Sudan University of science and technology
College of graduate studies

Characterization of different types of hepatitis using Ultrasonography

توصيف أنواع التهاب الكبد المختلفة بإستخدام التصوير بالموجات فوق الصوتية

A thesis Submitted for Partial Fulfillment for the requirement of MSc Degree inmedical Diagnostic ultrasound

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الآية

قال تعالى:

﴿ وَلَقَدْ خَلَقْنَا الْإِنسَانَ مِن سُلَالَةٍ مِّن طِينٍ {12} ثُمَّ جَعَلْنَاهُ نُطْفَةً فِي قَرَارٍ مَّكِينٍ {13} ثُمَّ خَلَقْنَا النُّطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا الْمُضْغَةَ عِظَامًا فَكَسَوْنَا الْعِظَامَ لَحْمًا ثُمَّ أَنشَأْنَاهُ خَلْقًا آخَرَ فَتَبَارَكَ اللَّهُ أَحْسَنُ الْخَالِقِينَ﴾ {14}

سورة المؤمنون

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First and above all, thanks and praises to Allah, the almighty for providing me this opportunity and granting me the capability to proceed successfully, and the prayers and peace be upon the merciful prophet Mohamed.

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Dedication

To my father

My mother

My wife

My brother

My sisters

My sons

My daughters

And My friends

Abstract

Viral hepatitis is one of the diseases that affect the liver and occurs worldwide; it is responsible of millions of deaths secondary to acute hepatic necrosis or chronic hepatitis which in turn may lead to portal hypertension, cirrhosis and hepatocellular carcinoma (HCC).

The objective of this research was to characterize different types of hepatitis using medical ultrasonography. 60 patients with positive laboratory test of hepatitis of one of the three types (A, B & C) were enrolled in the study and scanned with ultrasonography.

The study showed that the males are common affected than female (71.7% male &28.3% female). The frequency of viral hepatitis increased in child and younger adults. Furthermore the liver echogenicity of different types of hepatitis, the study showed that 75 % (15 of 20 patients) with hepatitis-A had hypoechoic liver echogenicity(starry night appearance),the rest of patients with hepatitis-A appear normal. Furthermore hepatitis-B and C the most (75%) are normal in echogenicity. The study showed 56.7% (34 of 60 patients) had wall thickening(more than 3 mm) and43.3% showed normal wall thickness, although it is not specific finding for hepatitis, because another diseases like heart failure, metabolic disease and bacterial infection cause gall wall thickening.

The study concluded that the ultrasound only is not efficient modality to characterize hepatitis but sometimes can suggest the diagnosis of hepatitis A in the correct clinical situation.

The study recommend that follow up ultrasound scanning is recommended for infected patients when develop changes in liver and gallbladder.

ملخص البحث

التهاب الكبد الفيروسي من الامراض التي تصيب الكبد وهو منتشر في جميع انحاء العالم . تسبب في ملاييين الوفيات نتيجة لقرقرينة الكبد أو التهاب الكبد المزمن الذي يؤدي الى ارتفاع ضغط الدم في الوريد البابي , تليف الكبد وفي بعض الحالات سرطان الكبد .

الهدف من هذه الدراسة هو تشخيص أنواع التهاب الكبد الفيروسي المختلفة بواسطة التصوير الطبي بالموجات فوق الصوتية . أجريت الدراسة على (60) مريض مصابين بأحد أنواع التهاب الكبد الفيروسي (A ,B ,C) .

وجدت الدراسة أن الرجال أكثر إصابة من النساء بالتهاب الكبد الفيروسي وكذلك أن معدل الإصابة أكثر شيوعا وسط الأطفال والشباب .

وجدت الدراسة أن الرجال أكثر إصابة من النساء بالتهاب الكبد الفيروسي بنسبة (71.7% من الرجال و28.3% من النساء) , وكذلك أن معدل الإصابة أكثر شيوعا وسط الأطفال والشباب .

بالاضافة إلي ذلك وجدت الدراسة ان قوة الصدي المتولدة بالنسبة لانواع التهاب الكبد الفيروسي المختلفة ان 75% (15- 20 مريض) من المرضي المصابين بالتهاب الكبد A أظهرت قوة صدي متولدة منخفضة من الكبد (منظر النجوم بالليل) .وماتبقي من المرضي المصابين بالتهاب الكبد A لم تظهر لديهم تغيرات , أما عن المصابين بالتهاب الكبد (B,C) الأغلبية 75% أظهروا قوة صدي متولدة طبيعية من الكبد , كذلك أظهرت الدراسة ان65.7% (34من 60 مريض) لديهم تضخم في جدار الحويصلة المرارية(أكثر من 3ملم), و34.3% ليس لديهم تضخم في جدار الحويصلة المرارية, وبالرغم من ذلك ليست خاصية مميزة للمرض لان بعض الأمراض كفشل القلب وأمراض سوء التغذية والالتهاب البكتيري تتسبب في تضخم جدار الحويصلة المرارية .

وكذلك وجدت الدراسة أن الموجات فوق الصوتية وحدها لا تكفي لتشخيص التهاب الكبد الفيروسي لكنها قد تشير إلي حدوث الإصابة في حالة التهاب الكبد الفيروسي-A في الحالات السريرة المثالية . و التي وجد فيها انخفاض في مستوى قوة الصدى المتولد وتضخم في الكبد وتضخم جدار الحويصلة المرارية .

وقد أوصت الدراسة بعمل صور بالموجات فوق الصوتية للمرضى المصابون بالتهابات الكبد الفيروسية لمتابعة التغييرات الناتجة في الكبد والحويصلة المرارية .

List of figures

List of tables

Table of contents

List of abbreviations

US	Ultrasound
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCC	Hepatocelular carcinoma
HCV	Hepatitis C virus
GB	Gall bladder
I.V.C	Inferior vena cava
PV	Portal vein
VLDLS	Very low- density lipoproteins
HDLS	High density lipoproteins
LCAL	Lecithin –cholestrol acyltransferase
IDLS	Intermediate-density lipoproteins
LDLS	Low –density lipoproteins
RNA	Ribo -neuclic acid
DNA	Deoxy ribo-neuclic acid
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase

Chapter one
Introduction

Chapter one

1-1 Introduction:

The liver is the largest organ in the human body, weighing approximately 1500g in the adults. It is very important organ in the body due to it is metabolic functions, synthetic function, conjugating function and secretary function. It is frequently involved in systemic and local disease. (CarolM.Rumack.2010)

Viral hepatitis is one of the diseases that affect the liver and occurs worldwide; it is responsible of millions of deaths secondary to acute hepatic necrosis or chronic hepatitis which in turn may lead to portal hypertension, cirrhosis and hepatocellular carcinoma (HCC). (Seeft L B.1996)

Recent medical advances have identified six distinct hepatitis viruses .hepatitis A, B, C, D, E and G. in Sudan only A, Band C .

Medical ultrasonography is a noninvasive, rapid, inexpensive and available diagnostic method used to visualize muscles, tendons, and many internal organs, to tomographic images .this technology is relatively inexpensive and portable especially when compared with other techniques. Ultrasound is used to visualize fetuses during routine and emergency prenatal care as currently applied in the medical field, properly performed ultrasound poses no known risks to the patient, sonography does not use ionizing radiation and the power levels used for imaging is too low to cause adverse heating or pressure effects in tissue, so the benefits to the patient are more than the risks. (H. T. Lutz et al. 2006)

The patient should be instructed to fast for at least 6 hours to eliminate bowel gas and assure the fullness of gall bladder. CarolM.Rumack.2010)

The liver is examined with patient in a supine or right anterior oblique position, usually with deep inspiration to allow the liver to move inferior to

the rib cage. The liver is then examined in a transverse, coronal, subcostal oblique and sagittal view to completely survey the organ. CarolM.Rumack.2010)

Within the homogeneous parenchyma lie the thin walled hepatic veins, the brightly reflective portal veins, the hepatic arteries, and the hepatic duct. The system gain should be adjusted to adequately penetrate the entire right lobe of the liver as a smooth, homogeneous echo-texture pattern.

In ultrasonography the acute stage of viral hepatitis and even in the beginning of fulminate hepatitis, ultrasound shows an almost normal liver, which may sometimes be slightly but not significant enlarged. The gall bladder may be slightly enlarged, with normal or sometimes thickened wall, as asign of mal function. in the later stage of fulminate hepatitis, the size of the liver decreases and the surfaces became irregular.

Now a day's medical ultrasonography is Avery important diagnostic tool in emergency department because it spends a very short time, so it decreases the patient waiting time. (CarolM.Rumack etal.2010)

1-2 Problems:

Now a days hepatitis is a common disease in Sudan and wildly spread in Khartoum state, early detection by ultrasonography can help management of the disease.

1-3 Objectives:

1-3-1General objective:

To characterize different types of hepatitis using medical ultrasonography.

1-3-2 Specific objectives:

- To demonstrate any change in the liver size with different type of hepatitis.
- To visualize the variation in echogenicity and architecture of the liver with different types of hepatitis.

- To detect any change in the gall bladder and common bile duct caused by hepatitis.

1-4Thesis out line

This study falls into five chapters :

1) Chapter one : introduction ,problem ,and objective .
2) Chapter two :Theoretical background and literature reviews .
3) Chapter three : Material and methods .
4) Chapter four : Results .
5) Chapter five : discussion , conclusion and recommendation.

Chapter two
Theoretical background and literature reviews

Chapter two:

Theoretical background and literature reviews

2-1Anatomy of the liver:

The liver is soft and pliable and occupies the upper part of the abdominal cavity just beneath the diaphragm the greater part of the liver is situated under cover of the right costal margin, and the right hemidiaphragm separates it from the pleura, lungs, pericardium, and heart. The liver extends to the left to reach the left hemidiaphragm. The liver may be divided into a large right lobe and a small left lobe by the attachment of the peritoneum of the falciform ligament (Fig.). The right lobe is further divided into a quadrate lobe and a caudate lobe by the presence of the gallbladder, the fissure for the ligamentum teres, the inferior vena cava, and the fissure for the ligamentum venosum. (Richard S Snell 2012)

The portahepatis, or hilum of the liver, is found on the postero inferior surface and lies between the caudate and quadrate lobes. In it lie the right and left hepatic ducts, the right and left branches of the hepatic artery, the portal vein, and sympathetic and parasympathetic nerve fibers A few hepatic lymph nodes lie here; they drain the liver and gallbladder and send their efferent vessels to the celiac lymph nodes. The liver is completely surrounded by a fibrous capsule(Glisson's capsule) but only partially covered by peritoneum. (Richard S Snell 2012)

2-1-1 Relations of the liver:

Anteriorly diaphragm, right and left costal margins right and left pleura and lower margins of lungs ,xiphoid process, and anterior abdominal wall

in the subcostal angle Posteriorly diaphragm, right kidney, hepatic flexure of the colon, duodenum, gallbladder, inferior vena cava and esophagus and fundus of the stomach. (Richard S Snell 2012)

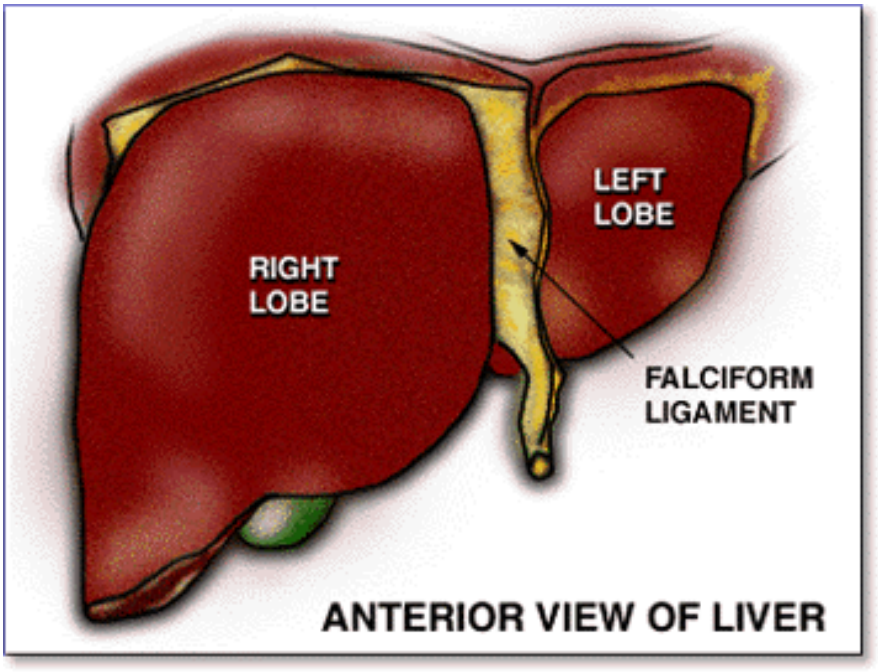

Figure 2-1Anterior view of liver (Richard S Snell 2012)

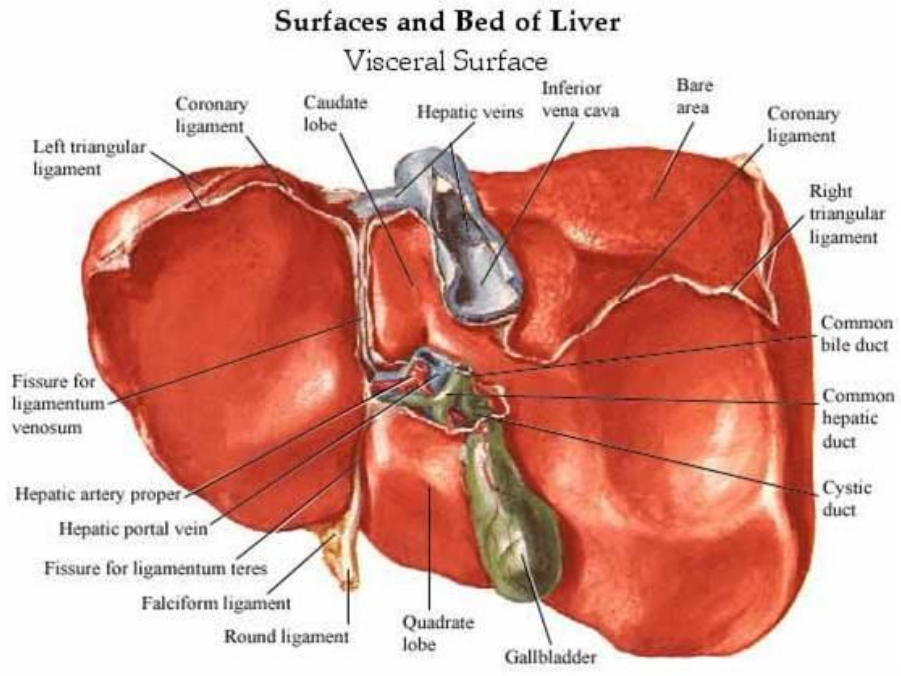

Figure 2-2 Postero-inferior view of liver(Richard S Snell 2012)

The liver is further subdivided into a total of eight segments by divisions of the right, middle and left hepatic veins. Each segment receives its own portal pedicle, permitting individual segment resection at surgery. (3)

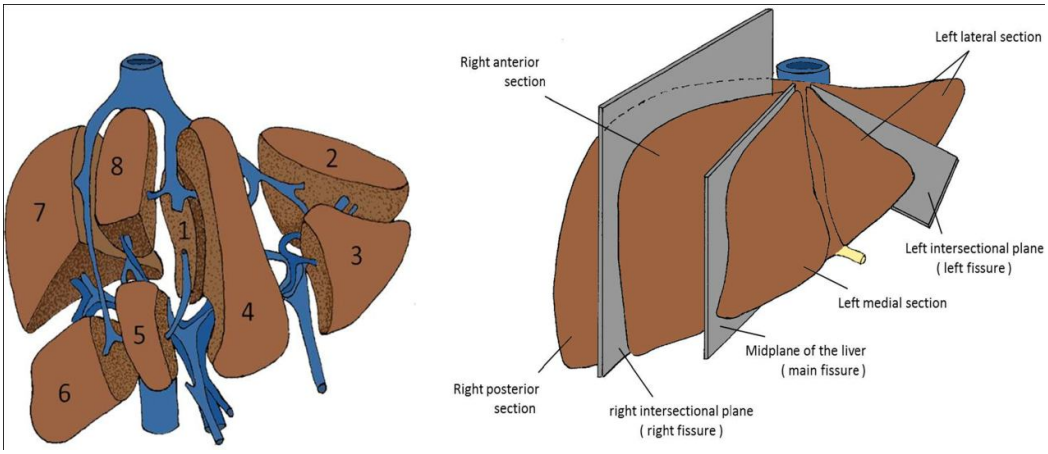

Figure 2-3 liver segments Kumar et al. 2007)

2-1-2 Blood Supply:

The liver has a dual afferent blood supply, receiving an afferent blood supply through both the portal vein and hepatic artery:

The hepatic artery, a branch of the celiac artery, divides into right and left terminal branches that enter the portahepatis.

The portal vein divides into right and left terminal branches that enter the portahepatis behind the arteries. The hepaticveins (three or more) emerge from the posterior surface of the liver and drain into the inferior vena cava. The blood vessels conveying blood to the liver are the hepatic artery (30%) and portal vein (70%).The hepatic artery brings oxygenated blood to the liver, and the portal vein brings venous blood rich in the products of digestion, which have been absorbed from the gastro intestine attract. The arterial and venous blood is conducted to the central vein of each liver lobule by the liver sinusoids.

The central veins drain into the right and left hepatic veins and these leave the posterior surface of the liver and open directly into the inferior vena cava.

The liver produces a large amount of lymph—about one third to one half of all body lymph. The lymph vessels leave the liver and enter several lymph nodes in the portahepatis**.**

The efferent vessels pass to the celiac nodes. A few vessels pass from the bare area of the liver through the diaphragm to the posterior mediastinal lymph nodes. .(Richard S Snell 2012)

2-2 Histology of the liver:

The functional unit of the liver is the acinus. This consists of parenchyma supplied by the smallest portal tracts containing portal vein radicles, hepatic arterioles and bile ductules. The hepatocytes near this triad are well supplied with oxygenated blood and are more resistant to damage than the

cells nearer the terminal hepatic (central) veins

The sinusoids lack a basement membrane and are loosely surrounded by specialist fenestrated endothelial cells and Kupffer cells (phagocytic cells). Sinusoids are separated by plates of liver cells (hepatocytes). The subendothelial space that lies between the sinusoids and hepatocytes is the space of Disse, which contains a matrix of basement membrane constituents and stellate cells. .(Kumar et al . 2007)

2-3 The biliary system:

Bile canaliculi form a network around the hepatocytes .these join to form thin bile ductules near the portal tracts .these then combine to form the right and left hepatic ducts that leave each liver lobe .the hepatic ducts join at the portahepatis to form the common hepatic duct. the cystic duct connects the gall bladder to the lower end of the common hepatic duct . the gall bladder lies under the right lobe of the liver and stores and concentrates hepatic bile .it has capacity of approximately 50 ml. the common bile duct is formed by the connection of cystic and hepatics ducts about 8 mm in diameter , narrowing at its distal end to pass into duodenum with the pancreatic duct (ampulla of vater).the lower end of the common bile duct contains muscular sphincter of oddi which contract rhythmically and prevents bile from entering the duodenum in the fasting state. .(Kumar et al . 2007)

2-4 Physiology of the liver:

2-4-1 Metabolism:

Protein synthesis, storage, and degradation (nitrogen excretion**):**The liver is the principal site of synthesis of all circulating proteins apart from γ-globulins, which are produced in the reticuloendothelial system. The liver receives amino acids from the intestine and muscles and, by controlling the rate of gluconeogenesis and transamination, regulates levels in the plasma. Plasma contains 60-80 g/L of protein, mainly in the form of albumin, globulin and fibrinogen.

Albumin has a half-life of 16-24 days and 10-12 g are synthesized daily. Its main functions are first to maintain the intravascular oncotic (colloid osmotic) pressure, and second to transport water-insoluble substances such as bilirubin, hormones, fatty acids and drugs. Reduced synthesis of albumin over prolonged periods produces hypoalbuminaemia and is seen in chronic liver disease and malnutrition. Hypoalbuminaemia is also found in hypercatabolic states (e.g. trauma with sepsis) and in diseases where there is an excessive loss (e.g. nephrotic syndrome, protein-losing enteropathy). Kumar & Clark CLINICAL MEDICINE(6th ed).2007

Transport or carrier proteins such as transferrin and caeruloplasmin, acute-phase and other proteins (e.g. α_1-antitrypsin and α-fetoprotein) are also produced in the liver.

The liver also synthesizes all factors involved in coagulation (apart from one-third of factor VIII) - that is, fibrinogen, prothrombin, factors V, VII, IX, X and XIII, proteins C and S and antithrombin as well as components of the complement system.

Degradation (nitrogen excretion) Amino acids are degraded by transamination and oxidative deamination to produce ammonia, which is

then converted to urea and excreted by the kidneys. This is a major pathway for the elimination of nitrogenous waste. Failure of this process occurs in severe liver disease.

Carbohydrate metabolism: Glucose homeostasis and the maintenance of the blood sugar is a major function of the liver. It stores approximately 80 g of glycogen. In the immediate fasting state, blood glucose is maintained either by glucose released from the breakdown of glycogen (glycogenolysis) or by newly synthesized glucose (gluconeogenesis). Sources for gluconeogenesis are lactate, pyruvate, amino acids from muscles (mainly alanine and glutamine) and glycerol from lipolysis of fat stores. In prolonged starvation, ketone bodies and fatty acids are used as alternative sources of fuel and the body tissues adapt to a lower glucose requirement.

Lipid metabolism: Fats are insoluble in water and are transported in the plasma as protein-lipid complexes (lipoproteins). The liver has a major role in the metabolism of lipoproteins. It synthesizes very-low-density lipoproteins (VLDLs) and high-density lipoproteins (HDLs). HDLs are the substrate for lecithin-cholesterol acyltransferase (LCAT), which catalyses the conversion of free cholesterol to cholesterol ester (see below). Hepatic lipase removes triglyceride from intermediate-density lipoproteins (IDLs) to produce low-density lipoproteins (LDLs) which are degraded by the liver after uptake by specific cell-surface receptors.

Bilirubin metabolism: Bilirubin is produced mainly from the breakdown of mature red cells in the Kupffer cells of the liver and in the reticuloendothelial system; 15% of bilirubin comes from the catabolism of other haem-containing proteins, such as myoglobin, cytochromes and catalases. Normally, 250-300 mg of bilirubin are produced daily. The iron and globin are removed from the haem and are reused. Biliverdin is formed from the haem and this is reduced to form bilirubin. The bilirubin produced

is unconjugated and water-insoluble, and is transported to the liver attached to albumin. Bilirubin dissociates from albumin and is taken up by the hepatic cell membrane and transported to the endoplasmic reticulum by cytoplasmic proteins, where it is conjugated with glucuronic acid and excreted into bile.

The microsomal enzyme, uridine diphosphoglucuronosyltransferase, catalyses the formation of bilirubin monoglucuronide and then diglucuronide. This conjugated bilirubin is water-soluble and is actively secreted into the bile canaliculi and excreted into the intestine within the bile. .(Kumar et al . 2007)

2-4-2 Storages (glycogen, vitamins ,iron).

2-4-3 Formation of bile (secretion and bile acid metabolism):

Bile secretion**:** Bile consists of water, electrolytes, bile acids, cholesterol, phospholipids and conjugated bilirubin. Two processes are involved in bile secretion across the canalicular membrane of the hepatocyte - a bile salt-dependent and a bile salt-independent process - each contributing about 230 mL per day. The remainder of the bile (about 150 mL daily) is produced by the epithelial cells of the bile ductules.

The average total bile flow is approximately 600 mL per day. In the fasted state half of the bile flows directly into the duodenum and half is diverted into the gall bladder. The mucosa of the gall bladder absorbs 80-90% of the water and electrolytes, but is impermeable to bile acids and cholesterol. Following a meal, cholecystokinin is secreted by the I cells of the duodenal mucosa and stimulates contraction of the gall bladder and relaxation of the sphincter of Oddi, so that bile enters the duodenum.

Bile acid metabolism**:** Bile acids are synthesized in hepatocytes from cholesterol. The rate-limiting step in their production is that catalysed by cholesterol-7α-hydroxylase. They are excreted into the bile and then pass

into the duodenum. The two primary bile acids - cholic acid and chenodeoxycholic acid - are conjugated with glycine or taurine (in a ratio of 3: 1 in humans) and this process increases their solubility. Intestinal bacteria convert these acids into secondary bile acids, deoxycholic and lithocholic acid. Shows the enterohepatic circulation of bile acids. .(Kumar et al . 2007)

2-4-4 Hormone and drug inactivation:

The liver catabolizes hormones such as insulin, glucagon, oestrogens, growth hormone, glucocorticoids and parathyroid hormone. It is also the prime target organ for many hormones (e.g. insulin). It is the major site for the metabolism of drugs and alcohol. Fat-soluble drugs are converted to water-soluble substances that facilitate their excretion in the bile or urine. Cholecalciferol is converted to 25-hydroxycholecalciferol. .(Kumar et al . 2007)

2-4-5 Immunological function:

The reticuloendothelial system of the liver contains many immunologically active cells. The liver acts as a 'sieve' for the bacterial and other antigens carried to it via the portal tract from the gastrointestinal tract. These antigens are phagocytosed and degraded by Kupffer cells, which are macrophages attached to the endothelium. .(Kumar et al . 2007)

2-5 Pathology of hepatitis in the liver:

2-5-Acut hepatitis:

Although some histological features are suggestive of the aetiological factor, most of the changes are essentially similar whatever the cause. Hepatocytes show degenerative changes (swelling, cytoplasmic granularity, vacuolation), undergo necrosis (becoming shrunken, eosinophilic Councilman Bodies) and are rapidly removed. The distribution of these changes varies somewhat with the aetiological agent, but necrosis is usually maximal in zone 3. The extent of the damage is very

variable between individuals affected by the same agent: at one end of the spectrum, single and small groups of hepatocytes die (spotty or focal necrosis), while at the other end there is multiacinar necrosis involving a substantial part of the liver (massive hepatic necrosis) resulting in fulminant hepatic failure. Between these extremes there is limited confluent necrosis with collapse of the reticulin framework resulting in linking (bridging) between the central veins, the central veins and portal tracts, and between the portal tracts. The extent of the inflammatory infiltrate is also variable, but portal tracts and lobules are infiltrated mainly by lymphocytes. Other variable features include cholestasis in zone 3 and fatty change, the latter being prominent in hepatitis that is due to alcohol or certain drugs.(Kumar et al . 2007)

2-5-2 Chronic hepatitis:

Chronic inflammatory cell infiltrates comprising lymphocytes, plasma cells and sometimes lymphoid follicles are usually present in the portal tracts. The amount of inflammation varies from mild to severe. In addition, there may be:

- loss of definition of the portal/periportal limiting plate - interface hepatitis (damage is due to apoptosis rather than necrosis)
- lobular change, focal lytic necrosis, apoptosis and focal inflammation
- confluent necrosis
- fibrosis which may be mild, bridging (across portal tracts) or severe cirrhosis.

The overall severity of the hepatitis is judged by the degree of the hepatitis and inflammation (grading) and the severity of the fibrosis or cirrhosis (staging) using various scoring systems.(Kumar et al . 2007)

2-5-3 Viral hepatitis:

2-5-3-1Hepatitis A virus(HAV):

Picornaviridae (pico=very small) RNA family. The virus is acquired by ingestion. It multiplies in the intestine and invades the blood, liver and saliva before any clinical manifestation of the disease appears. This period of incubation lasts an average of 4 (2-6) weeks. The virus disappears soon after the peak of serum transaminase is reached at which time the immune response and the hepatocellular damage start. This indicates that the damage is immunologically mediated. Indeed at this time NK (natural killer) cells, circulating or local in the liver (Pitt cells), are activated. CD8+ cytotoxic T lymphocytes that secrete gamma interferon infiltrate the field.

Clincal features**:** Most infections occur in children in whom the disease in most cases is either asymptomatic or symptomatic without jaundice. In adults, the infection is more severe with general symptoms malaise and jaundice, Gastro-enteric form ; however hepatitis A is not very debilitating even in the presence of jaundice. Fever does not go above 39 degrees centigrade. Jaundice lasts for 7-10 days and the whole illness lasts about 4 weeks. Relapses however do occur. .(Dr.orfel 2007)

Laboratory diagnosis:

1-Serum IgM antibody is present during the acute phase and disappears in 3 months. It may last up to 2 years in a few cases. The test is 100% sensitive and very specific.

2-Serum IgG antibody develops after the acute illness and persists for life, representing immunity.

3-Demonstration of virus in liver, feces and blood is impractical. The virus is present in these fluids before the symptoms appear therefore the patient is infectious before he is known to be sick.

4-Jaundice usually lasts 7-10 days and its degree is not related to the outcome of the illness.

5-Serum transaminase rise with the acute illness and return normal with recovery. They seldom are higher than 1000. There is no correlation between their level and prognosis.(.(Dr.orfel 2007)

Portal and periportal inflammation: Presence of both lobular and portal inflammation. This illustration shows marked protal and periportal inflammation with some hepatocellular ballooning degeneration.

❖ Lobular inflammation: Notice intralobular inflammatory cell, few shrinking apoptotic cells (Councilmann bodies), many swollen hepatocyte and binucleate hepatocytes indicating accelerated liver cell renewal.

❖ Confluent necrosis :Death of adjacent groups of hepatocyte throughout the lobule. Confluence of many spotty necroses. Notice glycogen (red granules) depletion on damaged hepatocyte..

❖ Hepatocelular damage : Some hepatocytes are swollen and clear (hydropic degeneration). One is shrunken and dark with rests of nuclear disintegration (apoptotic cell, Councilmann body). There is a group of Kupffer cells with bile and lipofuscin granules in their function as scavenger cells.

❖ Cholestatatic form of viral hepatitis: Marked cholestasis with intracytoplasmic yellow granules of bile and bile thrombi in canaliculi. Thescholestatic changes are seen in cases of prolonged jaundice. .(Dr.orfel 2007)

2-5-3-2 Hepatitis B virus (HBV):

is a Hepadnavirus (from Hepa=liver, dna=DNA)

The virus may produce :

1 - An asymptomatic transient infection

- **HBV-DNA** is of low titre and limited in time. The virus disappears before serum transaminases rise.
- ALT elevation is slight or moderate.
- Serum HbsAg is detectable for a few (2-3-) months and soon will convert to antibody.
- Serum anti-HBs indicates the end of the infection and will be present for life.
- IgM anti-HBc antibody will appear toward the end of transaminase (ALT) elevation and will last for 2-3 months.
- IgG anti-HBc antibody together with anti surface antibody will be present for life.
- Clinical disease is non existent.

2 - An acute resolving hepatitis

- The course of the infection is similar to the asymptomatic transient infection with the difference that there is the symptomatology of jaundice with marked elevation of ALT and AST and all viral antigens ,HBs, Hbc, He HBV-DNA. At 6 months the antigens convert to antibodies, the symptoms disappear, the infection resolves. IgM anti-HBs persists for about a year than IgG anti-HBs remains for life.

3 - An acute chronic hepatitis B

- Chronicity is characterized by persistence of viral replication with attached viral antigens for over 6 months, sometimes returning to normal in many years or advancing to induce cirrhosis and/or hepatocellular carcinoma. The chronicity of hepatitis B may follow either a symptomatic acute icteric hepatitis or, more commonly, an asymptomatic silent infection. .(Dr.orfel 2007)

Pathology of acute icteric hepatitis B:

❖ "Lobular disarray": Loss of hepatocyte, inflammatory reaction, Kupffer cell mobilization an hepatocellular swelling distort the pattern of the liver plates somewhat confusing the lobular architecture.(H&E stain).

❖ Focal necrosis**:** In the center of this slide there is a focus of cell dropout with inflammatory reaction

❖ Confluent necrosis: It is the confluence of many groups of focal necrosis. Note multiple foci of cell dropout. The tissue was stained with PAS technique which stains glycogen granules red.

❖ Bridging necrosis: It is the confluence of many groups of focal necrosis. Note multiple foci of cell dropout. The tissue was stained with PAS technique which stains glycogen granules red.

❖ Massive and submassive hepatic necrosis**:** Massive necrosis is fatal, involving the entire liver parenchyma. Submassive necrosis may not be fatal involving more severely large areas of the liver but less severely in other areas. It is , however, complicated by cirrhosis. Here is an example of submassive necrosis. Only a few periportal liver cell plates are viable in this open liver biopsy but other parts of the liver were less damaged.

❖ Portal and periportal inflammation: Portal inflammation is always present in most portal tracts. The inflammatory cell s are mostly lymphocytes sometimes forming lymphoid follicles, plasma cell containing gamma globulins mostly IgG type, macrophages containing iron granules. There may be bile duct damage. Periportal inflammation with disruption of periportal limiting plate and piecemeal necrosis is also present. An acute hepatitis with portal inflammation and many segmented leucocyte and eosinophils is usually not viral. In this case of acute hepatitis B there is marked portal inflammation and periportal piecemeal necrosis with ballooned hepatocyte.

❖ Hepatocellular damage**:** Hepatocyte suffer shrinkage with formation of acidophilic bodies (Councilman bodies), swelling ('ballooning degeneration"), accumulate bile pigment and drop out leaving gaps which in resolving cases will be filled with new cells. Notice in this slide swollen hepatocyte and two Councilman bodies.

❖ Fulminant fatal acute viral hepaptitis**:** The liver is soft, flabby, friable, yellowish-green, collapsed, shrunken ("acute yellow atrophy")..(Dr.orfel 2007)

2-5-3-3 Hepatitis c virus (HCV):

The virus contains a single-stranded genome of **RNA** with approximately 10,000 nucleotides, a **capsid**, a **matrix** and an **envelope**.

Clinical Course

Incubation period is 2-26 (mean. 7.8) weeks, Most infected patients, 80-85%, are asymptomatic. 25% of post blood transfusion patients are symptomatic and develop jaundice and ALT to high levels. 40 % of all infected patients develop a chronic course. .(Dr.orfel 2007)

Complications

1--Cirrhosis may take 10-20 years or more to appear and will have a long indolent course

2--Hepatocellular carcinoma develops in the presence or absence of cirrhosis

3--Essential cryoglobulinemia-which produce purpura, arthralgia and weakness.

4--Porphyria cutaneatarda due to decrease of Uroporphyrinogen Decarboxylase consists of cutaneous vesicles in exposed areas.

5--Lichen planus. It can be exacerbated by alpha-interferon treatment

. **6--Mooren's corneal** ulcers. They improve with alpha-interferon.

Infection in special subjects Children

The course is similar to that in adults. There is no growth retardation. Children don't die of hepatitis C because in this disease cirrhosis takes 10-20 years to develop and cause death. Treatment with alpha-interferon has produced same results as in adults. .[Dr.orfel 2007]

2-6 Sonographic evaluation of the liver and gallbladder :

2-6-1Liver:

Evaluation of the hepatic structures is one of the most important procedures in sonography for many reasons. The normal, basically homogeneous parenchyma of the liver allows imaging of the neighboring anatomic structures in the upper abdomen. Echo amplitude, attenuation, and transmission and parenchymal textures may be physically assessed with proper evaluation of the hepatic structures. The patient should be instructed to fast for at least 6 hours to eliminate bowel gas and assure the fullness of the gallbladder. The liver is examined with the patient in a supine or right anterior oblique position, usually with deep inspiration to allow the liver to move inferior to the rib cage. The liver is then examined in a transverse, coronal, subcostal oblique, and sagittal views to completely survey the organ.

Within the homogeneous parenchyma lie the thin walled hepatic veins, the brightly reflective portal veins, the hepatic arteries, and the hepatic duct.

The normal texture of the liver is homogeneous with fie, low-level echoes. When compared to the renal cortex of the kidneys, the liver texture is minimally hyperechoic to isoechoic. When compared to the texture of the spleen, the liver is hypoechoic. (Sandra L. et al . 2012)

2-6-2Gallbladder:

To ensure maximum dilation of the gallbladder, the patient should be given nothing to eat for at least 4 to 6 hours before the ultrasound examination. The patient isinitially examined in the supine position in full inspiration. Transverse , sagittal , andoblique scans are made over the upper abdomen to identify the gallbladder, biliary system, liver, right kidney, and head of the pancreas. The patient should also be rolled into a steep decubitus or upright position (to ensure there are no stones within the gallbladder) in an attempt to separate small stones from the gallbladder wall or cystic duct. The gallbladder may be identifid as a sonolucentoblong structure located anterior to the right kidney, lateral to the head of the pancreas and duodenum.

The normal sonographic findings of gallbladder are ≤ 4 cm transverse ≤ 10 cm longitudinal in size, wall thickness < 3 mm and lumen anechoic.(Sandra L. et al . 2012)

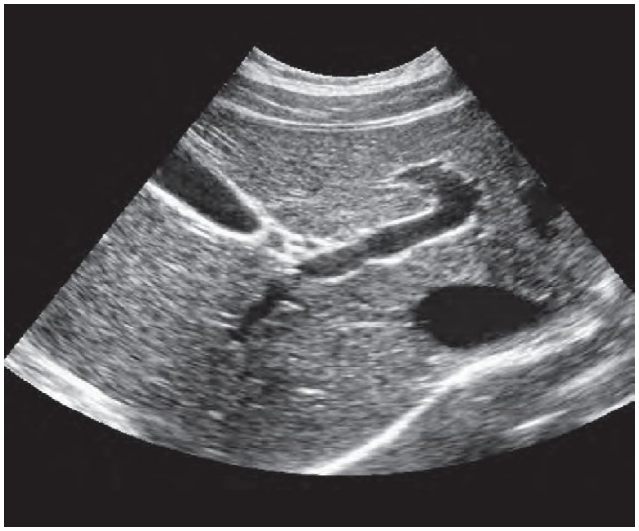

image 1 : Normal lobar anatomy of the liver

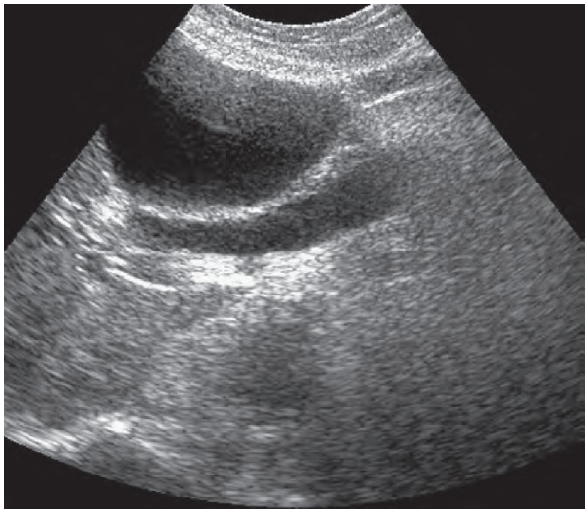

image 2 : Harmonic imaging of biliary Tree

2-7 Previous studies:

- 2-7-1 Wilson SR et al said in their study of Gastrointestinal disease; In acute hepatitis there is diffuse swelling of the hepatocytes, proliferation of kupffer cells lining the sinusoids and infiltration of portal areas by hepatocytes and monocytes. The sonographic features parallel the histologic fidings. The liver parenchyma may have a diffusely decreased echogenicity, with accentuated brightness of the portal triads or periportal cuffing.The liver parechymalmay have a brightness of the portal traids or periportal cuffing. Hepatomegaly and thickening of the gallbladder wall are associated findings. (Wilson SR.2004)
- 2-7-2 Zwiebel WJ found in his study of Sonographic diagnosis of diffuse liver disease ; In most patients the liver appears normal. Most cases of choronic hepatitis are also sonographicaly normal. when cirrhosis develops, sonography may demonstrate a coarsened echotecture and other morphologic changes of cirrhosis.((Zwiebel WJ.1995
- 2-7-3 Sudhamshu KC in his study of Ultrasound findings in acute viral hepatitis found that Gall bladder findings in ultrasound are present in over 80% of enterically transmitted hepatitis virus. Thus, it can be used to diagnose acute hepatitis when serological tests are not available. (Sudhamshu KC.2006)
- 2-7-4 HishamTchelepi et al in his study of Sonography of DiffuseLiver Disease found that there are no specific sonographic findings in acute hepatitis. The findings are quite variable because of many different etiologic factors that cause hepatic inflammation. The most common sonographic finding in hepatitis is probably hepatomegaly. The so-called “starry night liver” pattern, increased periportal echoes coupled with decreased parenchymal echogenicity, is not useful clinically. One series showed the starry night liver pattern in only 19 of 791 patients.4 In the

same study, there was no difference in sonographic findings between a control group without abnormalities and patients with acute viral hepatitis. Striking irregular gallbladder wall thickening is sometimes present in patients with acute hepatitis, especially hepatitis A .Direct inflammation and edema cause wall thickening, sometimes reaching 20 mm (normal,<3 mm). This finding alone, although nonspecific, can sometimes suggest the diagnosis of hepatitis A in the correct clinical situation. Hepatomegaly and inhomogeneous patchy or diffuse increased echogenicity are common in chronic hepatitis and are related to the amount of fatty infiltration and fibrosis present. The liver surface is smooth, unless cirrhosis is also present. (Hisham Tchelepi et al.2002)

- 2-7-5 Another study done by H.T Lutz et al found that In the acute stage of viral hepatitis and even in the beginning of a fulminant hepatitis, ultrasound shows an almost normal liver, which may sometimes be slightly but not significant enlarged.The gall bladder may be slightly enlarged, with a normal or sometimes thickened wall, as a sign of malfunction. (H. T. Lutz et al. 2006)

Chapter Three

Material and methods

Chapter three

Material and methods

3-1 Materials:

3-1-1 Subjects:-

The total populations included in this study were 60 patients whom had positive laboratory test of hepatitis of one of the three types (A, B & C) in Sudanese patients only .

Exclusive criteria:

1- Patient who had negative hepatitis laboratory test

2- Patient who are not Sudanese.

3-1-2 Machine used:-

Different marks of ultrasound machines was used in this study which are sonoscape portable ultrasound machine model A 5 made in china in 2014 , with multiple frequency curvilinear probe and Aloka SSD-500 ultrasound machine made in japapn with multiple frequency curvilinear probe which has variable focal zone and frequency capability

3-2 Method:

3-2-1 Technique used:

The patients were instructed to fast for at least 6 hours to eliminate bowel gas and assure the fullness of the gallbladder. The liver is examined with the patient in a supine or right anterior oblique position, usually with deep inspiration to allow the liver to move inferior to the rib cage. The liver is then examined in a transverse, coronal, subcostal oblique, and sagittal views to completely survey the organ.

Also for gallbladder scanning The patient was initially examined in the supine position in full inspiration. Transverse , sagittal , andoblique scans are made over the upper abdomen to identify the gallbladder, biliary system, liver, right kidney, and head of the pancreas. The patient should

also be rolled into a steep decubitus or upright position (to ensure there are no stones within the gallbladder) in an attempt to separate small stones from the gallbladder wall or cystic duct.

3-2-2 Image interpretation:

The represented ultrasonographic images of the liver and gallbladder were interpreted for different variables ,which include :

- ❖ Liver size.
- ❖ Liver echogenicity.
- ❖ Gallbladder wall thickness.
- ❖ Periportal area.

3-2-3 Data analysis:

The data was analyzed using Statistical Packaged for Social Studies (SPSS) by using various statistics computerize methods.

Chapter Four

Results

Chapter four

Results

Table 4-1Gender distribution

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	17	28.3	28.3	28.3
	Male	43	71.7	71.7	100.0
	Total	60	100.0	100.0	

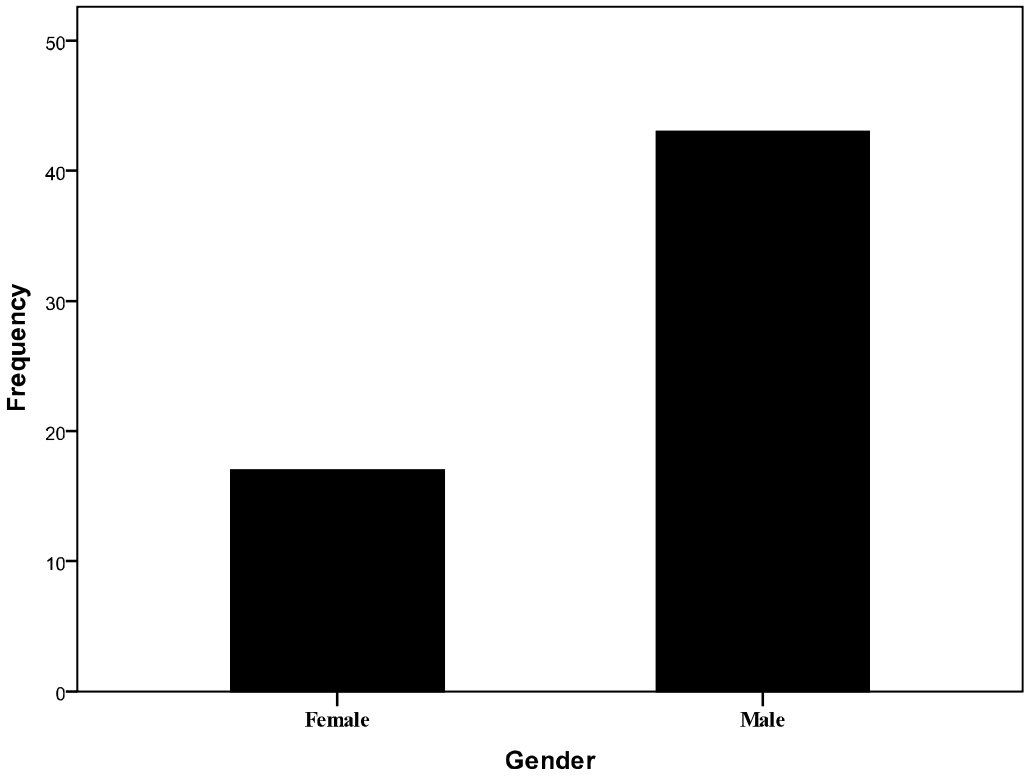

Figure 4-1 **Gender distribution**

Table 4-2 Age Group

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1-20	15	25.0	25.0	25.0
	21-30	14	23.3	23.3	48.3
	31-40	12	20.0	20.0	68.3
	41-50	11	18.3	18.3	86.7
	51-60	4	6.7	6.7	93.3
	61-70	4	6.7	6.7	100.0
	Total	60	100.0	100.0	

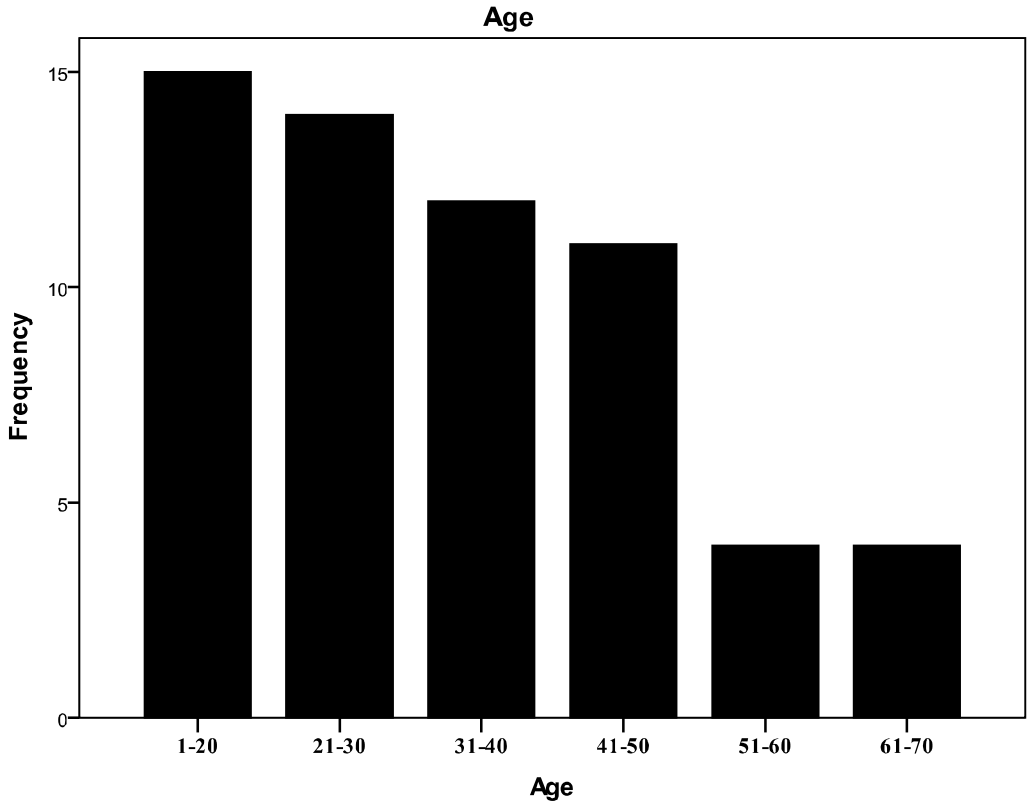

Figure 4-2 **Age Group**

Table 4-3 Hepatitis Type

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	hepatitis A	20	33.3	33.3	33.3
	hepatitis B	20	33.3	33.3	66.7
	hepatitis C	20	33.3	33.3	100.0
	Total	60	100.0	100.0	

Table 4-4 liver Echogenicity

	Frequency	Percent	Valid Percent	Cumulative Percent
Hyperechoic	4	6.7	6.7	6.7
Hypoechoic	21	35.0	35.0	41.7
Normal	35	58.3	58.3	100.0
Total	60	100.0	100.0	

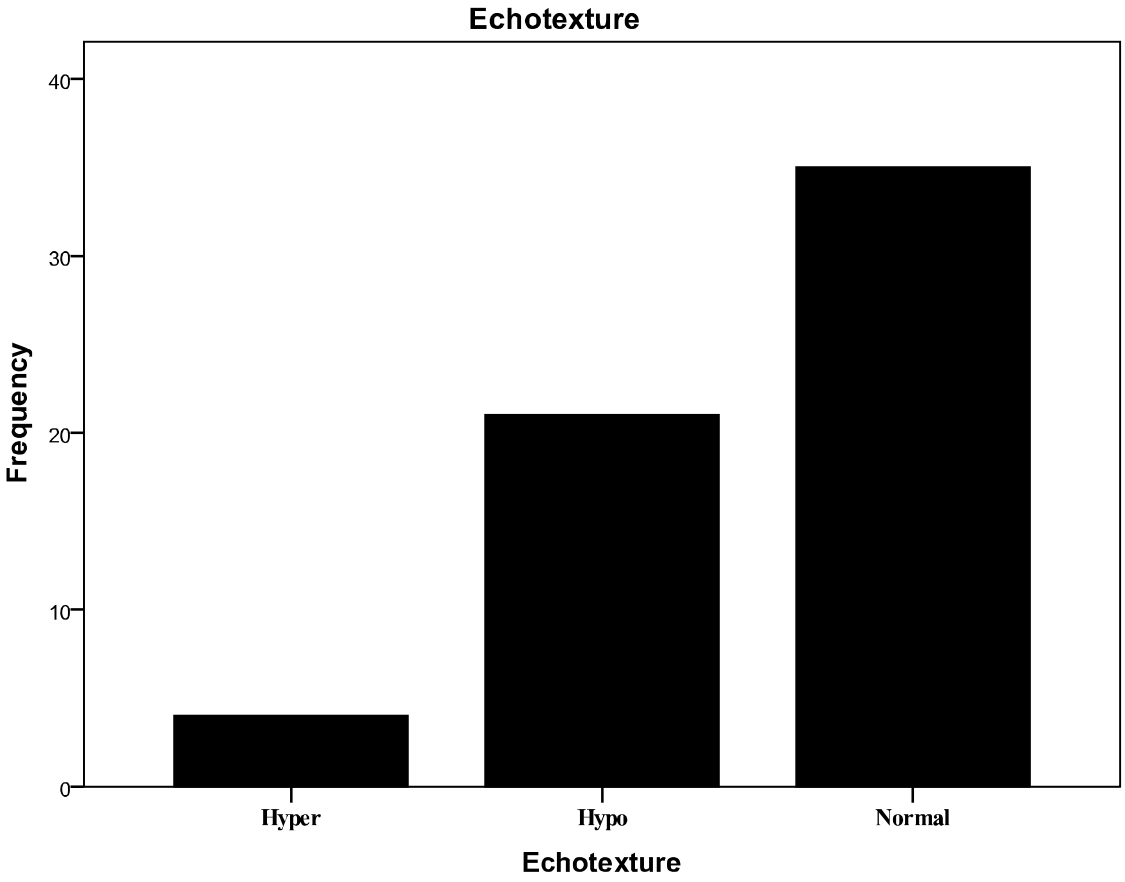

Figure 4-3 **liver Echogenicity**

Table 4-5 Age * Liver Size Cross tabulation

		Liver Size					
		0-10	11-12	13-14	15-16	17-18	Total
Age	1-20	2	4	5	2	2	15
	21-30	0	6	5	2	1	14
	31-40	0	0	8	4	0	12
	41-50	0	5	4	2	0	11
	51-60	1	0	1	2	0	4
	61-70	1	1	1	0	1	4
Total		4	16	24	12	4	60

Table 4-6 Hepatitis *liver echogenicity cross tabulation

		Echogenicity			
		Hyper	Hypo	normal	Total
Hepatitis	hepatitis A	0	15	5	20
	hepatitis B	2	3	15	20
	hepatitis C	2	3	15	20
Total		4	21	35	60

Table 4-7 Hepatitis * Gallbladder Wall thickness Crosstabulation

		Gallbladder Wall				
		0 -0.2	0.3-0.6	0.7-0.8	0.15-0.16	Total
Hepatitis	hepatitis A	6	10	4	0	20
	hepatitis B	9	9	1	1	20
	hepatitis C	11	9	0	0	20
Total		26	28	5	1	60

Table 4-8 Hepatitis * Periportal Changes Crosstabulation

		Periportal Changes			
		Fibrosis	Cuffing	normal	Total
Hepatitis	hepatitis A	1	0	19	20
	hepatitis B	2	2	16	20
	hepatitis C	2	0	18	20
Total		5	2	53	60

Table 4-9 Hepatitis * Liver Size Crosstabulation

		Liver Size					
		0-10	11-12	13-14	15-16	17-18	Total
Hepatitis	hepatitis A	2	4	6	6	2	20
	hepatitis B	1	4	10	5	0	20
	hepatitis C	1	8	8	1	2	20
Total		4	16	24	12	4	60

Chapter Five

Discussion, conclusion and recommendation.

Chapter five

Discussion, conclusion and recommendation.

5-1 Discussion:

The study done in 60 patients had a positive laboratory hepatitis test in three groups (HAV, HBV & HCV) and showed the sonographic appearance of the liver and gallbladder.

Regarding to the gender distribution the males are common affected than female (71.7% male &28.3% female). That might be due to the more activities of male than female.

The study found that the frequency of viral hepatitis increased in child and younger adults peoples, because hepatitis-A is common in school ages (oro-fecal transmission), also hepatitis-B is common in adults (sexual and blood transfusions), and the incidence less common in elder, so as the peoples increased in their contacts with other the incidence will increased.

Regarding to the liver echogenicity of different types of hepatitis, the study showed that 75 % (15 of 20 patients) with hepatitis-A had hypoechoic liver echogenicity(starry night appearance),the rest of patients with hepatitis-A appear normal. Furthermore hepatitis-B and C the most (75%) are normal in echogenicity. So the ultrasound is more sensitive in patients with hepatitis-A than those with hepatitis-B and C. this result was in line with

Wilson et al in their study. The liver parenchyma may have a diffusely decreased echogenicity, with accentuated brightness of the portal triads or periportal cuffig in acute hepatitis. So that it can be a useful for assessing the patients with hepatitis-A more than them with hepatitis-B&C. also it agree with Hisham chelapi T et al in their study . they found that the so called (starry night view) pattern increased periportal echoes coupled with decreased parenchymal echogenecity is not usefull clinically .

Concerning to the liver size the study found that peoples of ages less or equal to 20 years (15 patients) most of them had hepatomegaly (9 patients) which is associated with hepatitis-A. The peoples with age more than 20 years had normal liver size in most of them ,which in this finding agree with Zwiebel et al : in their study, in most patients the liver appears normal.
It is also agree with Hisham T chelepi et al in their study .they found that the most common sonographaic findings in hepatitis is probably hepatomegally .
Regarding to gallbladder wall thickness in patients with hepatitis, the study showed 56.7% (34 of 60 patients) had wall thickening(more than 3 mm) and43.3% showed normal wall thickness, although it is not specific finding for hepatitis, because another diseases like heart failure, metabolic disease and bacterial infection cause gall wall thickening. The study agree with Sudhamshu KC in his study , he found that gallbladder wall thickening are present in over 80% of entrically transmitted hepatitis .
Regarding the periportal area the most of patients (88.3%) showed normal periportal area appearance with less evidence of periportal fibrosis and periportal cuffing, so also it is not reliable finding in patients infected with hepatitis.

5-2 Conclusion:

By the end of this research the study found that the ultrasound only is not efficient modality to characterize hepatitis but sometimes can suggest the diagnosis of hepatitis A in the correct clinical situation.

The incidence of hepatitis more in male than female.

The incidence of hepatitis increased in children and younger adults.

The liver echogenicity is decreased in patients with hepatitis-A and normal in hepatitis-B&C.

Hepatomegaly presented in most of hepatitis-A patients and normal liver size in most of patients with hepatitis-B&C.

Gall bladder wall thickening is seen in most of patients with hepatitis-A and some patients with hepatitis-B&C, but is not specific sign.

5-3 Recommendation:

- Follow up ultrasound scanning is recommended for infected patients when develop changes in liver and gallbladder.
- Ultrasound is recommended to be use only to detect the changes with hepatitis A .
- Another research studies should be done with expanding period of time and include more sample data for precise and accurate results.
- Avoiding of crowding in schools , Orientation of youth and adolescent about hepatitis transmission and risk factors and Carrying must be taken during blood transmission and during delivery.

REFRENCES:

Carol M. Rumack, Stephanie R. Wilson, and Deborah Levine- 2010 Diagnostic ultrasound .4th ed. Mosby ;USA..

Dr.orfel,Emiliofromwww.meddean.luc.edu/lumen/meded/orfpath/pthcntnt.htm.

HishamTchelepi , MD ,Philip W. Ralls ,MD , Randall Radin , MD , Edwerd Grant -2002 .by the American Institute of Ultrasound in Medicine J Ultrasound;.

H. T. Lutz & H.A. Gharbi -2006.Manual of Diagnostic Ultrasound in Infectious Tropical Diseases.firstedition . Springer-Verlag Berlin Heidelberg.

Kumar & Clark- 2007CLINICAL MEDICINE(6th ed).

Richard S. Snell (2012) – accessory organs of the gastrointestinal tract /liver. Clinical Anatomy by Regions (9th ed).

Sandra L. Hagen-Ansert -2012. Textbook of diagnostic sonography .7th ed.Andrew Allen;USA.

Seeft L B -1996.. acute viral hepatitis in: Kapleowicz N, editor. Liver and biliary disease.2nd ed. Baltimore:Williams & Wilkins;

Sudhamshu KC-2006. Kathmandu University .Medical Journal. Nepal.
Wilson SR-2004. The gallbladder. In: Gastrointestinal disease. 6th series.Test and syllabus. Reston, Va: American College of Radiology;
Zwiebel WJ- 1995;16:8-15 Sonographic diagnosis of diffuse liver disease. Semin Ultrasound CT MR .

Appendix A

Ultrasound image from the study

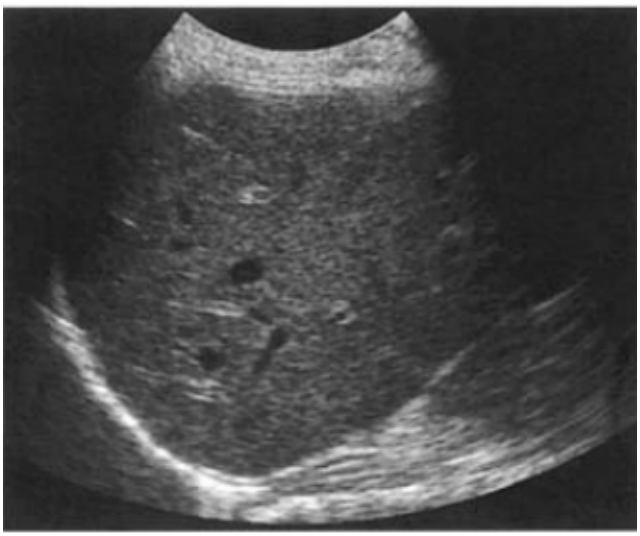

Image 3:Normal sonograhic appearance of the liver of patient with positive HBV

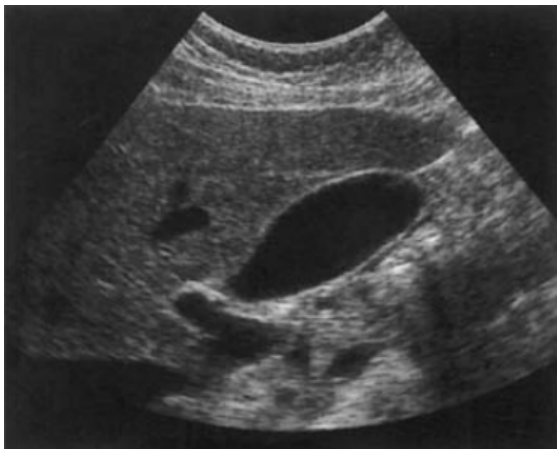

Image 4: Normal sonograhic appearance positive of the gallbladder of patient with HBV

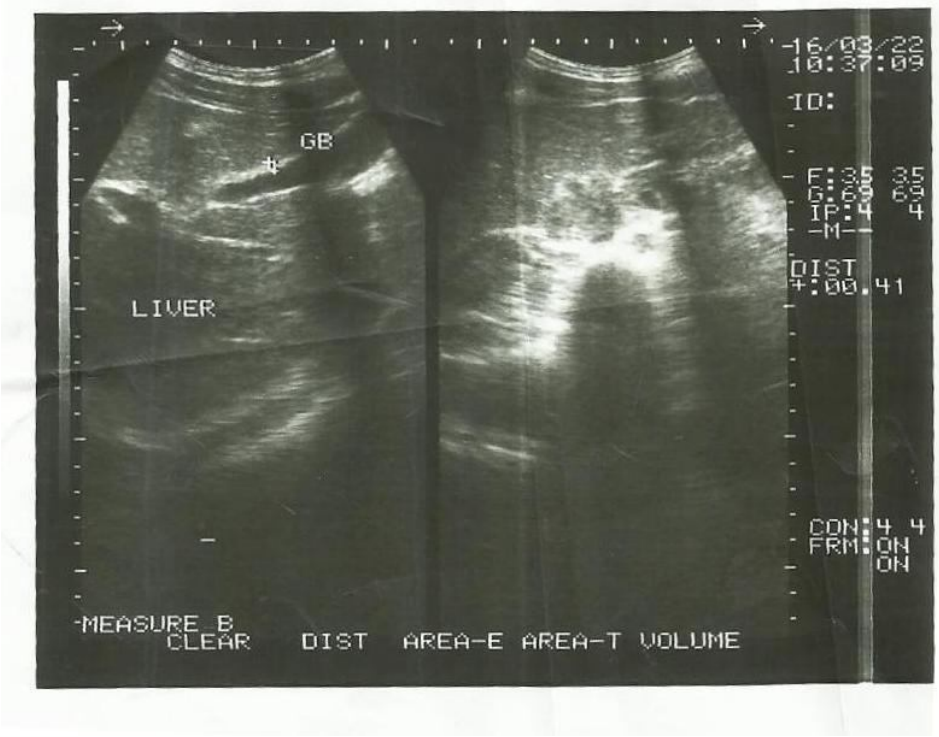

Image5 :Ultrasound of 28y old male,positive HCV showed normal liver finding with thickened GB wall(4mm).

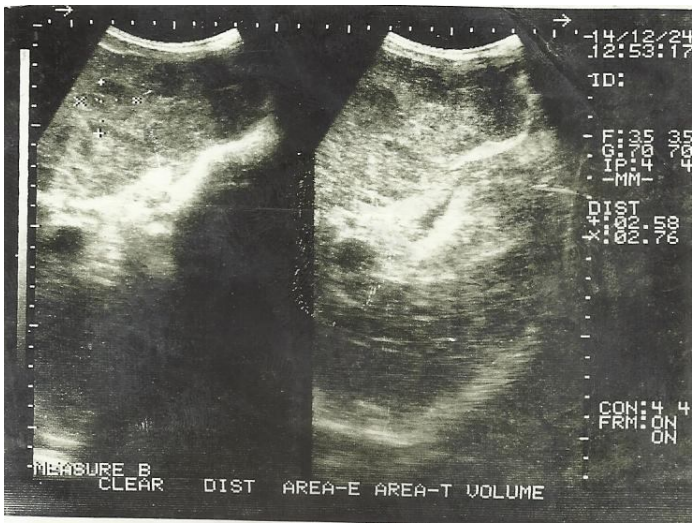

Image 6A: 30 y old male complain of Juandice , positive HBV US show enlarged liver with cirrhotic changes and contains large hetrogenious mass (HCC)

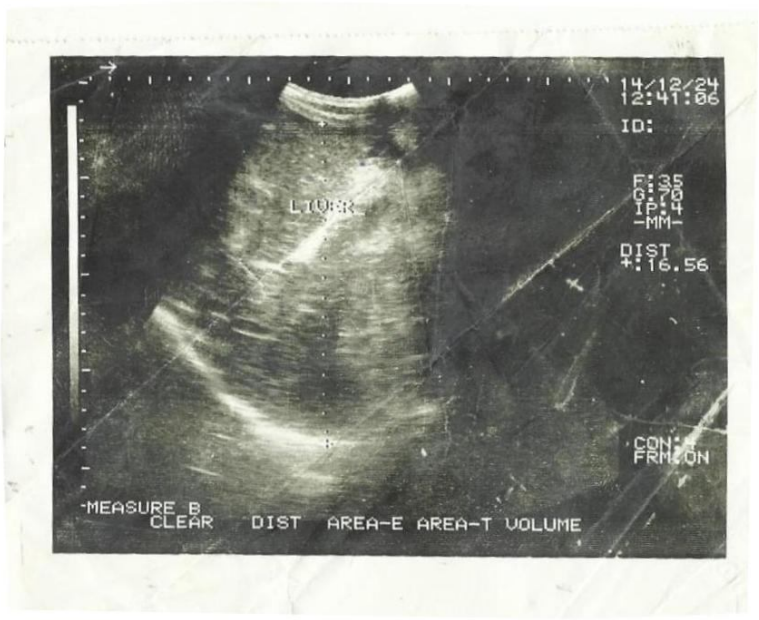

Image 6 B : Ultrasound of Same above patient showed thickened edeamatous GB wall (16mm)

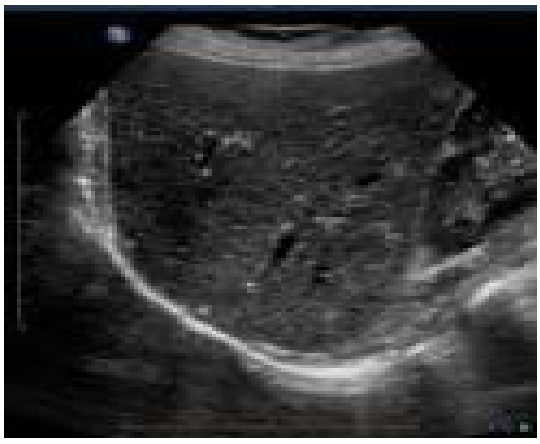

Image 7 :US of patient with positive HAV showed diffuse decreased liver echogenicity with prominent portal triads(starry night appearance)

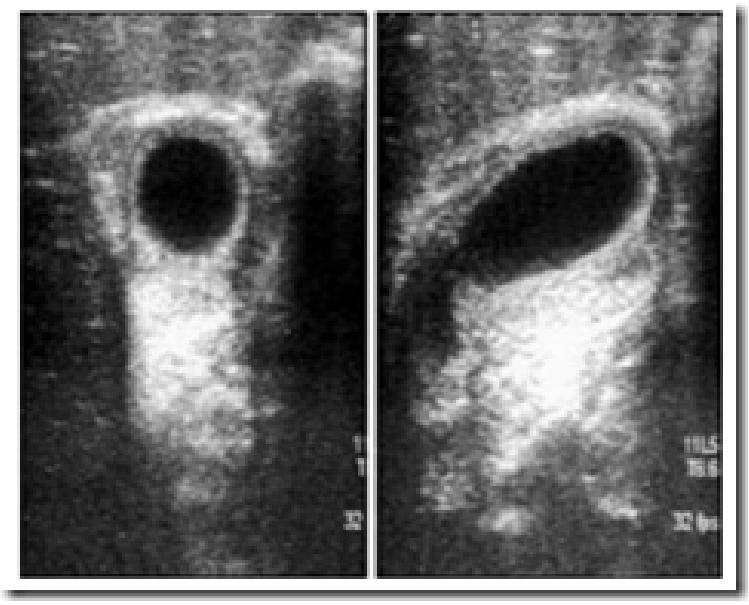

Image 8 US of patient with positive HCV showed odematous GB wall thickening

Characterization of different types of Hepatitis using U/S

Data collection table

No	Gender	Age	Hepatitis screening			Liver echogenicity			Liver Size (cm)	Gall Bladder Wall (cm)	Periportal			Findings		
			A	B	C	Hypo	Hypo	Normal			Fibrosis	Cuffing	Normal	Cirrhosis	Focal lesion	Ascites