edward**, for her help, supervising and encouragement during my research and also my colleagues in CT department, for their help in completing this work in success.

Special thanks to the radiologists for their help in diagnosis the image.

My Thank also extend to the whole staff in Elamal and Royal Scan diagnostic center.

ABSTRACT

The aims of this study were to evaluate liver measurements (linear, volume) and texture on computed tomography scan, to test their reflection in interpretation of the pattern of liver enzymes abnormality and to assess the ability of laboratory tests and liver imaging tests to detect hepatic diagnosis. Prospective study of 100 patients (41 males & 59 females) with ages ranged between 25-85 years was conducted at Royal diagnostic center during the period extended from June 2014 to July 2017.

Total bilirubin, direct bilirubin, Alkaline Phosphatase (ALP), Aspartate Transaminase (AST), Alanine Transaminase (ALT), albumin, globulin, total protein and prothrombin time (PT) were evaluated and clearly correlated with computed tomography imaging results and with liver measurements.

The linear hepatic measurements were evaluated including: mid hepatic point cranio caudal (MHP CC), maximum cranio caudal (Max CC), maximum transverse dimension (Max LL) and mid hepatic point anteroposterior (MHP AP) dimension. Hepatic volume measurements were performed depended on linear hepatic measurements: (MHP AP * Max LL * Max CC * 0.31) and the texture was evaluated for both right and left hepatic lobes and was measured in (Hounsfield). Cholangiocarcinoma was correlated significantly with AST level at $p=0.038$. Total bilirubin, direct bilirubin and ALP was correlated significantly with right lobe hepatocellular carcinoma (HCC) at $p=0.004$, 0.000 and 0.004 and with left lobe HCC at $p=0.000$, 0.025 and 0.042 respectively. Liver metastases decreased albumin level and was correlated significantly at $p=0.030$ and with total protein at $p=0.025$, while the PT was increased significantly with the presence of liver metastases at $p=0.007$ and cirrhosis at $p=0.030$. In the presence of Klatskin tumor the increasing of globulin was correlated significantly at $p=0.003$ and with total protein at $p=0.001$.

Results showed that there were no significant relation between the presence of focal nodular hyperplasia, fatty liver disease, abscess and simple cyst with the total bilirubin, direct bilirubin, ALP, AST, ALT, albumin, globulin, total protein and PT. The results showed that there was no significant relation between the changing in hepatic measurements done by CT and the biochemical markers values and showed no significant relationship between the liver volume and the liver function test results except with the serum albumin at $p=0.030$. The evaluation of the liver density by measuring the CT Hounsfield was obtained showing only significant relation with globulin results at $p=0.047$ and total protein at $p=0.017$.

مستخلص الدراسة

تهدف هذه الدراسة إلى توصيف الكبد بتقييم طول وعرض وحجم وكثافة نسيج الكبد وذلك بإستخدام تقنية التصوير بواسطة الاشعة المقطعية لإختبار إنعكاسهم في تفسير نمط شذوذ إنزيمات الكبد ايضا إهتمت الدراسة بتقييم قدرة نتائج إختبارات وظائف الكبد المعملية ونتائج تصوير الكبد في تصنيف أمراض الكبد. إشتملت هذه الدراسة على 100 مريض (41 ذكور و59 إناث) أعمارهم بين 25 إلى 85سنة، إختبروا لتحديد نوع المرض ثم تحليل البيانات للتحقق من الإرتباط بين إختبارات وظائف الكبد وتقنية التصوير بواسطة الأشعة المقطعية. وقد أجريت الدراسة في مركز رويال التشخيصي أثناء الفترة الممتدة من يونيو 2014 إلى يوليو 2017.

الفحوصات المعملية التي أجريت إشتملت على: بليروبن (ياقوتين الصفراء) الكلي، بليروبن المقترن، فوسفاتاز قلوي، إنزيمات حفز انتقال المجموعة الأمينية (ألانين، أسبارتات)، زلال، غلوبيولين (بروتينات)، البروتين الكلي الرئيسي، زمن توليد الخثرين، قيمت وربطت بشكل واضح بنتائج التصوير بواسطة الأشعة المقطعية.

المقاييس الكبدية الخطية إشتملت على: جمجمي ذنبي مرورا بالنقطة الكبدية الوسط، أعظم بعد جمجمي ذنبي الى طرف الكبد، أعظم قياس مستعرض، أمامي خلفي مرورا بالنقطة الكبدية الوسط. حجم الكبد معتمد على المقاييس الكبدية الخطية (أعظم قياس مستعرض × جمجمي ذنبي × أمامي خلفي مرورا بالنقطة الكبدية الوسط × 0.31). تقنية تحليل النسيج أجريت لإيجاد إختلاف المستوى الرمادي (هونسفيلد) للفصين الأيمن والأيسر في صور الأشعة المقطعية.

أوجدت الدراسة أن هناك إرتباط بشكل ملحوظ بين ورم قناة الصفراء و بمستوى إنزيم أسبرتاتي ناقل المجموعة الأمينية بقيمة إحتمالية تساوي 0.038، أيضا هناك إرتباط بين بليروبن الكلي، بليروبن المقترن، فوسفاتاز قلوي وبين سرطان الكبد الخلوي في الفص الأيمن بقيم تساوي 0.004، 0.000، 0.004 وبين سرطان الكبد الخلوي في الفص الأيسر بقيم 0.000، 0.25، 0.042 على التوالي. الإنبثاث السرطاني للكبد قلل الزلال؛ هناك ارتباط بين الزلال بقيمة 0.030 وبين البروتين الكلي بقيمة 0.025 بينما زمن توليد الخثرين زاد بشكل ملحوظ بسبب الإنبثاث السرطاني للكبد و الكبد المتشمعة بقيمة تساوي 0.007 و 0.030 على التوالي. ورم كلاتسكين زاد مستوى غلوبيولين و البروتين الكلي الرئيسي أي هناك إرتباط بقيم 0.003، 0.001 على التوالي.

أشارت الدراسة إلى أن بعض الأمراض الظاهرة في صور الأشعة المقطعية مثل الفرط النسيجي العقدي البؤري والكبد المدهنة والخراج والأكياس الغشائية البسيطة ليس لها تأثير على وظائف الكبد: بليروبين الكلي، بليروبين المقترن، فوسفاتاز قلوي، إنزيمات حفز انتقال المجموعة الأمينية (ألانين، أسبارتات)، ألبومين، غلوبيولين، البروتين الكلي الرئيسي، بروثرومبين. كما أوضحت النتائج بأنه ليس هناك إرتباط بين التغير في المقاييس الكبدية الخطية وحجم الكبد وبين إنزيمات وظائف الكبد الطبيعية والغير طبيعية بإستثناء الألبومين هناك إرتباط بينه وبين حجم الكبد بقيمة تساوي 0.030. أوضحت النتائج أن هناك إرتباط بين كثافة نسيج الكبد و الغلوبيولين بقيمة 0.047 وبين البروتين الكلي بقيمة 0.017 .

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List of abbreviations

ALP	Alkaline Phosphatase
ALT	Alanine Transaminase
AP	Anteroposterior
AST	Aspartate Transaminase
ATCM	Automatic tube current modulation
Ca	Carcinoma
CC	Cranio caudal
CBD	Common bile duct
CECT	Contrast enhanced computed tomography
CHD	Common hepatic duct
Cm	Centimeter
CM	Contrast material
CT	Computed tomography
CTAP	Computed tomography during arterial portography
DFOV	Display field of view
ERCP	Endoscopic retrograde cholangiopancreatography
FNH	Focal nodular hyperplasia
G	Gram
^{67}Ga	Gallium-67
GB	Gall bladder
GGT	Gamma glutamyltransferase
GIT	Gastrointestinal tract.
g/L	Gram per liter
HA	Hepatic artery
HBV	Hepatitis B virus
HCC	Hepato cellular carcinoma
HELLP	Hemolysis elevated liver enzymes and low platelets

HIDA	Hepatobiliary iminodiacetic acid
HU	Hounsfield units
HV	Hepatic vein
^{131}I	Iodine-131
IDA	Iminodiacetic acid
IgA	Immunoglobulin A
IU/L	International units per liter
IV	Intra venous
IVC	Inferior vena cava
Kg	Kilo gram
KVp	Peak kilo voltage
LFTs	Liver function tests
Lt	Left
MA	Millie ampere
Max LL	Maximum laterolateral
MCL	Midclavicular
MDCT	multi- detector computed tomography
mg/dl	Milligrams per deciliter
MHP	Mid hepatic point
Ml	Milliliter
ml/sec	Milliliter per second
Mm	Millimeter
µmol/L	Micromoles per liter
MPR	Multiplaner image reformatting
MRI	Magnetic resonance imaging
MRCP	Magnetic resonance cholangio pancreatography
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis

NTP	5'-nucleotidase
PT	Prothrombin time
PTC	Percutaneous transhepatic choleangiography
PV	Portal vein
Rt	Right
RUQ	Right upper quadrant
SPSS	Statistical package for social science
^{99m}Tc	Technetium-99m
T1-W	T1-weighted image
U/L	Units per liter
U.S	United State
US	Ultra sound
WL	Window level
WW	Window width
3D	Tree-dimension

Chapter one

1.1 Introduction

The liver is the largest and most versatile and complex organ in the body. It consists of two main lobes.The liver parenchyma consist of two major cell types, the polygonal cells which comprise 85% of the cellular population and the reticulo endothelial cell which make up the remaining 15%. In addition to this cellular population, the liver is fed, drained and otherwise traversed and indented by the portal and hepatic venous systems, the hepatic arteries and the biliary duct system (David et al, 1977). The normal adult liver spans 10 to 12 cm for men and 8 to 10 cm for women (Epstein et al, 1998). Generally, it can vary between 6 and 12 cm in all subjects when percussion is performed in the midclavicular line (Silva, 2005).

Estimation of liver measurements can be used as directory to observe many liver disease and response to treatment (Strunk et al, 2003). Mid clavicular (MCL), craniocaudad (CC), or midhepatic (MHP) CC measurements have been used in ultrasound (US) to estimate liver size (Naylor et al, 1987). Standard LFTs which are very sensitive for the abnormality occurred may be considered as biochemical marker of liver dysfunction consists of the enzymes Alanine Transaminase (ALT), Aspartate Transaminase (AST), Alkaline Phosphatase (ALP) and Gamma Glutamyl Transferase (GGT), together with bilirubin, albumin, total protein and globulin; when considered together, these analytic open a diagnostic window into multiple organ systems (Dr/Sydney S). Laboratory and radiologic tests have three major roles including screening, diagnosis and management (Black, 1997). The primary modalities currently used for diagnostic imaging of the liver and biliary tract are US, CT, MRI (Taylor et al, 1998). While radionuclide studies are additional useful noninvasive modalities, however they are less frequently requested for the initial investigation of abnormal laboratory test results

(Saini, 1997). US are currently the most common method for screening asymptomatic patients with elevated liver enzymes (H Osawa et al, 1996). CT allows for a more quantitative assessment with measurement of liver attenuation in Hounsfield units (HU) compared to US (JE Jacobs et al, 1998). A common indication for abdominal imaging is to assist in the evaluation of abnormal liver function test (LFT) results.

The various biochemical tests, their pathophysiology and an approach to the interpretation of abnormal LFTs are discussed in chapter two.

1.2 Problem of the Study:

Among the most important are group of blood tests known as liver function tests. Such blood tests represent a non-invasive way to screen for the presence of liver disease (hepatitis in blood donation) and to measure the severity and progress of liver disease and its response to treatment; however, the term is somewhat misleading because most such test does not test the metabolic or bile-secreting functions of liver. Rather, they detect inflammation or damage of the liver. In the current study, we find it helpful on inspecting a set of LFTs to first pose the simple question: Is this pattern likely to be due to liver pathology or not? For that point we find the answer when the CT images were taken and were diagnosed pre and post contrast

1.3 Objectives of the study:

1.3.1 General objective:

The general aim of this study to characterize the liver in patients with liver function tests by using computed tomography scan.

1.3.2 Specific objectives:

1. To inspect a set of liver function tests.
2. To evaluate the measurements (linear & volume) and texture of the liver on CT scan

3. To test their reflection in interpretation of the pattern of liver enzymes abnormality.

4. To classify liver lesions.

5. To correlate the CT findings with laboratory results.

6. To assess the ability of laboratory tests and liver imaging tests to detect hepatic diagnosis.

Chapter two
Literature review

2.1 Anatomy of the liver:

The liver is the largest organ of the abdomen, occupying a major portion of the right upper quadrant. The liver weight about 1.5 kg in the adult and composed of many cellular plates radiating between the central veins and the portal tracts. The hepatic plates are two cells thick. Between the cells there are bile canaliculi, which drain into biliary ducts, and between the plates are found the blood sinusoids which receive the blood from branches of the portal veins and branches of hepatic artery (Sukkur et al, 2006).The liver can be divided into eight segments according to the vascular supply (Figure 2.4) (Kelly et al, 1997) and divided into lobes according to surface anatomy. The Rt hepatic lobe is much larger than the Lt (Peter, 2009). On occasion, the Lt lobe of the liver extends lateral to the spleen, which can mimic a perisplenic collection or mass (David, 1992).

The fissure of the gallbladder (GB) divides the liver into right and left lobes and the falciform ligament divides the Lt lobe into medial and lateral segments (Peter, 2009). The Rt lobe contains four separate segments and the Lt has three segments with the quadrate lobe comprising the most medial and antero-inferior surface of the Lt lobe between the GB and the ligamentumteres (The round, cord-like, and runs along the free edge of the falciform ligament). The caudate lobe remains a separate segment (Figure 2.2). It is the smallest lobe located on the postero- inferior and medial to the Rt lobe, sandwiched between the IVC and the ligament venosum (Kelley et al, 1997). Each segment has its own HA & PV inflow, HV& biliary drainage. This classification is important in hepatic surgery as each segment can be

resected without damaging those remaining (Peter, 2009). The inferior and posterior surface of the Rt lobe is bordered by the porta hepatic (hilum of the liver), GB and IVC. The falciform ligament provides the structural support that attaches the upper surfaces of the liver to the diaphragm and upper abdominal wall (Kelly et al, 1997).
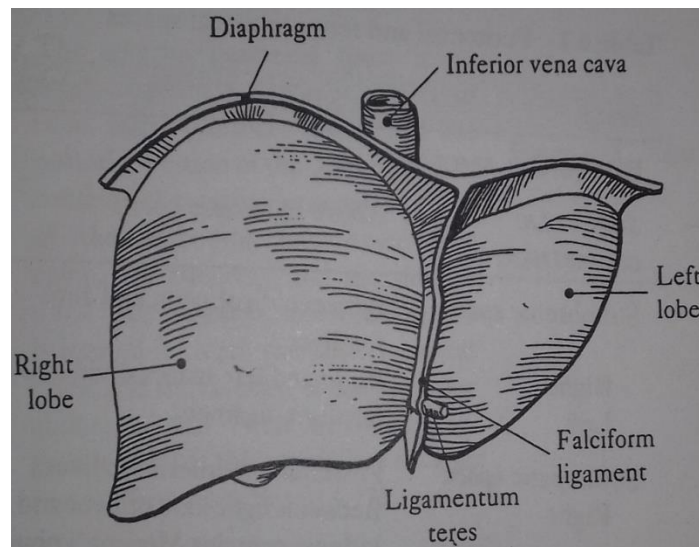
Figure 2.1: Anterior view of liver surface (Kelley et al, 1997).
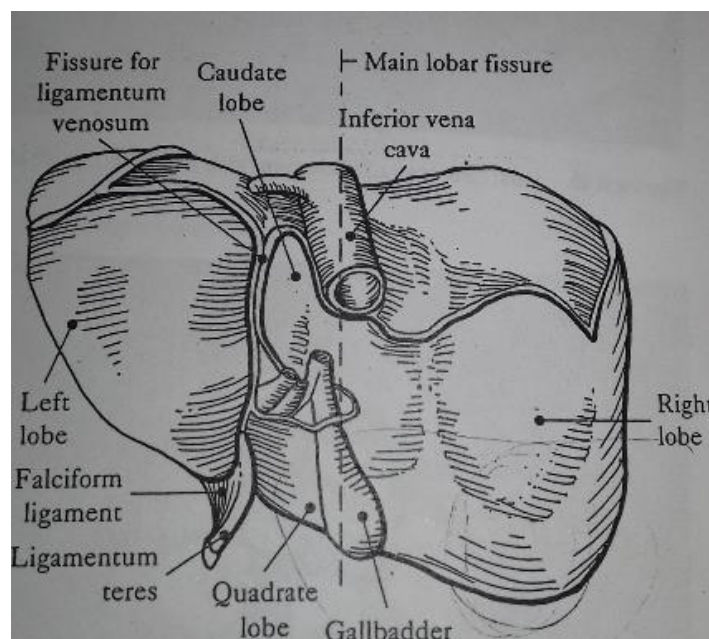
Figure 2.2: Posterior view of liver surface (Kelley et al, 1997).

2.2 Anatomy of the gall bladder (GB):

The pear-shaped GB is located in a fossa on the antero-inferior portion of the Rt lobe of the liver. It acts as a reservoir for bile. The body of the GB tapers into the neck of the GB and then continues as the cystic duct. Normal GB size is variable according to the amount of bile it is storing. Up to 3cm wide and 7cm to 10cm long is normal size for the GB. The wall of the GB is less than 3mm.The GB has a capacity of 30-50ml. It stores, concentrates bile and regulates its discharge into the duodenum (Dykstra et al, 1999).
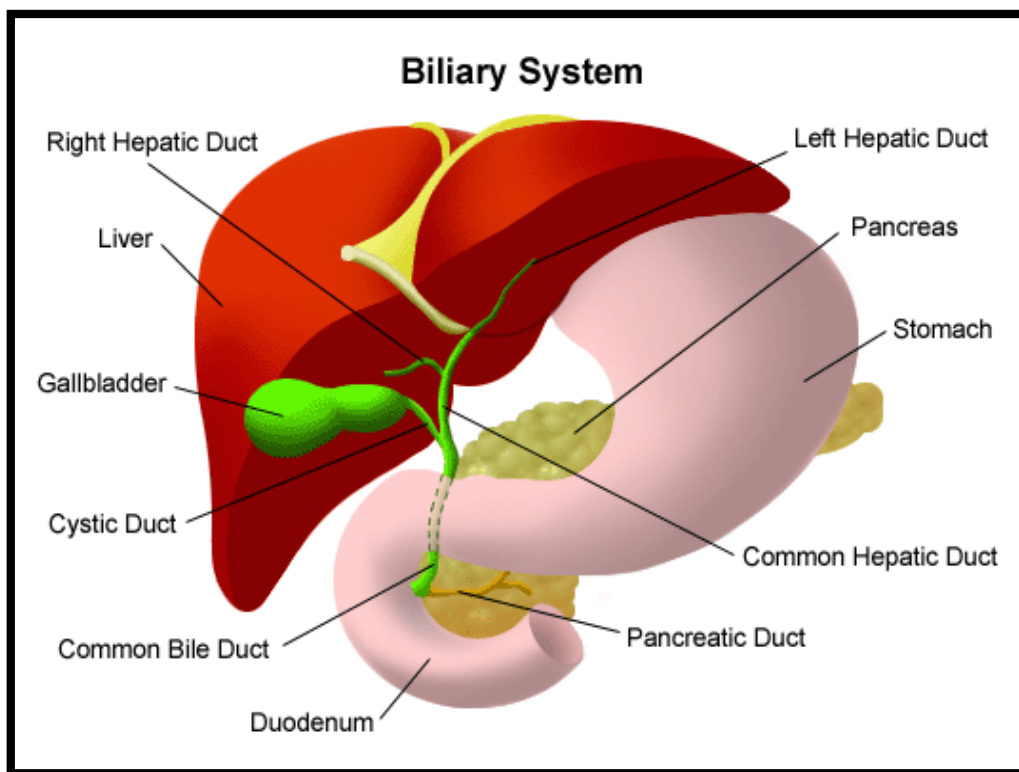
Figure 2.3: Anatomy of the biliary system

(https://www.beaumonthospitals.com/health-library/p07694).
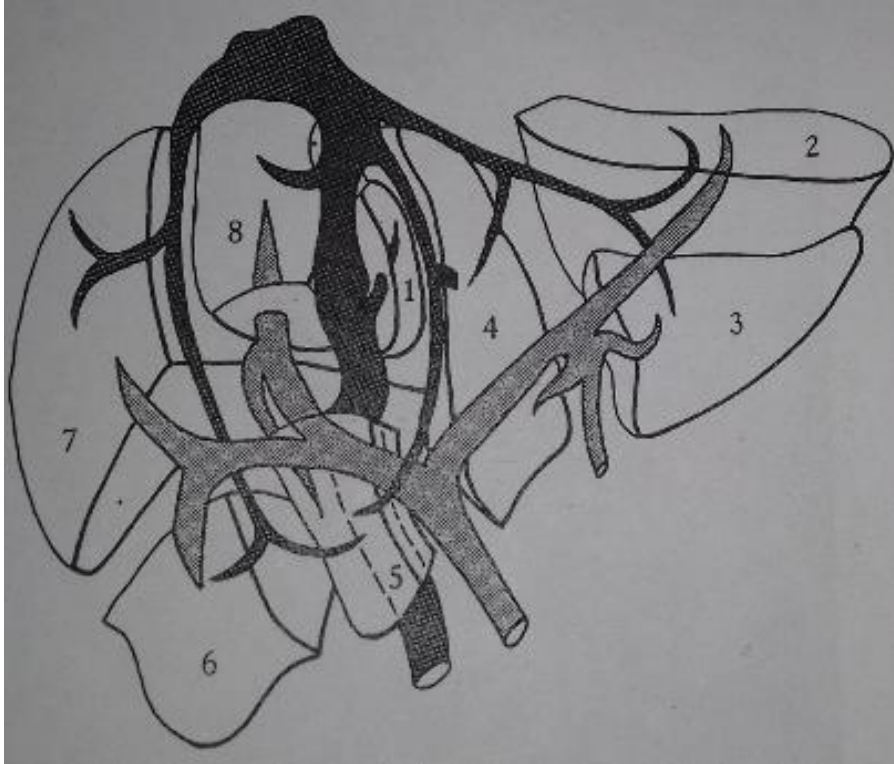
Figure 2.4: Coronal view with segmental anatomy of the liver (Kelley et al, 1997).

2.3 Physiology of the liver:

2.3.1 Vascular function:

2.3.1.1 Storage:

Since the liver blood flow is 30% of blood volume, it is one of the important reservoirs of blood in the body. In case of strenuous exercise or hemorrhage, part of the hepatic blood is diverted towards the exercising muscles or vital organ (Sukkur et al, 2006).

2.3.1.2 Antigen clearance:

The liver filters the blood coming from the gut and remove bacteria, debris, particulate matter or any other antigens contained in the blood arriving from the gut (Sukkur et al, 2006).

2.3.2 Metabolic functions:

The liver has a central role in the metabolism of the major types of foodstuffs as well as substances of endogenous or exogenous origin (Sukkur et al, 2006).

2.3.3 Synthesis function:

The liver synthesizes many useful substances such as albumin and the coagulation factors. Hepatic failure therefore results in bleeding disorders (Sukkur et al, 2006).

2.3.4 Secretary function:

The liver continuously secretes bile, which after storage and concentration in the GB, is discharged into the duodenum. It needs to be stored between meals to aids in digestion.

Bile is a viscous golden-yellow or greenish fluid with a bitter taste. It is iso-osmotic with plasma and slightly alkaline. The liver produces about 5 liters of bile per day but only 500-600ml is poured into duodenum daily (Sukkur et al, 2006).

2.4 Disorder of the hepatobiliary system:

2.4.1 Jaundice:

Jaundice or icterus refers to the yellowish discoloration of the skin and sclera (Krebs et al, 1992). Although the upper limit of normal for total serum bilirubin is 1mg/dl, jaundice is not clinically apparent until the bilirubin level exceeds 2 to 3 mg/dl. Except in infants, physiological jaundice is common and generally well tolerated and doesn't produce serious clinical side effects and often disappears within two weeks after birth. Less common causes of newborn jaundice include: biliary atresia, certain blood abnormalities, certain inherited disorders and infection (Stuart et al, 2007). For suspected stone disease or a hilar stricture, MRCP is often more helpful than CT in delineating the biliary tree. Conversely, CT is more often used for further evaluation and staging of a distal obstruction secondary to an underlying pancreatic malignancy (Peter, 2009).

2.4.1.1 Radiographic appearance of the jaundice:

Imaging is used to determine the site of obstruction (distal CBD or hilar) and if possible, the cause of obstruction such as impacted stone in the CBD, Ca of the head of the pancreas, Ca of the ampulla of vater and cholangiocarcinoma. Dilatation of the intra and extra hepatic biliary system (CBD >7mm or CHD >5mm) can be identified at CT. The intra hepatic bile ducts may not dilate at all within the first 48 hours following obstruction (Peter, 2009).
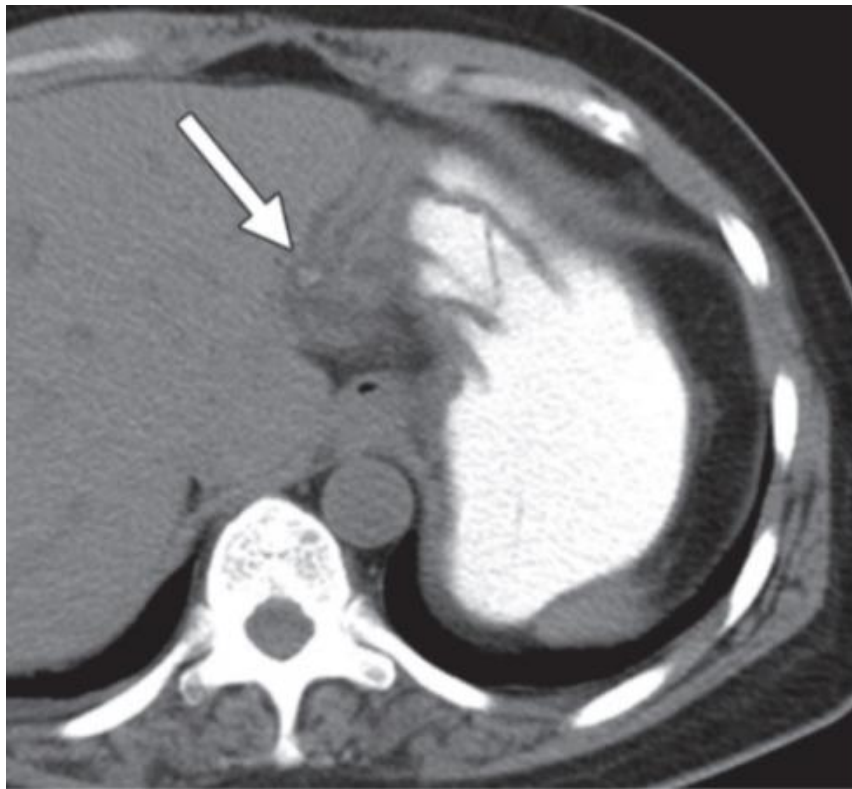
Figure 2.5: Intra-hepatic stone disease. Axial pre-contrast CT scan shows hepatolithiasis (arrow) in the dilated Lt intrahepatic duct (Yong et al, 2009).

2.4.1.2 Levels of the jaundice:

2.4.1.2.1 Pre-hepatic jaundice:

Pre-hepatic jaundice is caused by an increased rate of hemolytic, malaria can cause jaundice. Certain genetic diseases, such as sickle cell anemia, spherocytosis, thalassemia and glucose 6-phosphate dehydrogenate deficiency can lead to increased red cell lyses (Kumar et al, 2003).

2.4.1.2.2 Hepatocellular jaundice:

Hepatocellular (hepatic) jaundice can be caused by inflammatory destruction of intrahepatic bile ducts (e.g. primary biliary cirrhosis, primary sclerosing cholangitis and liver transplantation), hepatocellular damage or toxicity (viral or drug-induced hepatitis), deficiency in canalicular membrane transports (Dubin-Jonson syndrome, Rotor syndrome), and drug-induced canalicular membrane dysfunction (oral contraceptives, cyclosporine) (Kumar et al, 2003).

2.4.1.2.3 Post-hepatic jaundice:

Post-hepatic jaundice also called obstructive jaundice, caused by an interruption to the drainage of bile in the biliary system. The most common causes are Ca of head of pancreas, gallstones, obstruction of the biliary tree, Ca of the ampulla of vater, biliary strictures, extrahepatic biliary artesia, primary sclerosingcholengitis (extrahepatic), pancreatitis (Kumar et al, 2003).

2.4.2 Diffuse liver diseases:

2.4.2.1 Cirrhosis:

Cirrhosis is chronic destructive disease. Common causes of cirrhosis are hepatitis and chronic alcoholism (Daniel, 2011). Other causes of cirrhosis include hemochromatosis, post-necrotic cirrhosis (which occurs as a late consequence of hepatitis) and primary biliary cirrhosis which is an autoimmune disorder (David, 1992).

2.4.2.1.1 Radiographic appearance of the cirrhosis:

The signs of cirrhosis of the liver at CT are characterized by variety of features, including hepatomegaly, fatty infiltration and irregular nodular contour, enlargement of the Lt and caudate lobes of the liver, portal hypertension and reduction in size of the Rt lobe together with splenomegaly. Ascites may be present as well. At CT, the parenchyma appears normal until late in the disease (Peter, 2009). In many cases, the anterior segment of the Rt

lobe atrophies more than does the posterior segment, causing flattening of the surface of the former. These features are only "seen" at the end stage of disease, however, not always present. Regenerative nodules are characteristically present in cirrhotic livers, caused by grossly distorted hepatic architecture, heterogeneous regeneration, and heaptocellular dysplasia, these nodules, usually less or larger than 5 mm or larger than 10 mm in diameter (Wada et al, 1988). The resulting nodular appearance on CT can mimic malignancy. Occasionally regenerative nodules are hyper dense on unenhanced CT. regenerative nodules can also displace hepatic vessels, producing mass effect on angiograms (Rabinowitz et al, 1974).
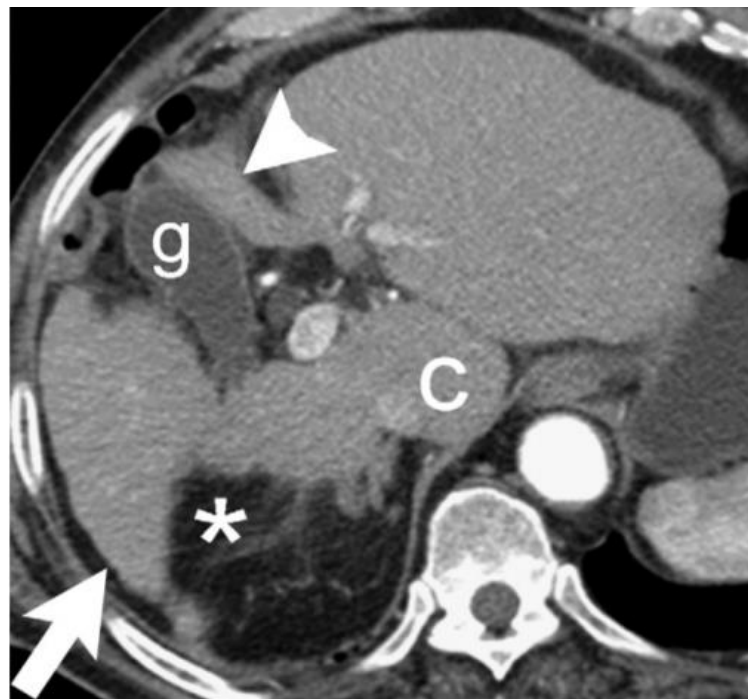
Figure 2.6: CT of liver cirrhosis.

Portal venous phase shows an enlarged Lt & caudate lobe (C), an enlarged gallbladder fossa with the gallbladder (g), atrophy of the medial segment of the Lt lobe (arrowhead) and Rt posterior hepatic lobe (arrow) (Giuseppe et al, 2007)

2.4.2.2 Fatty liver disease (FLD):

NAFLD is the term caused by a build-up of fat in the liver in response to nutritional, chemical or vascular insults such as ethanol abuse, diabetes mellitus and obesity (Nomura et al, 1987). It is also observed in many patients with advanced malignancy, possibly because of poor nutrition and hepato-toxic effects of chemotherapy (David, 1992). Fatty infiltration may involve the whole liver or individual subsections. However, some patients infrequently progress to outright hepatic inflammation, so called NASH (Clark et al, 2003). Over time, NASH may progresses into fibrosis, cirrhosis, liver failure or HCC (Chavez et al, 2009).

2.4.2.2.1 Radiographic appearance of FLD:

Fatty change is frequently diffused, patchy or even focal with CT. Most likely reflecting regional differences in perfusion; areas of decreased portal flow tend to accumulate less fat than better perfus eareas, the probably because less dietary lipid reaches the hepatocytes (Arai et al, 1988). Areas of focal sparing of fatty infiltration appear hyper dense to surrounding tissue and may mimic hepatic neoplasm (Daniel, 2011). Fatty infiltration leads to a reduction in the attenuation of the affected parenchyma causing low density on CT scans. The vessels are then seen as relatively high attenuation structures against a background of low-density parenchyma, even on images taken without intravenous CM (Itai et al, 1987).
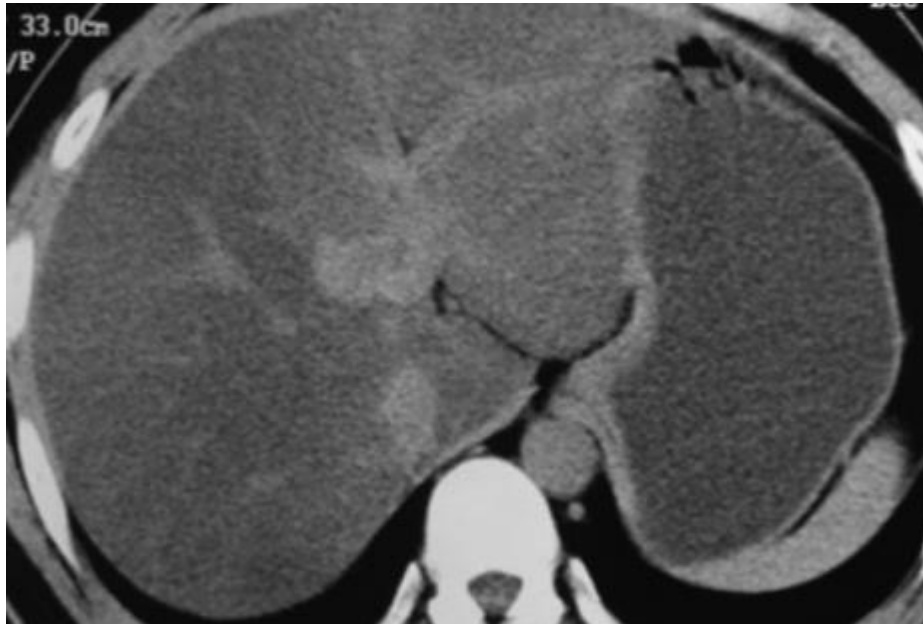
Figure 2.7: CT of fatty liver (Chang, 2011).

2.4.3 Masses:

2.4.3.1 Malignant neoplasm of the liver:

2.4.3.1.1 Hepatocellular carcinoma (HCC):

Hepatocellular carcinoma the most common primary malignant neoplasm of the liver (Daniel, 2011). HCC is usually associated with chronic liver disease such as alcoholic cirrhosis, chronic active hepatitis or hemochromatosis (Jorge et al, 2012).

2.4.3.1.1.1 Radiographic appearance of HCC:

HCC typically appears hypodense on non-contrast CT scans and hyperdense or hyper vascular (Figure 2.8) on arterial phase imaging (Daniel, 2011). HCC and cholangiocarcinoma are usually solitary but they may be multifocal (Peter, 2009). On occasion, HCC has a central scar that may be vascular, inflammatory or fibrotic. Fibrous scares are more common with HCC and vascular scars are more common with FNH (Rummeny et al, 1989). Slow growing HCC is frequently surrounded by a fibrous capsule (Yoshida et al, 1989).
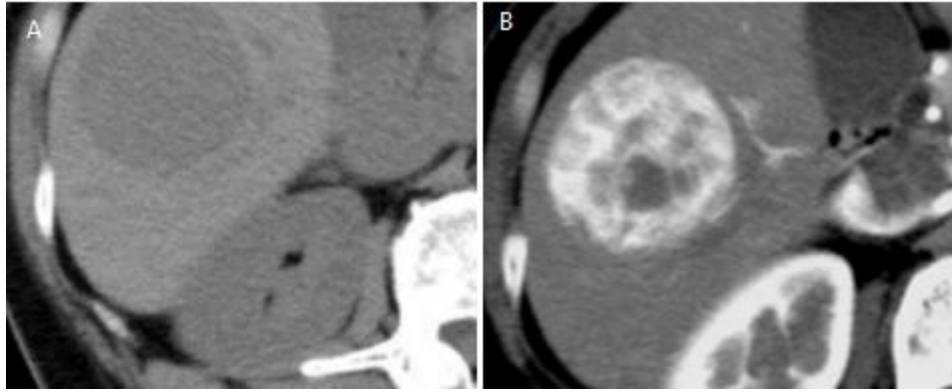
Figure 2.8: CECT images demonstrating a mass.

(A) A low-density mass in the plain phase. (B) A heterogeneous high-density mass (Noritaka et al, 2012).

2.4.3.1.2 Metastases:

The liver is common sites for the metastatic spread of Ca. Primary neoplasm that commonly metastasize to the liver include those of the colon, lung, breast, pancreas and stomach (Daniel, 2011).

2.4.3.1.2.1 Radiographic appearance of metastases:

Metastases are often solitary or multiple, situated peripherally and of variable size. At times, they undergo central necrosis described as a target lesion they may even resemble cysts (Peter, 2009). The CT appearance of hepatic metastases varies greatly and is nonspecific. They may appear hypodense or hyperdense in arterial phase images (Figure 2.9), necrotic or calcified (Daniel, 2011). Intense contrast enhancement is sometimes seen within the tumor, or immediately surrounding it, a useful differentiating feature, which is not seen with cysts (Peter, 2009).
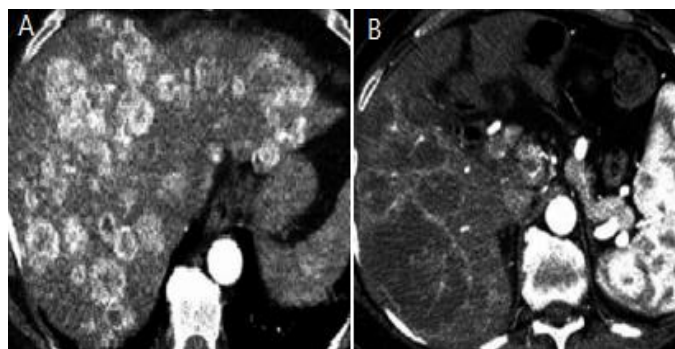
Figure 2.9: Arterial phase CECT of metastatic liver tumors

were grouped into hypervascular tumors (A) and hypovascular tumors (B) (Koichi et al, 2013).

2.4.3.1.3 Malignancy of the biliary tract:

2.4.3.1.3.1 Cholangiocarcinomas:

Cholangiocarcinomas are epithelial cancers of the biliary tree. They are broadly classified into intra-hepatic tumors, hilar tumors and distal bile duct tumors. Majority arise in the absence of risk factors, however, identified risk factors include age, primary sclerosing cholangitis, chronic choledocholithiasis, bile duct adenoma, parasitic biliary infestation and chronic typhoid carrier state (Malhi H et al, 2006). Hilar cholangiocarcinoma accounts for two thirds of all cases of extra-hepatic cholangiocarcinoma (Ortner M et al, 2001).

2.4.3.1.3.1.1 Radiographic appearance of cholangiocarcinomas:

Arterial phase CT scan shows a tumor with ragged rim enhancement at the periphery and gradual centripetal enhancement of the tumor at portal venous phase (Yong EC et al, 2009).
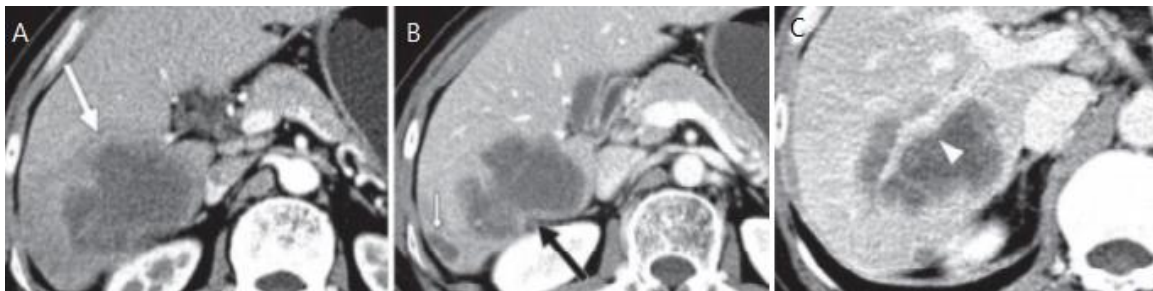
Figure 2.10: CT cholangiocarcinoma.

(A) Arterial phase CT scan shows a tumor with ragged rim enhancement at the periphery (arrow). (B) Axial portal venous phase CT scan shows gradual centripetal enhancement of the tumor with capsular retraction (black arrow). A satellite nodule is also seen (white arrow). (C) three-minute delayed phase CT scan shows gradual centripetal enhancement with tumor encasement of the posterior branch of the Rt PV (arrowhead) (Yong ECet al, 2009).

2.4.3.2 Benign liver masses:

2.4.3.2.1 Cavernous hemangioma:

Cavernous hemangioma is vascular lesion (Daniel ND, 2011). Cavernous hemangioma is the most common benign hepatic neoplasm. Cavernous

hemangiomas are composed primarily of large vascular lakes and channels. Many of these channels undergo thrombosis and fibrous organization. Complications are rare and ensue only when large lesions rupture (Takayasu K et al, 1990).

2.4.3.2.1.1 Radiographic appearance of cavernous hemangioma

On CT, hemangioma is characterized by diminished attenuation on the precontrast scan, peripheral globular enhancement during initial post-contrast imaging, Progressive fill-in of enhancement occurs over time, until the mass becomes isodense with surrounding hepatic parenchyma (Daniel ND, 2011). Cavernous hemangiomas frequently show complex internal architecture. Cavernous hemangiomas frequently degenerate, forming internal cysts or fibrotic scars that occasionally calcify (Choi BI et al, 1989).

Figure 2.11: CT of hepatic hemangioma.

(A)Nonenhanced image shows hypoattenuation lesion. (B) Arterial phase shows peripheral, globular enhancement of the lesion. (C) Venous phase shows centripetal enhancement that progress to uniform filling (S Florimet al, 2017).

2.4.3.2.2 Cysts:

Liver cysts are usually congenital in origin; some are due to infection (Peter AS, 2009). Cysts of the liver are less common than cavernous hemangiomas (David DS, 1992).

2.4.3.2.2.1 Radiographic appearance of cysts:

Simple cysts of the liver may be single or multiple, variable in size and are scattered through the liver. At CT, cysts show very well-defined, thin-walled round or oval masses and have attenuation values similar to that water (0_20 HU). The hallmark feature is lack of enhancement with IV contrast agent administration (Daniel ND, 2011).It is often not possible to characterize small lesions, and with lesions below 1 cm in diameter it may be difficult to distinguish cyst from neoplasm.
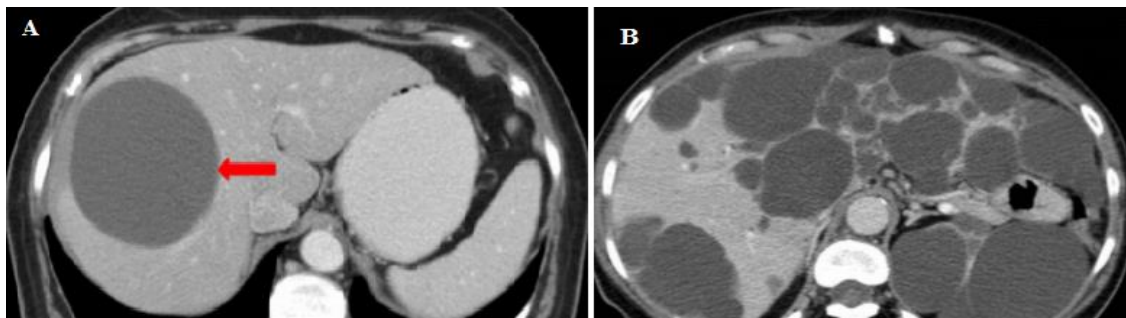
Figure 2.12: CECT of hepatic cyst.

 (A) Simple cyst (arrow). (B) Polycystic liver and kidneysdisease (E Rosado et al, 2014).

Cysts due to echinococcus (hydatid) disease may be single or multiple; a few shows calcified wall and may prove indistinguishable from simple cysts. Daughter cysts may be seen within a main cyst at both US and CT. Occasionally; metastases can have a cystic appearance (Peter AS, 2009).
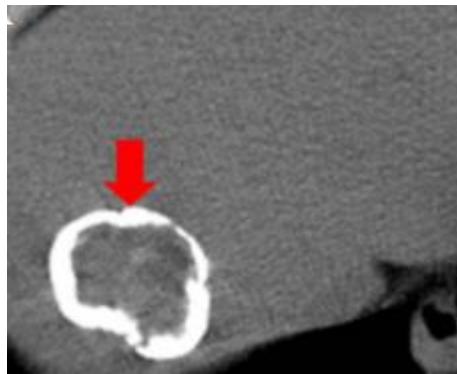
Figure 2.13: Unenhanced CT of hydatid cyst

in the Rt lobe of liver (E Rosado et al, 2014).

2.4.3.2.3 Focal nodular hyperplasia (FNH):

FNH is another common vascular lesion often identified along the surface of the liver (Daniel, 2011). FNH is rare benign tumor of the liver that contains hepatocytes, bile duct elements, kupffer cells and fibrous tissue. The distinction between FNH and hepatocellular adenomais important, since FNH can be treated conservatively, where as hepatocellular adenoma is resected because of its propensity to hemorrhage (David DS, 1992).

2.4.3.2.3.1 Radiographic appearance of the FNH:

The CT appearance of FNH varies and can be hypodense or isodense relative to the liver on either noncontrast or contrast-enhanced scans. The finding of a central stellate low-attenuation region by CT is uncommon (Kerlin P et al, 1983). FNH appear as hyper vascular masses on arterial phase on CT (Figure 2.10) (Peter AS, 2009). FNH is characterized on CT by intense homogeneous enhancement with CM administration. There is usually a central scar that remains hypodense until delayed imaging (Rahman ME et al, 1989).
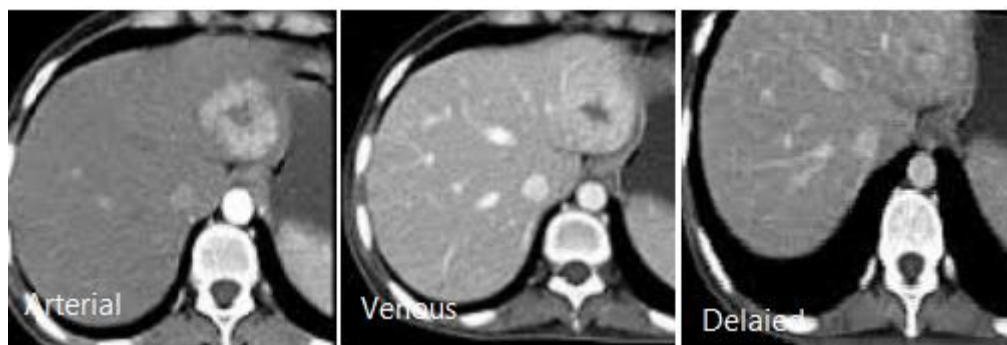
Figure 2.14: CT of FNH.

28 years old female showing well defined arterial enhancing lesion in the Lt lobe of liver with central non-enhancing scar (Manjunath, 2009)

2.4.3.2.4 Hepatocellular adenoma:

The incidence of hepatocellular adenoma is greatest in women of childbearing age, especially those who use oral contraceptives (Kerlin P et al, 1983). Necrosis and hemorrhage are common causes of pain, and life-threatening hemorrhage in the peritoneum can occur. Malignant potential has not been established (David DS, 1992).

2.4.3.2.4.1 Radiographic appearance of hepatocellular adenoma:

Hepatocellular adenoma appears as hyper vascular masses on arterial phase on CT and MRI (Peter AS, 2009). Pathologically, the typical features of hepatocellular adenoma are a thin pseudocapsule, intracellular glycogen deposition, lack of architecture, paucity of bile ducts and necrosis (Kerlin P et al, 1983).
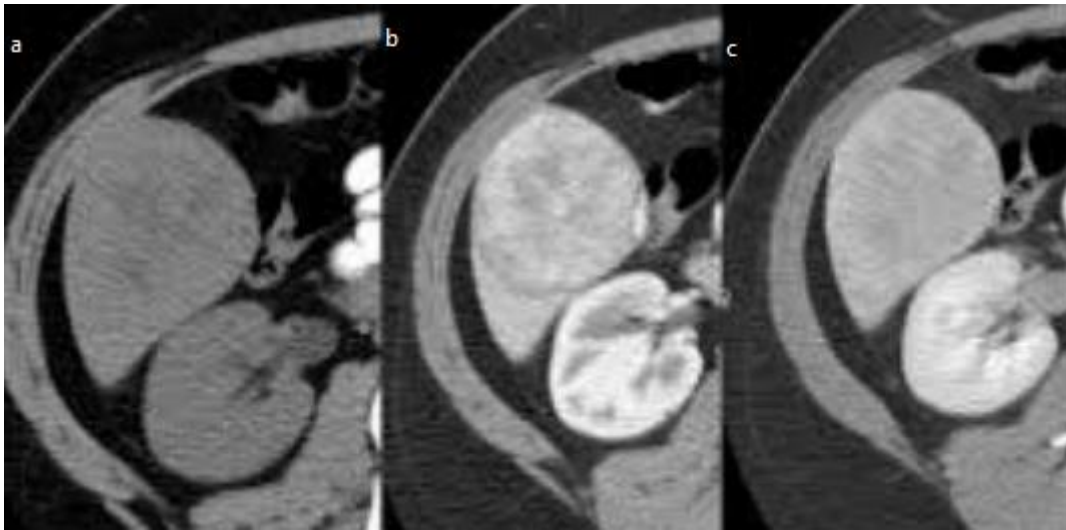
Figure 2.15: CT of hepatic adenoma

In patient with breast Ca. (a) Axial unenhanced shows low density hepatic mass. (b) Inhomogeneous contrast enhancement on arterial phase image. (c) Gradual washout on delayed phase (Gore RM et al, 2012)

2.4.4 Abscess:

Pyogenic liver abscess occurs most commonly in older patients with Ca or biliary disease. The symptoms and signs of hepatic abscess are often nonspecific, delaying diagnosis and therapy (David DS, 1992).

2.4.4.1 Radiographic appearance of abscess:

Abscesses appear somewhat similar to cysts. Hepatic abscesses tend to have fluid centre, with walls that are thicker, more irregular and more obvious than those of simple cysts. Although the CT attenuation values in the centre of an abscess may be the same as water, usually they are higher. Occasionally, chronic abscess calcify. Abscesses cannot usually be distinguished from necrotic tumors at US, CT or MRI (Peter AS, 2009).
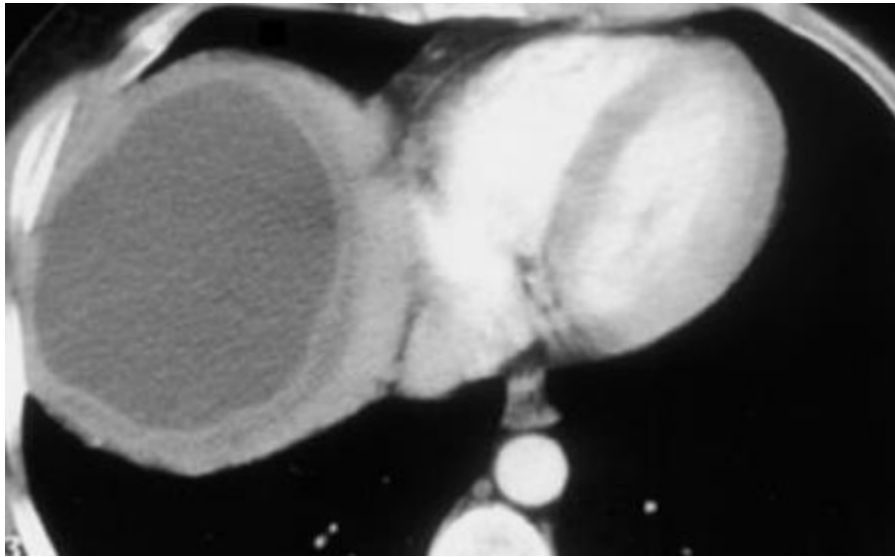
Figure 2.16: A CT of amebic liver abscess

Shows a large, round, hypoattenuated area in the Rt lobe of the liver (Jaspreet KG et al, 2001)

2.4.5 Hepatitis:

Hepatitis means inflammation of the liver which may be caused by viruses, bacteria, parasites, radiation, drugs and chemicals or toxins. Among the viruseshepatitis types A, B, C, D (or delta) and E and several others. Acute hepatitis can be diagnosed by clinical and serologic studies, and imaging is not part of the standard initial work-up, in patients with chronic hepatitis, however, imaging studies are used to detect cirrhosis or ascites and to exclude HCC (David DS, 1992).

2.4.6 Liver trauma:

Trauma to the liver is the commonest abdominal injury that leads to death. US have become part of the standard assessment of patients. CT scanning for evaluation of free intra peritoneal fluid (Peter AS, 2009).

2.4.6.1 Radiographic appearance of the liver trauma:

CT scanning, however, is more sensitive and specific; lacerations and hematomas are recognized as low density areas relative to the contrast-

enhanced parenchyma. Leakage of contrast indicates active bleeding (Peter AS, 2009).

Figure 2.17: CECT of abdominal trauma

showing a complex hepatic laceration: hepatic fracture (Abdominal Blunt Trauma 2013 from: www.imagingpathways.health.wa.gov.au)

2.4.7 Gall stones and cholecystitis:

Gall stones are a frequent finding in adults; particularly middle-aged females. Calcified sludge within the GB is also known as "milk of calcium" bile.Together with accompanying chronic cholecystitis, they are a major cause of recurrent upper abdominal pain (Peter AS, 2009).

2.4.7.1 Radiographic appearance of the gall stones and cholecystitis:

Some 20% of gall stones contain sufficient calcium to be visible on plain film. They vary greatly in size and shape and typically have a dense outer rim with a more lucent centre. Stones that have high lipid content are supported by low x-ray attenuation observed on CT. In acute cholecystitis, the GB wall is thickened and there isa rim of fluid in the GB fossa or fluid within the GB

wall itself and surrounding inflammatory change seen as stranding in the adjacent fat. In chronic cholecystitis, the GB is often contracted and thick-walled (Peter AS, 2009).

Figure 2.18: CECT of necrotizing cholecystitis (Fuszek P, 2016).

2.5 Common methods of diagnosing liver diseases:

There are three main types of methods that are performed in liver disease diagnosis: laboratory tests, radiological studies and biopsies.

2.5.1 Laboratory Evaluation:

Commonly available tests include ALT, AST, ALP, GGT, serum bilirubin, PT and albumin. They reflect different functions of the liver that is, to excrete anions (bilirubin), hepatocellular integrity (tranaminases), formation and the subsequent free flow of bile (bilirubin and ALP) and protein synthesis (albumin).

A detailed history should be taken and full physical examination performed with a particular emphasis on alcohol consumption, risk factors for viral hepatitis (intravenous drug use, sexual promiscuity, homosexual relations and blood transfusions), medications used currently or previously, herbal or alternative remedies and occupational exposure to toxins. Other factors such as diabetes, obesity and hyperlipidaemia in non- alcoholic fatty liver disease and family history for (Wilson's disease, haemochromatosis, autoimmune disease) may be significant (JK Limdiet al, 2003).

Table 2.1: Normal values of LFTs (Jk Limdi et al, 2003).

Liver enzymes	Normal values
AST	0-35 IU/L
ALP	30-120 IU/L
GGT	0-30 IU/L
Bilirubin	2-17μmol/L
PT	10.9-12.5 seconds
Albumin	40-60 g/L

2.5.1.1 Enzyme Tests in Liver Disease:

2.5.1.1.1 Bilirubin:

Bilirubin is the end product of heme degradation. Most of the daily production (0.2 to 0.3 g) (80%) is derived from breakdown of senescent erythrocytes, with the remainder (20%) derived primarily from turnover of heme-containing proteins and from premature destruction of newly formed erythrocytes in the bone marrow. In the laboratory, conjugated bilirubin is the fraction that reacts directly with the reagents. Thus it is reported as "direct" bilirubin. The unconjugated fraction requires the addition of an accelerator compound and is referred to as "indirect" bilirubin (Kaplan MM, 2005).
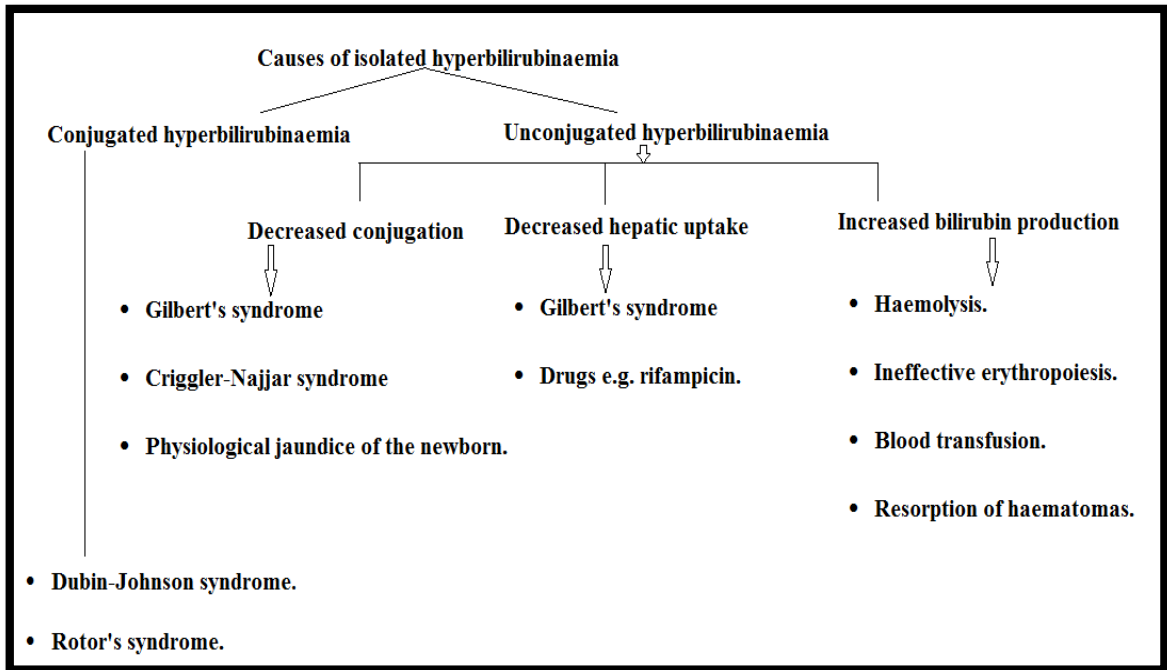
Figure 2.19: Shows Causes of isolated hyperbilirubinaemia

(JK Limdi et al, 2003).

2.5.1.1.2 Alkaline Phosphatase (ALP):

ALP is found in a number of tissues but is used most often in the clinical diagnosis of bone and liver disease such as hepatitis and cirrhosis. ALP is present in mucosal epithelia of small intestine, proximal convoluted tubule of kidney, bone, liver and placenta. The serum ALP activity is mainly from the liver with 50% contributed by bone. It performs lipid transportation in the intestine and calcification in the bone (Mauro P et al, 2006).

Common causes of raised ALP

Pathological causes

- Bile duct obstruction.
- Primary biliary cirrhosis.
- Primary sclerosing cholangitis.
- Drug induced cholestasis (anabolic steroids)
- Metastatic liver disease.
- Adult bile ductopenia.
- Bone disease.

Physiological causes

- Women in the third trimester of pregnancy,
- Adolescents.
- Benign, familial (due to increased intestinal ALP).

Figure 2.20: Shows common causes of raised ALP

(JK Limdiet al, 2003).

2.5.1.1.3 Aminotransferases (Transaminases):

AST and ALT are two enzymes widely used to assess hepatocellular damage. AST mitochondrial and cytoplasmic catalyze transamination reaction. ALT is purely cytoplasmic catalyzing the transamination reaction. AST is found in highest concentration in heart compared with other tissues of the body such as liver, kidney, erythrocyte sand skeletal muscle. ALT is present primarily in the liver and to a lesser extent in the kidney and skeletal muscle, making it more (liver specific) (Mauro P et al, 2006).

Any type of liver cell injury can reasonably increases ALT levels. Elevated values up to 300 U/L are considered nonspecific. Marked elevations of ALT levels greater than 500U/L observed most often in persons with diseases that affect primarily hepatocytes such as viral hepatitis, ischemic liver injury (shock liver) and toxin-induced liver damage. The absolute peak of the ALT elevation does not correlate with the extent of liver cell damage (Kallei L et al, 1964).
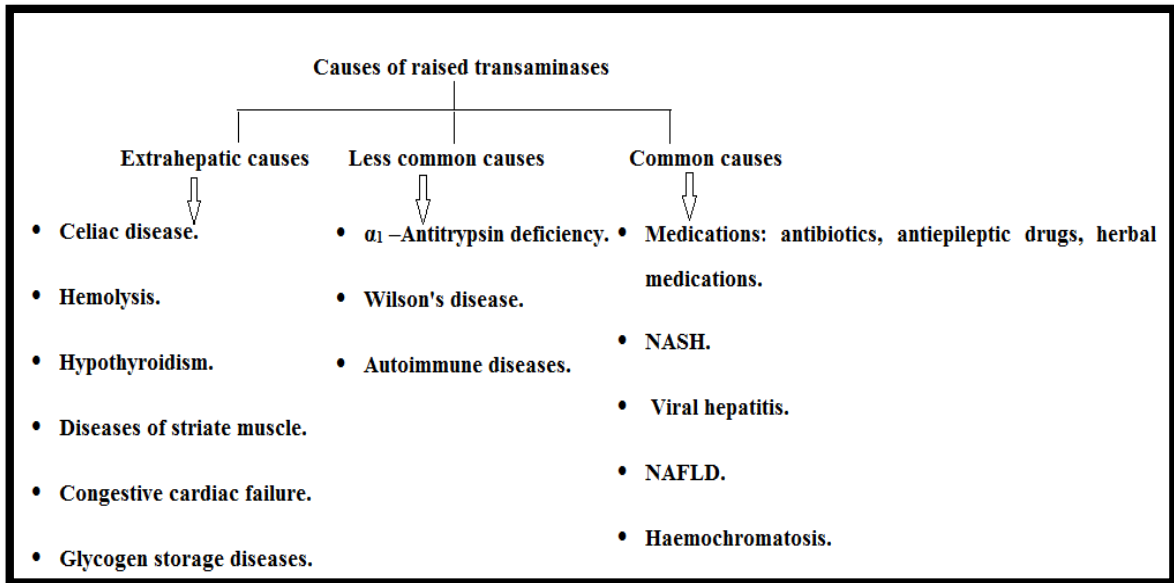
Figure 2.21: Shows causes of raised transaminases

(JK Limdi et al, 2003 and Robert C et al, 2011).

2.5.1.1.4 5'-nucleotidase (NTP):

5'-nucleotidase is another phosphatase. NTP is a glycoprotein generally disseminated throughout the tissue of the body localized in cytoplasmic membrane catalyzing release inorganic phosphate from nucleoside-5-phosphates. The normal range is 0 to 15U/L (Mauro Pet al, 2006).

Raised levels of NTP activity were found in patients with obstructive jaundice, parenchymal liver disease, hepatic metastases and bone disease (Daniel SP et al, 2007). NTP is precise marker of early hepatic primary or secondary tumors. ALP is also increased conjugation with NTP showing intra or extra hepatic obstruction due to malignancy (Smith K et al, 1966). It originates largely in the liver and is used clinically to determine whether an elevation of the ALP is caused by liver or bone disease. Levels of both 5'-nucleotidase and ALP are elevated in liver disease, whereas in primary bone disease, ALP level is elevated, but the 5'-nucleotidaselevel is usually normal or only slightly elevated. This enzyme is much more sensitive to metastatic liver disease than is ALP because, unlike ALP, it's not markedly elevated in other conditions such as pregnancy or childhood. In addition, some increase

in enzyme activity may be noted after abdominal surgery. Elevation of NTP is found in acute infective hepatitis and also in chronic hepatitis (Pratibha K et al, 2004).

2.5.1.1.5 Gamma-glutamyl transferase (GGT):

GGT is a microsomal enzyme present in hepatocytes and biliary epithelial cells, renal tubules, pancrease and intestine. It is also present in cell membrane performing transport of peptides into the cell across the cell membrane and involved in glutathione. It is found in more concentration in renal tissue (Mauro P et al, 2006). The normal level of GGT is 9 to 85U/L (Diana NC et al, 2007).

In acute viral hepatitis the level of GGT will reach the peak in the second or third week of illness and in the some patients remain elevated for 6 weeks (Rosalki SB et al, 1999). Increased level is seen in about 30% of patients with chronic hepatitis C infection (Giannini E, et al 2001). Other conditions like uncomplicated diabetes mellitus, acute pancreatitis, myocardial infarction, anorexia nervosa, hyperthyroidism and obesity caused elevated level GGT (Rosalki SB et al, 1999). It is elevated in the serum of almost all patients with hepatobiliary disorders. The highest levels are seen in biliary obstruction. It is not specific for any type of liver disease but is frequently the first abnormal LFT demonstrated in the serum of heavy drinkers. It is, therefore, a sensitive test for alcoholic liver disease. Elevated serum GGT levels of more than 10 times is observed in alcoholism. GGT level may be 2-3 times greater than the upper reference value in more than 50% of the patients with NAFLD (Mccullough AJ, 2002). Measurement of this enzyme is also useful if jaundice is absent for the confirmation of hepatic neoplasms and is a useful test to confirm hepatic disease in patients with elevated ALP. Serum GGT activity was significantly lowers in the second and the third trimesters of normal asymptomatic pregnancy (Bacq Y et al, 1996).

2.5.1.2 Uses of liver function tests:

➢ Screening.

➢ Pattern of disease (Simple and complex patterns).

➢ Assess severity.

➢ Follow up (BR Thapa et al, 2007).

Table 2.2: Simple patterns of liver function tests (Dr Sydney Sacks).

Analyte	Comment	Likely causes
Elevated albumin	Usually benign	Tight tourniquet, prolonged erect posture, Dehydration
Elevated globulin	+\-↑ total protein	Chronic infection or monoclonal gammopathy (myeloma).
Elevated Bilirubin (other LFTs normal)	Unconjugated	Gilberts Syndrome, haemolysis.
	Conjugated	Some medications: anabolic steroids, sulphonamides. Dblin Johnson syndrome.
Elevated GGT (other LFTs normal)	High	Ethanol induced. Medications including anticonvulsants, tricycles and warfarin.
	Very high (>500IU/L)	Usually ethanol induced
Elevated ALP (other LFTs normal)	In Children and adolescence.	May be associated with growth spurt (Check vitamin D).
	Young women	Pregnancy third trimester.
	Elderly men	Bone secondary from prostate Ca.
	Any age	Healing fractures, vitamin D deficiency.
Elevated GGT+ALP	Cholestatic pattern	Medication: antibiotics, phenytoin. Hepatic space occupying mass. (more probable if accompanied by ↑AST) Post viral hepatitis, cirrhosis.
Elevated AST+ALT With AST>>ALT	GGT typically Not elevated	Muscle damage. Haemolysis.

Table 2.3: Complex patterns of liver function tests (Dr Sydney Sacks).

Pattern	Comment	Likely causes
Mild Hepatitic	↑ALT Slight ↑AST Slight ↑GGT	Common in overweight patients with metabolic syndrome and NAFLD, medications.
Acute severe hepatitis	↑↑↑ALT+AST ↑GGT+ALP	Acute viral infection. Toxins and drugs (e.g. paracetamol, valproate)
Conjugated bilirubin	↑↑GGT ↑↑ALP ↑↑Bilirubin (conjugated) Dark urine and pale stooles	Exclude pancreatic, biliary Ca Consider bile stones Viral hepatitis, medication.
Mixed hepatic/ cholestatic	Similar elevations of ALT, AST, GGT, ALP	Viral, medication, auto immune hepatitis, biliary pathology, hepatic space occupying mass
Ethanolic hepatitis	↑AST>↑ALT ↑↑GGT+/-↑ALP	Acute binge drinking
Chronic end stage liver disease/ hepatic failure	↓Alb ↑Globulin ↑Bilirubin ↑AST ALT often normal	May be due to ethanol, chronic viral or auto immune hepatitis.
Abnormal LFTs in pregnancy (usually 3rd trimester)	Normal rise in ALP (placental) occurs in 3rd trimester.	For other abnormal liver enzymes, consider possibility of intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy or HELLP syndrome as well as other Non-pregnancy related causes.

2.5.1.3 Limitations:

2.5.1.3.1 Lack sensitivity:

The LFTs may be normal in certain liver diseases like cirrhosis, non cirrhotic portal fibrosis, congenital hepatic fibrosis, etc.

2.5.1.3.2 Lack specificity:

Parameters may be elevated for pathological processes outside the liver. Serum albumin may be decreased in chronic disease and also in nephritic syndrome. Aminotransferases may be raised in cardiac diseases and hepatic diseases (Daniel SP et al, 1999).

2.5.2 Imaging studies:

2.5.2.1 Ultrasonography:

US has important role in the diagnosis of abnormalities of the liver and biliary system. Diagnosis of hepatic metastases and primary solid neoplasm of the liver is not very successful even in experienced hands. In addition to fluid-filled pathologic lesions such as cysts, abscesses and hematomas a variety of solid lesions become apparent on sonograms including primary benign and malignant lesions as well as secondary deposits (David N, 1977).

2.5.2.2 X- ray computed tomography (CT):

IV contrast medium is usually given in order to increase the density of normal liver parenchyma and to emphasize the density difference between the normal parenchyma and lesions that enhance poorly, such as tumors or abscesses. Most metastases are best demonstrated as low attenuation areas during the portal venous phase on a scan taken 60-70 seconds after injection of contrast. Scanning during the arterial phase, about 30 seconds after the injection of contrast, will show lesions such as hemangiomas and some neoplasms, particularly hepatomas and highly vascular metastases (e.g. carcinoid), as areas of greater enhancement than the surrounding parenchyma(Peter AS, 2009). Until recently, CT has been accepted as the "gold standard" for preoperative detection of focal liver lesions (Bernardino ME et al, 1986). However, CM administration may obscure metastases from hyper vascular Ca (Bressler EL et al, 1987). Therefore both non-contrast and contrast-enhanced scans would be desirable, but expensive.

2.5.2.2.1 Normal appearance of CT liver

The normal hepatic parenchyma has a relatively high density prior to contrast enhancement; higher than that of muscle and higher or equal in density to the spleen. On images taken without IV contrast medium, the HV and PV are seen as branching, low density structures coursing through the liver. As CT is

a sectional technique, some of these branches may be seen as round or oval low density areas, which should not be confused with metastases. After contrast enhancement the veins clearly opacified against a background of uniform density. The biliary system distal to the Rt and Lt hepatic ducts can be identified, but the smaller intra-hepatic bile ducts are not visible in the normal patient (Peter AS, 2009).

2.5.2.3 MRI of the liver:

MRI is used as a problem –solving technique to give additional information to US and CT. It is, however, an excellent technique for demonstrating primary and secondary tumors. Images can be obtained in the axial, coronal and sagittal planes. IV contrast is used to improve visualization and help characterize lesions. Malignant tumors do not normally possess hepatocytes or reticulo-endothelial cells, so there is heightened contrast between tumor and normal liver (Peter AS, 2009). MRI has shown great potential in the diagnosis of a variety of diffuse and focal hepatic diseases because of its capability to image selectively free water, fat, iron and blood flow (David DS, 1992).

2.5.2.4 Isotopic imaging of the liver:

^{99m}Tc sulfur colloid is distributed throughout the normal liver and provides a homogeneous pattern of uptake on scan.Variations in the configuration of the normal liver, especially common in the region of the portahepatis may result in "false positive" interpretations. Liver scan the limits of resolution of the imaging system. Such patients can be further evaluated by the use of tumor localizing agents such as ^{67}Gacitrate.^{67}Gascan should always be performed in conjunction with colloid liver scan. ^{131}I-labeled Rose Bengal has been used for hepatic parenchymal cells and the biliary excretory system. The^{131}I-labeled Rose Bengal scan provides poor anatomic detail.Recently, ^{99m}Tc-labeled HIDA has been introduced for parenchymal cell and biliary duct imaging. They provide good anatomic detail and may be extremely useful in the detection of biliary tract obstruction and cholecystitis (David N, 1977).

2.6 Common method of diagnosing a biliary system:

2.6.1 Ultrasound of the GB and bile ducts:

US is the initial method of imaging because it is the simplest test for showing gallstones, diseases of the GB and excluding bile duct dilatation (Peter AS, 2009). Specific advantages of US are that it requires no CM and that image quality is independent of hepatic or biliary function. US is highly valuable inpregnant patients with jaundice or suspected cholelithiasis.The US findings aid in selection additional invasive diagnostic procedures such as ERCP or PTC (David N, 1977). US gives information related to the disease (e.g. hepatic metastases, gallstones, hepatic parenchymal change), but it is unreliable for small stones or strictures in the bile ducts. It may also demonstrate tumors, cysts, or abscesses in the pancreas, liver, and surrounding structures (Lomas DJ et al, 2006). Endoscopic US enables the aspiration of cysts and biopsy of solid lesions.

2.6.2 Magnetic resonance cholangiopancreatography (MRCP):

MRCP uses special fluid-sensitive sequences to visualize the biliary and pancreatic ducts. The examination is non-invasive and no contrast agents are needed. MRCP is replacing ERCP in many instances, because it useful in patients who have contra indications for ERCP, although ERCP is necessary for any endoscopic biopsy or treatment (Peter AS, 2009). One of the disadvantages of MRCP is the inability of the current techniques to assess the length or asymmetry of bile ducts strictures (Lee MG et al, 2004).

2.6.3 Endoscopic retrograde cholangiopancreatography (ERCP):

ERCP consists of injecting CM directly into the CBD through a catheter inserted into the papilla of vater via an endoscope positioned in the duodenum.With obstruction due to tumor, biopsies can be obtained and the obstruction relieved with stents passed through the endoscope across the obstruction. It is still occasionally used for more detailed imaging of the intra-hepatic biliary ducts as resolution is better than with MRCP (Peter AS, 2009).

2.6.4 Percutaneous trans-hepatic cholangiogram (PTC):

PTC can demonstrate the bile duct system in order to show the site and cause of obstruction and is generally performed if an ERCP is unsuccessful in treating a distal CBD obstruction or as the primary procedure in treating a more proximal hilar stricture. The procedure is carried out under local anaesthesia and because it is far easier and safer to perform if the intrahepatic bile ducts are dilated, the patient is usually jaundiced at the time of examination. The examination consists of passing a fine needle (usually 22 or 23 gauge) through the abdominal wall into the liver and injecting contrast directly into intrahepatic bile ducts. Haemorrhage is an occasional problem, as are septicaemia and biliary peritonitis. PTC is also used to introduce stents across an obstruction if this cannot be achieved endoscopically at ERCP (Peter AS, 2009).

2.6.5 Biliary system radionuclide scanning:

IDA pharmaceuticals labeled with ^{99m}Tcare excreted by the liver following IV injection and may be used for imaging the bile duct system. The patient fasts for 4 hours prior to the injection of the radionuclide. Normally, the GB, CBD, duodenum and small bowel are all seen within the first hour. The main use of this technique is in patients with suspected biliary leak following biliary surgery. Excretion of the radionuclide tracer from the biliary tree into the peritoneal cavity is diagnostic of a leak. The technique may also be used in acute cholecystitis or in children, when biliary atresia is suspected (Peter AS, 2009).

2.7 Comparisons between CT and MRI:

CTAP is more sensitive than other current CT or MR techniques. However, CTAP may produce false-positive results because of heterogeneous hepatic perfusion, especially in patients with preexisting liver disease. Occasionally, MRI may detect lesions that are not seen optimally with CTAP (Heiken JP et al, 1989), allowing it to serve as a valuable complementary modality to optimize appropriate selection of candidates for surgical resection of hepatic malignancies.

Partial volume effects between an irregular hepatic surface and perihepatic fat can mimic low-density lesions on CT scans. This is not a problem with MRI, since low-density fat can cause increased intensity on T1-W images, unlike neoplasm, which are hypointense. MRI is also not affected by artifact from high- density structures such as bone or ingested oral contrast but MRI's inability to show micro calcifications. MRI was a better test than CT for screening patients at risk of developing hepatic metastases (David DS, 1992). One advantage of CT is its current superiority for detecting most extra hepatic lesions in the abdomen (Barakos J et al, 1990).

The choice between CT and MRI is complex (Heiken JP et al, 1989). The need to detect extra hepatic lesions must be balanced against the risk and cost of CT CM, the relative availability and cost of MRI and CT, and the superiority of MRI for imaging the liver itself (David DS, 1992).

MRI can substitute for angiography and CT in evaluating portal thrombosis without administration of CM and it is not restricted by body habitus or ascites (Levy HM et al, 1988). MRI is more sensitive than other imaging methods and at least as specific for diagnosing cavernous hemangiomas. In the general population cavernous hemangiomas are more common and can mimic the appearance of metastases when imaged by CT, US or scintigraphy (David DS, 1992). Metastases may also be isodense with fatty liver and thus be obscured on CT (Lewis E et al, 1983).

CT of the abdomen provides excellent visualization of the liver, GB, pancreas, kidneys, and retroperitoneum. It can differentiate between intra- and extra-hepatic obstructions with 95%. However, CT may not define incomplete obstruction caused by small gallstones, tumors, or strictures. CECT is very useful for assessment of biliary malignancies. CT is the best technique for evaluation of the wall of the extra hepatic bile ducts and MRI the best technique for showing the intra hepatic periportal tissue and determining the extent of malignant tumor (David DS, 1992).

2.8 CT techniques for hepatobiliary system:

The ability of MDCT to rapidly acquire large volumes (greater anatomic coverage) of extremely thin images has revolutionized the CT evaluation of the abdomen and pelvis. Patient radiation dose might also be reduced with the utilization of ATCM techniques, which are available on most CT systems.

Current MDCT technology allows for scanning of the liver during multiple phases of contrast enhancement. This improves characterization of both hypovascular and hypervascular lesions. Protocol considerations for a multiphasic MDCT scan of the liver department-specific but may include any or all of the following:

- Non-contrast survey of the liver to evaluate baseline lesion density, fatty infiltration, calcifications.
- Early arterial phase (15-20 seconds) for assessment of the hepatic arterial supply. Important in cases of preoperative planning for resection, transplantation or placement of a chemotherapy infusion pumps.
- Arterial phase (25-35 seconds) for optimal visualization of hypervascular hepatic lesions such as hemangioma and HCC.
- Portal venous phase (60-70 seconds) for evaluation of the maximally enhanced hepatic parenchyma and demonstration of hypovascular lesions such as hepatic metastases.
- Delayed phase (5-20 minutes) for demonstration of hemangioma fill-in and FNH central scar.
- Reconstructed images 3 to 5 mm thick from data obtained with detector collimation as low as possible. Section width may range from 2.5 mm in a 4-slice MDCT system to 0.6 mm in a 64-slice system.
- Thinner (0.5-2.5 mm), overlapping reconstructions may be used for angiographic, MPR and 3D applications.
- Automated bolus-tracking software can be utilized to improve the timing accuracy of multiphasic acquisitions of the liver (Daniel, 2011).

2.9 Previous studies:

Verma, Sachit K et al (2010) determined MHP CC, Max CC, Max LL and MHP AP dimensions of the normal liver and correlated with liver volume on contrast enhanced abdominal MRI between December 2006 and September 2007. The study group consisted of 116 (40 men, 76 women; age range 16-89, mean; 55.5 years). Hepatic volume measurements were performed by tracing the contours of liver on sequential 5mm axial images. There was a positive correlation between hepatic volume and linear measurements except with Max LL andthere was a positive correlation between hepatic volume and MHP CC*MHP AP & Max CC*MHP AP. The study validate; MHP CC, Max CC and MHP AP as good indicators of hepatic size.

Dr/Sydney Sacks (chemical pathologist) studied the various patterns of LFTs and showed the causes of mild persistent elevations of ALT (up to about 200 IU/L) with or without lesser elevations of AST and GGT constitute a very common pattern particularly in overweight patients with metabolic syndrome and resultant NAFLD. However, patients with NAFLD commonly have elevated LFTs secondary to liver damage. He said chronic hepatic disease may have totally normal LFTs due to the liver's reserve capacity. Also he founded the PT elevations and similar elevations of ALT, AST, GGT, ALP usually >200 IU/L and some times of bilirubin constitute in chronic disease

Torres DM and Harrison SA (2008) estimated 30% of U.S. and reported the common causes of mild elevation of transaminase were NAFLD and was become more prevalent as the obesity rate increases. NAFLD may be present with variations of this pattern; the majority of patients with NAFLD have completely normal LFTs.

Clark JM et al (2003) studied the chronic liver disease and the causes of morbidity and mortality in the United States. The data analyzed on adult ages 17years and older. The results showed; aminotransferase elevation was more common in men. Participants were classified as having elevated

aminotransferase levels if either aspartate aminotransferase or alanine aminotransferase was elevated above normal. Aminotransferase elevation was classified as explained if there was laboratory evidence of hepatitis B or C infection and high alcohol consumption. In both men and women unexplained aminotransferase elevation was significantly associated with higher body mass index, type 2 diabetes and hypertension in women. Liver can remain fatty without disturbing liver function.

ShivarajG and Prakash B et al (2009) mentioned the causes of ALT elevation constitute in the hepatic fat accumulation in obesity and nonalcoholic fatty liver disease.

Peter AS et al (2009) added that the majority of cases of jaundice were associated with liver disorders and may also result from erythrocyte destruction or hemolysis in patients with normal liver function.

Mathew W et al (2008) discussed in laboratory literature that the ALT and AST are two liver enzymes commonly used as markers of hepatocellular injury. A small fraction of asymptomatic patients can also have slight elevations. The absolute number of elevation is not specific for a particular cause of injury. He founded the elevations of ALP and bilirubin relative to the aminotransferases suggests intrahepaticor extrahepatic cholestasis.

Thapa BR and Anuj W (2007) reported that theelevated AST seen in extensive tissue necrosis during myocardial infarction and also in chronic liver diseases.

American Gastroenerological Association review (2002) on evaluation liver chemistry added that the AST elevations often predominate in patients with cirrhosis and even in liver diseases that typically have an increased ALT.

Rosalki SB and Mcintyre N (1999) noted that the tumors secrete ALP into plasma and there were tumor specific isoenzymes.

Erdem O et al (2014) studed 44-year old HBV carrier male presented with distention of the abdomen, nausea, vomiting and fever. CT revealed liver mass and had extrahepatic growth. Biochemical analyses performed at the time of admission indicated that his ALT value was 11U/L (normal value: 0-55) and AST value was 123U/L (normal value: 10-40).

Yoshihiko Yet al (2003) studed a 66-old woman was admitted to hospital on March 31, 2001 because she was detected a large space occupying lesions in the liver and sever esophageal varices. Laboratory examinations showed; elevated hepatobiliary enzymes; aspirate aminotransferase (AST) 120IU/l, alanine aminotransferase (ALT) 611IU/l, alkaline phosphatase (ALP) 983IU/l, total bilirubin 3.2 mg/dl and low albumin (2.4g/dl) levels. Abdominal CT showed two large nodules in both lobes.

Le NH et al (2015) studed 416 jaundice patients administered over 38 days. The study done to investigate the new-onset jaundice, map of causes, approaching method and risk factors for treatment failure in adult patients at a tertiary general hospital. Laboratory tests investigated were total bilirubin, direct bilirubin, ALP, AST, ALT and GGT. The results showed that the main causes of jaundice were pancreatic and biliary tract diseases (71, 17.1%), cirrhosis (68, 16.3%), liver tumor (61, 14.7%), sepsis (37, 8.9%), hepatitis (37, 8.9%), hematology diseases (33, 7.9%) and cardiac diseases (31, 7.5%).

Butch RJ et al (1986) studied patients with primary hepatic tumors were depicted by CT. The results mentioned that the LFTs were normal in 33% of patients in whom metastases.

Chapter Three
Material and Methods

3.1 Material:

3.1.1 Patients:

Prospective study of 100 consecutive Sudanese patients in both genders with evidence of liver function (LFT) tests was tested for correlation between the laboratory tests and CT imaging results and with the liver linear measurements, volume and CT Hounsfield.The sample included 59(59%) females and 41(41%) males. Their ages ranged between 25 and > 65years. Ages ranged from 25-34 were (12), 35-44 were (14), 45-54 were (15), 55-64 were (26) and > 65 constituting (33) patients. Mean age was 54.98±15.07 years. Study was extended during the period from June 2014 to July 2017.

3.1.1.1 Included criteria:

The patients were referred to the radiological department for CT abdomen in Royal diagnostic center with different clinical indications and their results of suspected liver disease based on patient's symptoms and previous modalities e.g. US. All patients had LFT. Patients who did not have lab results; we pulled blood sample from them and send it.

3.1.1.2 excluded criteria:

Samples show normal a computed tomography sequence.

3.1.2 Data collection:

The data were collected using the variables: age, gender, duration of illness, signs and symptoms, total bilirubin, direct bilirubin, ALP, AST, ALT, albumin, globulin, total protein and PT were evaluated.

All measurements of the liver in mm were taken by use Radiant DICOM Viewer program as follows:

➢ Linear hepatic measurements:

The following measurements of the liver were performed:-

1- Mid hepatic point craniocaudad (MHP CC).
2- Maximum CC to liver tip (Max CC).
3- Maximum transverse dimension.
4- MHP anteroposterior (AP) dimension of the liver.

The plane of the horizontal component of the main portal vein was identified and used as a reference point for measurements. The MHP was defined as half way between the mid vertebra and right lateral margin of the liver at the level of main portal vein on a transverse section (Figure 3.1). MHP CC was defined as a perpendicular measurement on the coronal images from the hepatic dome to the inferior margin of the liver passing through the midhepatic point (Figure 3.2). The Max CC was defined as the greatest obtainable craniocaudad dimension of the liver from the hepatic dome to the liver tip on coronal reconstructed images (Figure 3.2). Maximum transverse dimension was the maximum measurement from the right to left margins of the liver at the level of the portal vein (Figure 3.1). MHP AP measurement was taken at the level of the midhepatic point from anterior to posterior margin of the liver (Figure 3.1).

➢ Hepatic volume measurement:

Hepatic volume measurements were performed depended on linear hepatic measurements.Volume = **(MHP AP * Max LL * Max CC * 0.31)** in ml as proposed by (Verma et al.2010).
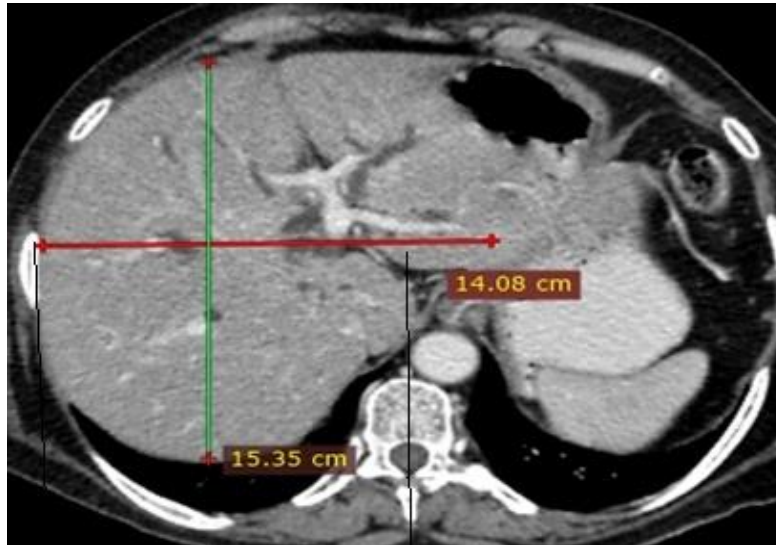
Figure 3.1: The Linear dimensions of the liver (Max LL & MHP AP).
Maximum transverse dimension (the maximum measurement from the Rt to Lt
margins of the liver). Mid hepatic point AP (MHP AP) measurement was taken at
the level of the mid hepatic point from anterior to posterior margin of the liver.
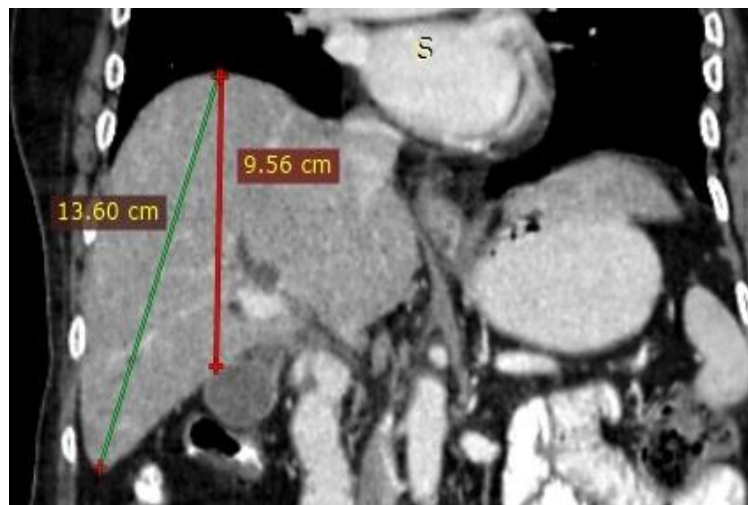
Figure 3.2: Linear dimensions of the liver (MHP CC & Max CC). MHP
CC was defined as a perpendicular measurement on the coronal images from
the hepatic dome to the inferior margin of the liver passing through the
midhepatic point. The Max CC was defined as the greatest obtainable
craniocaudad dimension of the liver from the hepatic dome to the liver tip on
coronal reconstructed images.

3.1.3 CT scanner machin:

3.1.3.1 Detector configuration and section width:

Toshiba MDCT system allows for detector collimation as thin as 0.5 to 0.625 mm, with images reconstructed at widths based on the anatomy or pathology in question. For general survey studies, section widths of 3 to 5 mm were sufficient. Section widths of 1 to 2 mm or less might be preferable during multi-phasic studies and in anticipation of 3D and MPR. MDCT system was capable of acquisitions in a short time, often within a single, comfortable breath-hold.The detector configuration, table speed and pitch were optimized according to the clinical indications of the exam while keep in scan time and patient radiation dose to a minimum.

3.1.3.2 Scan parameter:

The MA and KVP settings were based on patient size, yielding to the noise requirements of the particular exam. DFOV was patient specific, being set as small as possible while still including the abdomen and pelvis in their entirety. A standard soft tissue algorithm was used for reconstruction. When indicated, additional reconstruction with a high-resolution algorithm might be used to demonstrate bony detail. Sample WL and WW settings for optimal displaiedwere: Soft tissue of the abdomen: WL 40, WW 350, lung bases: WL 450, WW 1400 and bone: WL 300, WW 2000.

3.2 Methods:

3.2.1 Technique and protocol:

3.2.1.1Exam preparation:

When possible, patients fasted for 2 to 6 hours before the examination. Fasting results in an empty proximal GIT, facilitating its evaluation and also limiting the potential hazard of aspiration of stomach contents in the event of GI upset due to IV administration of a contrast agent. In most cases, an oral contrast agent is administered to distend the GIT and clearly demonstrate the

intestinal lumen. The agent used might be a dilute solution of an iodinated CM, barium sulfate, or water. For general studies of the abdomen and pelvis, 750 to 1,500 ml of oral contrast agent is administered 30 to 120 minutes before the exam.150 to 250 ml given just before scanning for opacification of the stomach and duodenum.

3.2.1.2 Patient position and instructions:

The patients were positioned supine head first with the arms placed overhead to eliminate scatter artifact. Whenever possible, the patient was instructed to suspend respiration during scan acquisition.

3.2.1.3 Administration of IV contrasts agents:

When not contra-indicated, the administration of an iodinated IV contrast agent improved the quality of abdominal and pelvic CT imaging.

3.2.1.4 Contrast agent dose & Injection rates:

Ranges from approximately 50 to 150 ml. The total dose depends on the patient's condition and the clinical indication for the study. Injection rates vary between 2 and 5 ml/sec. the rate selected depends on the enhancement phase(s) to be acquired and the capacity of the venous access.

Iodine was infused over 2 or 3 minutes while rapid sequential scans were performed with table incrementation through the liver.

Automated bolus-tracking software utilized to improve the timing accuracy of multiphasic acquisitions of the liver.

3.2.1.5 Phases of hepatic contrast enhancement:

Scanning of the liver during multiple phases of contrast enhancement:
- Non-contrast imaging for hepatic calsification, fatty infiltration and hemorrhage and characterize hepatic lesions.
- Arterial phases at 25 to 35 seconds.
- Portal venous phases at 60 to 70 seconds.
- Equilibrium phases at 2 to 3 minutes.

- Repeated scan after 4-6 hours may detect additional lesions.

The timing of each of these phases depends on:

- Cardiac output as its redused, arterial phases delayed.

- Injection duration

- Iodine concentration

3.3 Statistical Analysis:

The statistical evaluation of the data was descriptive. The data were stored by EXCEL program. Statistical analysis with SPSS version 16 under windows. The main statistics was descriptive with values presented as mean±SD, median, and range (minimum & maximum). Variable analysis with tables for relation ship between the laboratory tests and CT imaging results.

A p value of less than 0.05 was statistically significant.

3.4 Limitations of the study:

➢ Not all patients referred to the radiological department had LFT.

➢ Not all mesurments taken at the level of main portal vein (appraise Max section of the liver)

➢ Variation in the position of the liver during suspended respiration results in CT examination that skips some anatomic levels while duplication other.

➢ Estimation of the point of hepatic dome on coronal image not accurate because the liver is covered by the Rt lower thoracic cage.

Chapter Four

Result

Table 4.1: Distribution of the study sample according to gender

Gender	Frequency	Percent
Male	41	41%
Female	59	59%
Total	100	100%
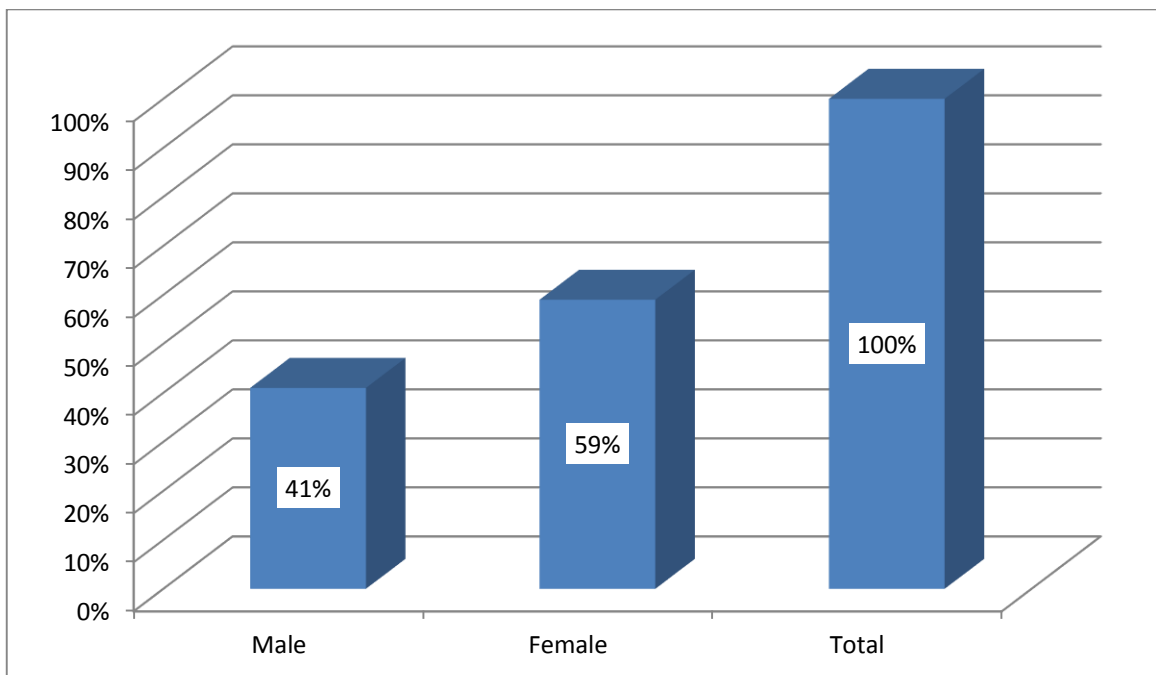
Figure 4.1: Distribution of the study sample according to gender

Table 4.2: Distribution of the study sample according to age group

Age group	Frequency	Percent
25-34	12	12%
35-44	14	14%
45-54	15	15%
55-64	26	26%
>65	33	33%
Total	100	100%
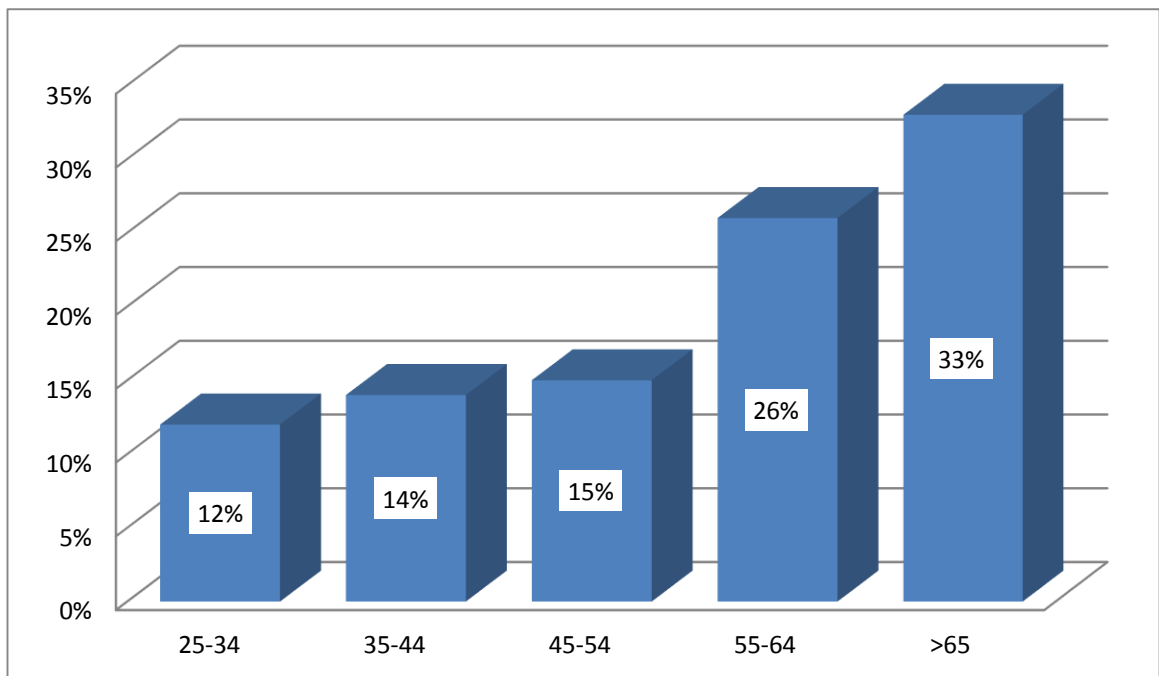
Figure 4.2: Distribution of the study sample according to age group

Table 4.3: Shows correlation between the liver CT findings &laboratory results

	Total bilirubin	Direct bilirubin	ALP	AST	ALT	Albumin	Globulin	Total protein	PT
Abscess	0.511	0.511	0.638	0.626	0.471	0.471	0.548	0.814	0.752
Fatty Liver	0.250	0.250	0.410	0.394	0.207	0.207	0.473	0.532	0.135
Cholangio Carcinoma	0.125	0.125	0.638	**0.038**	0.161	0.161	0.267	0.814	0.752
Rt lobe Hemangioma	0.198	0.198	0.591	0.164	0.319	0.076	0.369	0.385	0.354
Lt lobe hemangioma	0.133	0.133	0.189	0.017	0.771	0.208	0.619	0.493	0.378
FNH	0.350	0.350	0.503	0.489	0.305	0.629	0.528	0.575	0.653
Rt liver lobe simple cyst	0.594	0.594	0.730	0.527	0.129	0.434	0.619	0.650	0.817
Lt liver lobe simple cyst	0.467	0.467	0.118	0.444	0.091	0.325	0.961	0.663	0.907
Klatskin tumor	0.250	0.250	0.410	0.394	0.207	0.207	**0.003**	**0.001**	0.580
Rt liver lobe HCC	**0.004**	**0.000**	**0.004**	0.876	0.902	0.493	0.318	0.192	0.662
Lt liver lobe HCC	**0.000**	**0.025**	**0.042**	0.876	0.212	0.661	0.090	0.789	0.622
Rt lobe mets	0.834	0.834	0.987	0.375	0.861	0.395	0.619	0.391	0.259
Lt lobe mets	0.195	0.195	0.141	0.128	0.434	**0.030**	0.619	**0.025**	**0.007**
Cirrhosis	0.140	0.140	0.607	0.294	0.302	0.947	0.619	0.912	**0.030**
Other finding	0.148	0.148	0.888	0.060	0.335	0.555	0.325	0.780	0.341

P value of less than 0.05 was statistically significant.

Table 4.4: The liver measurements and CT Hounsfield

Descriptive Statistics			
Hepatic measured variables/mm	**Min**	**Max**	**Mean± STDV**
Maximum craniocaudal (Max CC)	14.80	269.50	169.15±49.46
Mid hepatic point craniocaudal (MHP CC)	13.00	321.70	129.27±50.40
Maximum transverse (Max LL)	17.20	314.00	181.34±52.95
Mid hepatic point anteroposterior (MHP AP)	13.70	215.70	155.98±37.29
Volume / ml	428.00	5076.00	1802.38±10.31
Lt liver lobe texture (Hounsfield)	0.06	58.00	36.70±11.46
Rt liver lobe texture (Hounsfield)	0.00	58.00	36.47±10.58

Table 4.5: Shows the liver measurements and CT Hounsfield correlated with ALP, AST, ALT values.

		ALP U/L		AST U/L		ALT U/ L	
		Mean	STDV	Mean	STDV	Mean	STDV
Maximum craniocaudal (Max CC) in mm	Normal	155.77	69.26	158.86	69.66	166.46	60.69
	High	172.09	43.99	171.56	43.64	170.53	43.017
	Total	169.15	49.46	169.15	49.46	169.15	49.46
	P-value	0.207		0.316		0.699	
Mid hepatic point craniocaudal (MHP CC) in mm	Normal	130.28	62.76	125.88	60.34	127.53	52.67
	High	129.05	47.72	130.07	48.17	130.17	49.58
	Total	129.27	50.40	129.2760	50.40	129.27	50.40
	P-value	0.926		0.746		0.806	
Maximum transverse (Max LL) in mm	Normal	180.74	60.80	190.47	59.98	180.27	65.60
	High	181.47	51.49	179.20	51.34	181.90	45.66
	Total	181.34	52.95	181.34	52.95	181.34	52.95
	P-value	0.958		0.407		0.885	
Mid hepatic point anteroposterior in mm	Normal	149.32	37.04	154.80	39.98	152.32	46.96
	High	157.44	37.41	156.26	36.89	157.87	31.42
	Total	155.98	37.29	155.98	37.29	155.98	37.29
	P-value	0.406		0.879		0.484	
Volume /ml	Normal	1695.44	1046.35	1878.94	1115.33	1982.72	1159.73
	High	1825.86	1033.20	1784.42	1017.36	1709.48	954.91
	Total	1802.38	1031.48	1802.38	1031.48	1802.38	1031.48
	P-value	0.630		0.721		0.211	
Lt liver lobe texture	Normal	40.82	8.87	38.12	8.44	38.17	8.70
	High	35.80	11.80	36.37	12.07	35.95	12.64
	Total	36.70	11.46	36.70	11.46	36.70	11.46
	P-value	0.092		0.551		0.362	
Rt liver lobe texture	Normal	35.16	8.31	37.68	7.27	37.05	8.91
	High	36.72	11.04	36.19	11.23	36.17	11.39
	Total	36.47	10.58	36.47	10.58	36.47	10.58
	P-value	0.565		0.582		0.695	

Table 4.6: Shows the liver measurements and CT Hounsfield correlated with total bilirubin and PT values

		Total Serum bilirubin*µmol/L		Prothorombin time(PT)** Second	
		Mean	STDV	Mean	STDV
Maximum craniocaudal (Max CC) in mm	Normal	167.24	61.49	167.81	49.73
	High	169.97	43.80	182.74	47.20
	Total	169.15	49.46	169.15	49.46
	P-value	0.801		0.390	
Mid hepatic point craniocaudal (MHP CC) in mm	Normal	132.94	54.34	128.12	50.48
	High	127.70	48.94	140.86	50.95
	Total	129.27	50.40	129.27	50.40
	P-value	0.636		0.472	
Maximum transverse (Max LL) in mm	Normal	183.66	61.82	181.80	51.20
	High	180.35	49.13	176.71	72.01
	Total	181.34	52.95	181.34	52.95
	P-value	0.776		0.785	
Mid hepatic point anteroposterior (MHP AP) in mm	Normal	156.76	42.84	156.29	35.75
	High	155.65	34.98	152.90	53.05
	Total	155.98	37.29	155.98	37.29
	P-value	0.892		0.796	
Volume /ml	Normal	2022.26	1220.16	1764.22	1010.75
	High	1708.15	933.16	2188.22	1220.33
	Total	1802.38	10.31	1802.38	10.31
	P-value	0.164		0.241	
Lt liver lobe texture	Normal	37.77	10.63	37.22	11.35
	High	36.2496	11.83	31.48	11.91
	Total	36.7083	11.46	36.70	11.46
	P-value	0.544		0.153	
Rt liver lobe texture	Normal	34.2567	10.25	36.74	10.76
	High	37.4257	10.65093	33.72	8.58
	Total	36.4750	10.58292	36.47	10.58
	P-value	0.171		0.416	

*Normal serum total bilirubin varies from 2 to 21µmol/L. **Normal PT 12-13 second.
Volume = (MHP AP * Max LL * Max CC * 0.31) in ml

Table 4.7: Shows the liver measurements and CT Hounsfield correlated with albumin, globulin, and total protein values

	Values	Serum albumin		Values	Globulin		Values	Total protein	
		Mean	STDV		Mean	STDV		Mean	STDV
Maximum craniocaudal (Max CC) in mm	N	162.71	52.89	N	182.43	47.32	N	165.23	52.32
	L	181.65	39.80	H	177.80	14.57	H	161.58	38.28
							L	185.28	40.81
	p value =0.069			*p value*=0.833			*p value* =0.241		
Midhepatic point craniocaudal (MHP CC) in mm	N	123.95	47.33	N	130.38	50.80	N	126.31	50.77
	L	139.59	55.15	H	132.36	35.47	H	118.65	38.34
							L	143.32	52.47
	p value=0.142			*p value* =0.936			*p value* 0.331		
Maximum transverse (Max LL) in mm	N	177.72	48.00	N	169.96	66.10	N	178.88	52.08
	L	188.37	61.61	H	178.60	37.45	H	174.46	37.18
							L	192.27	61.13
	p value 0.343			*p value* 0.783			*p value* 0.558		
Midhepatic point anteroposterior in mm	N	153.90	35.16	N	153.35	50.50	N	152.70	37.97
	L	160.01	41.36	H	155.22	7.10	H	160.68	16.16
							L	165.29	40.09
	p value =0.441			*p value*= 0.936			*p value* =0.375		
Volume/ml	N	1642.02	891.65	N	1945.00	938.36	N	1724.37	990.02
	L	2113.67	1214.33	H	1523.80	344.85	H	1436.00	512.50
							L	2205.71	1223.92
	p value= **0.030**			*p value*= 0.339			*p value* =0.098		
Lt liver lobe texture	N	38.16	11.70	N	36.08	11.46	N	36.85	11.49
	L	33.88	10.56	H	47.52	7.85	H	46.06	6.32
							L	32.65	11.02
	p value 0.076			*p value* =**0.047**			*p value* =**0.017**		
Rt liver lobe texture	N	37.52	10.41	N	33.12	12.65	N	37.09	10.86
	L	34.43	10.77	H	34.40	11.43	H	37.85	9.9
							L	33.84	9.8
	p value =0.169			*p value* =0.839			*p value* =0.436		

ChapterFive

Discussion, Conclusion & Recommendation

5.1 Discussion:

Standard liver function tests consist of the: total bilirubin, direct bilirubin, ALP, AST, ALT, albumin, globulin, total protein and PT have been evaluated. When considered together; these analyses open a diagnostic window into multiple organ systems (Dr Sydney S). All measurements were taken by CT scan.The liver measurements (linear and volume) in addition to CT Hounsfield were presented in (Table 4.4).

Elevated AST seen in extensive tissue necrosis during myocardial infarction and also in chronic liver diseases (Thapa BR et al, 2007). This was consigned with our results that the AST was increased in the presence of cholangiocarcinoma at $p=0.038$. Literature also has mentioned that the ratio of mitochondrial AST to total AST activity has diagnostic importance in identifying the liver cell necrotic type condition and alcoholic hepatitis (Panteghini M et al, 1983). AST elevations often predominate in patients with cirrhosis and even in liver diseases that typically have an increased ALT (AGA Technical Review 2002).But in our study the ALT dose not significantly affected with the AST elevations in presence of choleangiocarcinoma.

In the presence of Klatskin tumor the increasing of globulin was correlated significantly at $p=0.003$ and with total protein at $p=0.001$.The liver synthesizes most other serum proteins or globulin and thus has a major effect on the serum total protein level. Elevated globulin usually due to increased IgA and non-removal of antigenic compounds by the damaged liver (Dr Sydney S).

However our study showed that the Lt lobe metastases decreased albumin level and correlated significantly at $p=0.030$, while the PT is increased

significantly with the presence of Lt lobe metastases at $p=0.007$ and liver cirrhosis at $p=0.030$. Albumin, with biological half-life of about 3 weeks, is synthesized exclusively by the liver and levels are thus a measure of long term hepatic health. Albumin may be normal early in acute hepatitis (due to long half life) and only falls late in chronic liver damage (Dr Sydney S). Albumin levels are dependant on a number of other factors such as the nutritional status, hormonal factor, catabolism, urinary and GIT losses. This should be taken into account when interpreting low albumin levels. Having said that, albumin concentration does correlate with the prognosis in chronic liver disease (JK Limdi et al, 2003).

The signature features of chronic liver diseases are low albumin, elevated globulin and some times elevated bilirubin, AST is mildy elevated, ALT is often normal, GGT and ALP are mildy elevated or unremarkable. Once ascites and elevated bilirubin are present, prognosis is poor and hepatic failure is imminent. Variations on this pattern exist; occasionally quite severe chronic hepatic disease may have totally normal LFTs due to the liver's large reserve capacity (Dr Sydney S).

In acute viral hepatitis, ALP usually remains normal or moderately increased. Tumors secrete ALP into plasma and there are tumor specific isoenzymes (Rosalki SB et al, 1999). This was consigned with our result; the presence of HCC in Rt lobe was correlated significantly with total bilirubin at $p=0.004$, direct bilirubin at $p=0.000$ and ALP at $p=0.004$. Lt lobe HCC was correlated significantly with total bilirubin at $p=0.000$, direct bilirubin at $p=0.025$ and ALP at $p=0.042$.

Bilirubin, derived from the breakdown of red cell haemoglobin, is conjugated by the hepatocyte and excreted via the bile ducts into the bile (Dr Sydney S).

In one study done by Erdem O et al (2014) showed that in patients with HCC, AST is increased and ALT is normal (Erdem O et al, 2014), while in another study done by Yoshihiko Y et al (2003) said that the all of total bilirubin,

AST, ALT, ALP and GGT are raised while there is reduction in albumin values (Yoshihiko Y et al, 2003). Hepatic and bony metastasis can also cause elevated levels of ALP. While mildly elevated levels of ALP may be seen in cirrhosis and other diseases (Rosalki SB et al, 1999).

Results showed that there are no significant relation between the presence of the focal nodular hyperplasia, fatty liver, abscess and simple cyst with the total bilirubin, direct bilirubin, ALP, AST, ALT, albumin, globulin, total protein and PT that means many lesions can be present and diagnosed by imaging but not affected the LFT parameters.

The current study showed no significant relation between the changing in hepatic measurements done by CT and ALT, AST and the ALP valuesas presented in (Table 4.5).

The description of changing the values between normal to high in our study is that the hepatocellular damage releases ALT and AST into the blood stream. AST is found in highest concentration in heart compared with other tissues of the body such as liver, skeletal muscle and kidney (Mauro P et al, 2006). Normal serum AST is 0 to 35U/L (Diana NC et al, 2007). ALT is found primarily in the liver; therefore, elevations in ALT levels generally are more specific for hepatic injury (Green RM et al, 2002). It was appreciated that the measurement of liver enzymes is wide spread and frequent in primary care and asymptomatic patients may have mild elevations in ALT and AST levels. The National Health and Nutrition Examination Survey found elevated liver transaminase levels in up to 8.9 percent of the survey population (Clark JMet al, 2003 and Ioannou GN et al, 1999). At times, those enzymes values can suggest certain disease patterns including alcoholic liver disease or NAFLD or Wilson disease. Asymptomatic elevation of liver transaminase levels can be categorized into common hepatic, less common hepatic and extra hepatic causes (Green RM et al, 2002 and Morisco F et al, 2008).

Literature has stated that ALP is present in mucosal epithelial of small intestine, proximal convoluted tubule of kidney, bone, liver and placenta. The serum ALP activity is mainly from the liver with 50% contributed by bone (Mauro P et al, 2006). Normal serum ALP is 41to 133U/L (Diana NC et al, 2007). ALP is mainly located in the bile ducts; biliary obstruction induces increased levels of ALP (Dr Sydney S).Therefore understanding the basic disease processes that cause the elevation of liver enzymes (ALT, AST and ALP) levels may help guide the patient for further diagnostic testing.

As a result; hepatic measurements done does not reflect the changes in the enzymes values, therefore those measurements should not be considered to predict the changes detected in the enzymes.For that reasons studies suggested a complete blood count with platelet count, testing of prothrombin time and measurement of albumin to be considered if there are concerns about the synthetic function of the liver. A more advance refine may proceed if there is evidence of decreased liver function (Robert C et al, 2011).

To better understand the genesis of various patterns, the possible source of each LFT component needs to be appreciated; the hepatocytes are rich in ALT and AST, with ALT predominant in the cytoplasm and AST mainly intra mitochondrial. The typical hepatitic picture thus comprises ALT elevation, accompanied by usually lesser AST rise. Predominant elevation of ALP are thus termed the cholestatic pattern which may be due to intrahepatic obstruction where the bilirubin may be normal or raised, or less commonly extrahepatic obstruction where the bilirubin is elevated (Dr Sydney S).

This is what have been evaluated in this current study and the results of the tested values also showed no significant relation between those values PT level with the linear or volume measurements done for the liver as presented in (Table 4.6).

Liver mean volume was found to be 1802.38±10.31ml ranged from 428.00-5076.00ml which considered greater to what was mentioned in the literature.

A recent study reported hepatic volumes (mean 1186 cm^3, range; 639.3-2359.4 cm^3) (Verma SK et al, 2010). Another study, the mean was 1106 cm^3, range; 533-2417 cm^3 of normal healthy livers (Chandramohan A et al, 2007). Our justification may be due that a number of cases were found to have tumors that may have a role of changing the liver measurements. The results of the study showed that there is no significant relationship between the liver volume and the LFT results except with the serum albumin at *p value*=0.030 as noticed in (Table 4.7). However the CT volumetric measurement is currently the standard method to determine whether a patient can safely undergo liver treatment and surgery or not (Shoup M, 2003 and Clavien PA, 2004).

On the other hand, study has mentioned that liver volume does not necessarily reflect liver function, especially in patients with a compromised liver (de Graaf W, 2010).Therefore, it is important to reliably assess hepatic function before liver surgery in addition to CT volumetry.

The evaluation of the liver density by measuring the CT Hounsfield was obtained showing significant relation with globulin results *p*=0.047 and with total protein at *p*=0.017as presented in (Table 4.7).

From the results of this study, shoud be researcher found that interpreting LFTs would be of multifaceted because the liver is not the only source of the enzymes, in particular AST also found in muscle, red cells and etc. ALP also found in bone, placenta and tumors. Albumin, globulins and total protein levels may also be affected by non-hepatic pathology e.g. nephrosis as may bilirubin e.g. haemolysis, as well a single cause may result in multiple different patterns including medication effects.

5.2 Conclusion:

To conclude, laboratory liver tests can help to explain the alteration of markers which reflect the liver disease including: HCC, cholangiocarcinoma, Klatskin tumor, metastases and cirrhosis but a single laboratory liver test is of little value in screening for liver disease as many serious liver diseases may be associated with normal levels and abnormal levels might be found in asymptomatic healthy individuals.

Any injury to the liver that results in cytolysis and necrosis causes the liberation of various enzymes. The measurement of these hepatic enzymes in the serum is used to assess the extent of liver damage and to differentiate hepatocellular (functional) from obstructive (mechanical) disease. Among the many diverse metabolic functions of the enzymes are synthesized by the liver, but not all have been found to be useful in the diagnosis of hepatobiliary.

The ALT and AST are two liver enzymes commonly used as markers of hepatocellular injury but mild elevations in levels of liver enzymes (ALT&AST) are commonly discovered in asymptomatic patients in primary care. Many lesions may be present and diagnosed by imaging but not affected the LFT parameters. On the other hand, not all persons with one or more abnormalities in these tests actually have liver disease as the elevation of the laboratory tests may be caused by many different causes because the liver is not the only source of the enzymes asthey produced from many sources. Interpretation of abnormalities in liver function tests is a common problem faced by clinicians. This has become more common with the introduction of automated routine laboratory testing.

The pattern of enzyme abnormality, interpreted in the context of the patient's symptoms and imaging results can aid in directing the succeeding diagnosis. Less information is available regarding the evaluation of patients with abnormal LFT results as the primary indication for imaging requests.

However, at our departments, there is no clear guidance for selection of specific imaging test regarding specific abnormal liver function test.

From the presented study; I found that the knowledge of the radiological presentation is critical for interpreting LFT abnormalities correctly instead of measuring the liver alone linearly at different points or evaluating its volume and texture considering the CT diagnostic criteria as useful trend giving good value of diagnostic results. I have categorized the laboratory patterns seen and have tried to integrate some basic diagnostic hints as measuring the liver linearly in addition to its volume trying to cast some light in a few dark corners and concentrated on the questions regarding their relationship seen in daily clinical practice.

Pre and post contrast showing the different diagnosis results including: abscess, fatty liver, cholangiocarcinoma, hemangioma, FNH, simple cyst, HCC, mets, Klatskin tumor and cirrhosis showing the involved organs and enhanced characteristics of the lesions giving excellent feature for diagnostic imaging while the sectional study took place. However the linear, volume and hepatic texture measurements did not reflect the laboratory pattern changes.

5.3 Recommendation:

➢ The pattern of enzyme abnormality, interpreted in the context of the patient's symptoms and imaging results can aid in directing the succeeding diagnosis.

➢ Physicians of all specialties need a working knowledge of the meaning of these abnormalities.

➢ Follow up of 6 months to 2 years of abnormal LFT is very useful as any trend gives important diagnostic information and helpful in evaluating response to therapy.

➢ Other study about the use of CT compare to MRI in assessment of hepatobiliary lesion in sitting of LFTs interpretation is recommended.

➢ Other studies will be necessary for correlation LFT with mixed liver diseases.

➢ In the future will expand the clinical utility of biochemical markers and correlate with CT findings.

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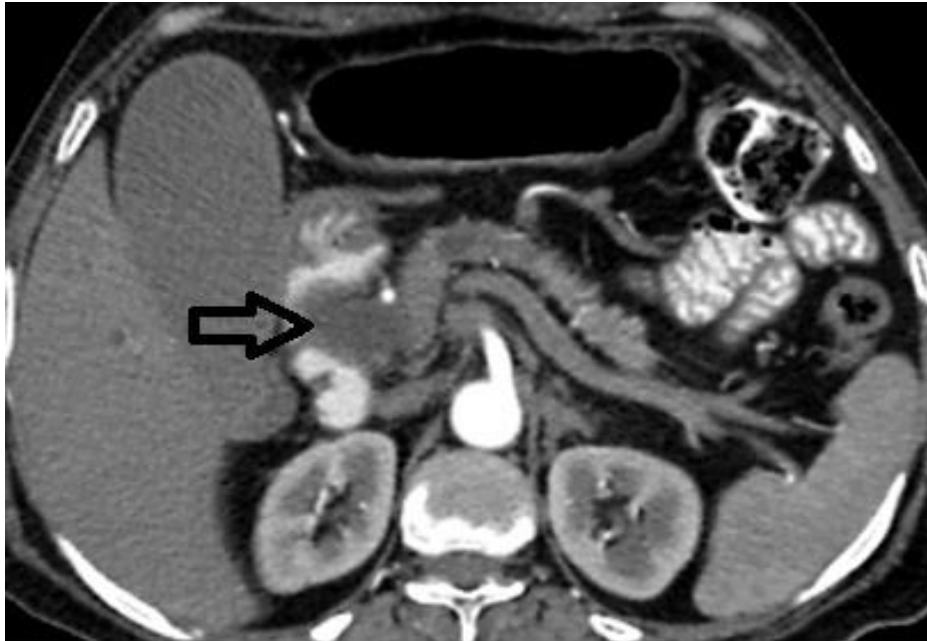
Appendix: 1

Image 1: Axial arterial sequence CT of Ca head of pancreas shows extra hepatic biliary obstruction. 85 years old female. Laboratory data showed elevated serum activity of total bilirubin, direct bilirubin, ALP, AST, ALT as 17.2 mg/dL, 14.3 mg/dL, 760 U/L, 171 U/L and 143 U/L respectively. Normal total protein and PT as 7.7g/dL and 10 seconds respectively and low albumin as 3.3 g/dL. Liver measurements Max CC, MHP CC, Max LL and MHP AP as 148.6mm, 84.1mm, 198.5mm and 149.7mm respectively. Liver volume 1369ml. Rt & Lt liver lobe texture as 41.3HU (Department of radiology, Royal scan diagnostic center-Khartoum, 2015).
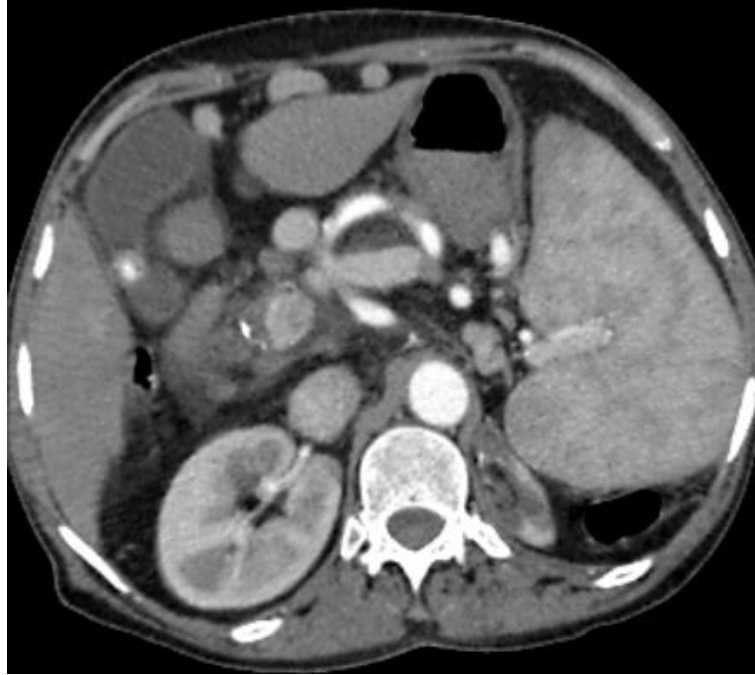
Image 2: CT of cholecystitis and GB stone. 55 years old male shows a thick-walled GB. Laboratory data showed elevated serum activity of total bilirubin, direct bilirubin, ALP, AST, ALT as 23mg/dL, 19.6 mg/dL, 391U/L, 80U/L, 77U/L respectively and normal albumin, total protein and PT as 3.5g/dL, 7.1 g/dL and 16 seconds respectively. Liver measurements Max CC, MHP CC, Max LL and MHP AP as 194.7mm, 124.8mm, 136.4mm and 185.6mm. Liver volume 1528ml. Rt & Lt liver lobe texture as 41.18 HU and 41.2 HU respectively (Department of radiology, Royal scan diagnostic center-Khartoum, 2015).

Image 3: CT of hepatoma. 70 years old male shows a large mass of variable density. Laboratory data showed elevated serum activity of AST and ALT as 256U/L, 49U/L. Normal total bilirubin, direct bilirubin, ALP, albumin, total protein and PT. Liver measurements Max CC, MHP CC, Max LL and MHP AP as 166.5mm, 145.3mm, 210mm and 158mm. Liver volume 1713ml. Rt & Lt liver lobe texture as 45.98 HU and 31.6 HU respectively (Department of radiology, Royal scan diagnostic center-Khartoum, 2015).

Image 4: Axial arterial sequence CT of portal hypertension.70 years old female showing varices due to portal hypertension, There is vascular calcification. Laboratory data showed elevated serum activity of total bilirubin, direct bilirubin as 1.44mg/dL, 0.54mg/dL. Normal ALP, AST, ALT, total protein and PT as 112.8U/L, 28.4U/L, 17.2U/L, 6.7g/dL and 15.4 seconds respectively. Liver measurements Max CC, MHP CC, Max LL and MHP AP as 101.6mm, 65mm, 161.7mm and 128.1mm. Liver volume 652ml. Rt & Lt liver lobe texture as 47.85 HU and 48.24 HU respectively (Department of radiology, Royal scan diagnostic center-Khartoum, 2015).
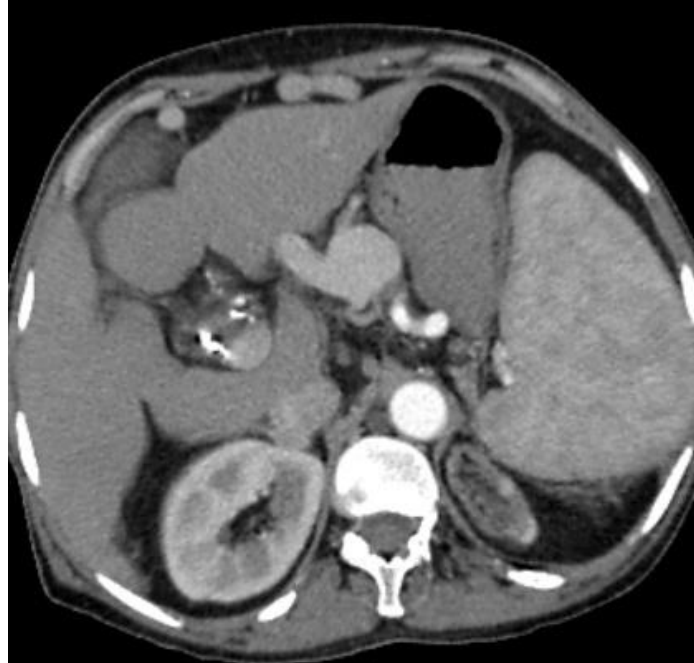
Image 5: Axial pre-contrast CT image of cirrhosis morphologic features. 60 years old female shows cirrhotic enlarged liver with tumor and irregular outlines. Laboratory data showed elevated serum activity of ALP as 482U/L and normal AST, ALT, albumin, total protein and PT as 37 U/L, 14 U/L, 4.6g/dL, 7.8g/dL and 18 seconds respectively. Liver measurements Max CC, MHP CC, Max LL and MHP AP as 216.9mm, 163.2mm, 250mm and 215.7mm respectively. Liver volume 1369ml. Rt & Lt liver lobe texture as 22.4 HU and 45 HU respectively (Department of radiology, Royal scan diagnostic center-Khartoum, 2015).

Image 6: Axial arterial phase CT of liver metastasis (Same patient in Image 4) shows the liver is enlarged due to a large number of low-density lesions in both lobes, which show enhancement around their edges& cirrhotic with irregular outlines (Department of radiology, Royal scan diagnostic center-Khartoum, 2015).

Image 7: CT of hydrated cyst and fatty liver disease. 50 years old female showing shows Lt liver lobe thin walled cyst with lateral wall calcification, its abutting the GB. Atrophy segments II & III noted. The rest of liver shows diffuse fatty information. Laboratory data showed normal serum activity of total bilirubin, direct bilirubin, total proteins and PT as 0.4mg/dL, 0.15 mg/dL, 8.8g/dL and 16 seconds respectively and elevated serum activity of ALP, AST, ALT as 160U/L, 118U/L and 155U/L respectively. Liver measurements Max CC, MHP CC, Max LL and MHP AP as 196.2mm, 125.4mm, 148.4mm and 177mm respectively. Liver volume 1598ml. Rt & Lt liver lobe texture as 21 HU and 6 HU respectively (Department of radiology, Royal scan diagnostic center-Khartoum, 2015).
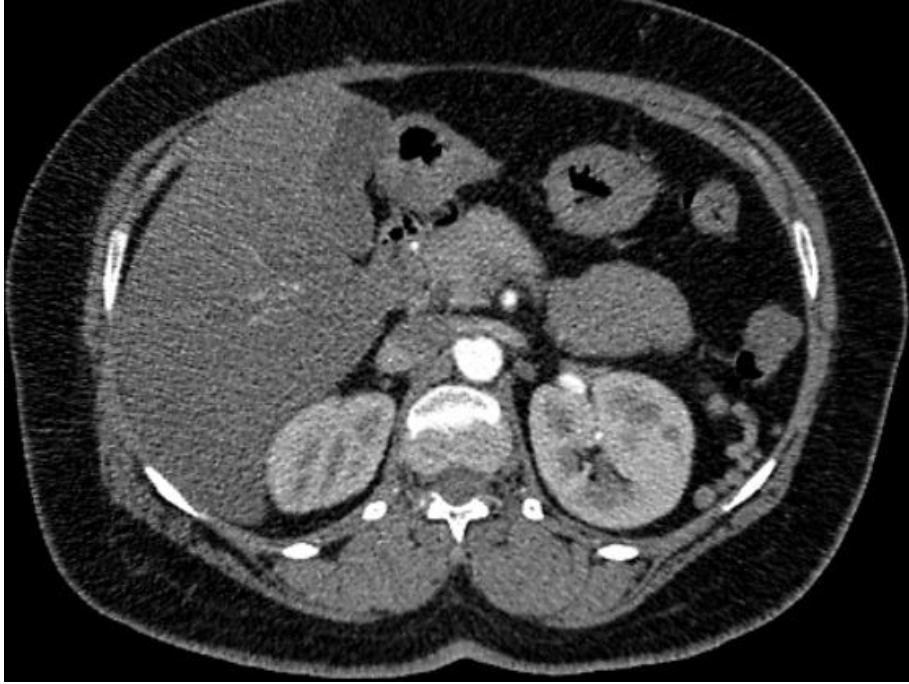
Image 8: Axial arterial phas CT of fattey liver disease or steatosis
(Same patient in Image 6). 50 years old obese (99 kg) female showingfatty
degeneration of the liver as reduced attenuation of the liver (Department of
radiology, Royal scan diagnostic center-Khartoum, 2015).
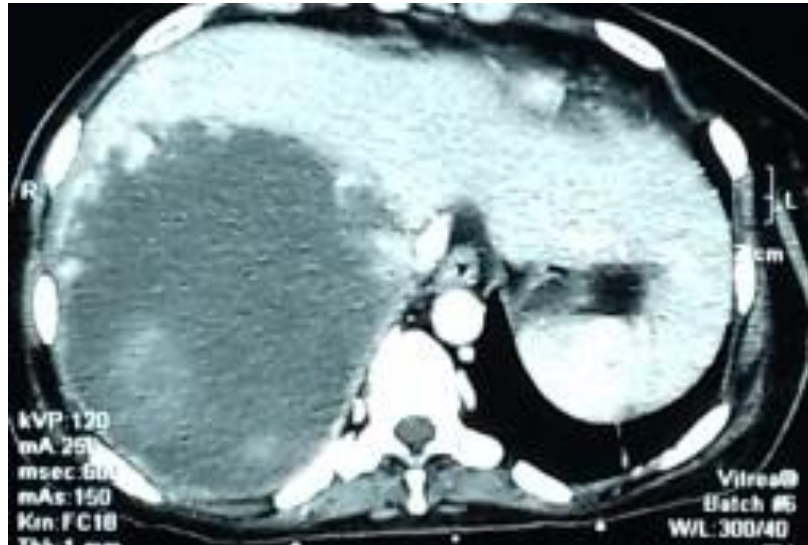
Image 9: CT of ruptured giant liver haemangioma. 38 years old female showing arterial phase CT shows heterogeneous mass lesion at the Rt liver lobe with peripheral, nodular & interrupted enhancement & centripetal filling. Laboratory data showed normal serum activity of total bilirubin, direct bilirubin, ALP, AST, ALT, albumin, total protein and PT as 1mg/dL, 0.37 mg/dL, 104U/L, 33U/L, 17U/L, 4.7g/dL, 6.7g/dL and 12 seconds respectively. Liver measurements Max CC, MHP CC, Max LL and MHP AP as 220.3mm, 130.3mm, 237.3mm and 170mm respectively. Liver volume 2755ml. Rt & Lt liver lobe texture as 34.3 HU and 43.8 HU respectively (Department of radiology, Ibn sina specialized hospital-Khartoum 2015)

Image 10: CT of cyst. 57 years old female showing (A) Sagittal, (B) Axial same patient CT shows well defined low detection multiple simple liver cysts wi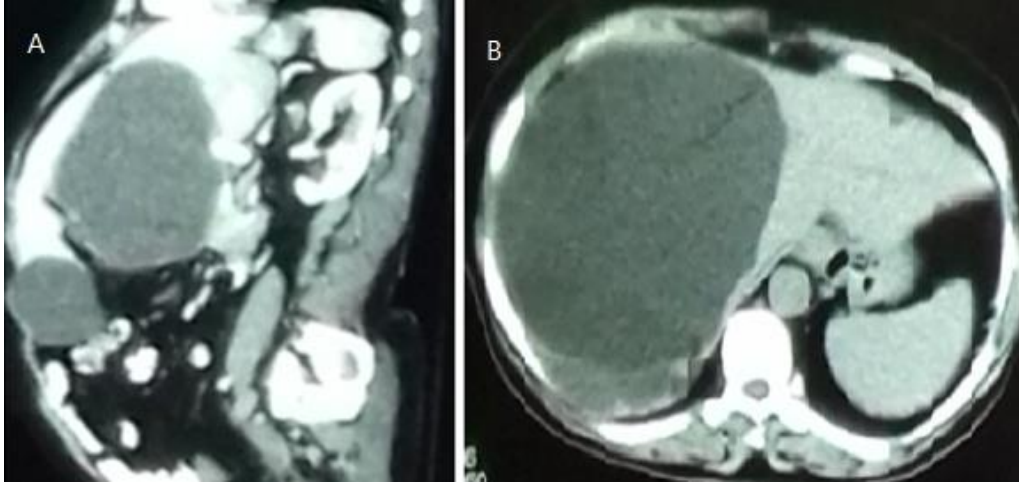th huge cyst. Laboratory data showed normal serum activity of total bilirubin, direct bilirubin, ALP, AST, ALT, albumin, total proteins and PT (Department of radiology, Ibn sina specialized hospital-Khartoum 2015).

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Data coolection sheet of measurement and characterization of liver in CT images among patients with abnormal liver function tests

Age	Gender	Clinical signs	Duration of illness	Total bilirubin	Direct bilirubin	ALP	AST	ALT	Albumin	Glubulin	Total protein	PT	CT findings

Max CC	Max LL	MHP CC	MHP AP	Liver volum	Rt lobe density	Lt lobe density