Sudan University for Sciences and Technology
College of Graduate Studies

Assessment of Gallbladder Diseases in Diabetic Patients Using Ultrasonography

تقييم امراض الحويصلة الصفراوية لدي مرضي السكر باستخدام التصوير بالموجات فوق الصوتية

A thesis submitted for partial fulfillment for the requirement of M.Sc. Degree in Medical Diagnostic Ultrasound

By:

Mai Ali Basher

Supervisor:

Dr. Ahmed Mostafa Abukonna

May 2016

بسم الله الرحم الرحيم

قال تعالى: (ويسألونك عن الروح قل الروح من أمر ربى وما أوتيتم من العلم إلا قليلا)

صدق الله العظيم

الإسراء(85)

This thesis dedicated:

To my parents

To my sisters and brothers

To my friends

Acknowledgment

I would like to thank God for enabling me to write this thesis.

I would like to specially thank Dr. Ahmed Abukonna the supervisor of my thesis.

I am particularly gratefully to ultrasound department staff at Alhasahesa hospital.

Thanks also to everyone who helped me.

List of figures

List of Tables

List of abbreviations:

CM	Computed Tomography**.**
DM	Diabetes Mellitus**.**
GB	Gallbladder**.**
GBS	Gallbladder stone**.**
IIDM	Insulin Independent Diabetes Mellitus**.**
MRI	Magnetic Resonance Image.
NIIDM	Non Insulin Independent Diabetes Mellitus**.**
PV	Portal Vein
US	Ultrasound .

Abstract

People with diabetes are at greater risk of gallbladder diseases due to damage from diabetes to the involuntary nerves that control movement of bowel and gallbladder. Also people with diabetes are generally over weight, and obesity is linked to gallbladder diseases especially gallbladder stones.

This is a cross-sectional study aimed to assess the gallbladder diseases in diabetic patients. 75 diabetic patients were enrolled in the study (42 female and 33 male), their age ranging from 40 to 80 years; presented at Alhasahesa hospital. All patients were scanned using ultrasonography in order to assess gallbladder abnormalities.

The result of this study showed that out of 75 cases, there were 16 cases of Gall stone (21.3%), one was polyp (1.3%), one sludge (1.3%), 5 case presented with a chalculus cholecystitis (6.7%), and 52 cases were normal gallbladder (69.3%).

Diabetic patients had a significantly higher prevalence of gallbladder diseases. Female diabetic patients were significantly more affected than males and the prevalence significantly increased with age particularly in males. Gender, was the most significant risk factors for gallbladder diseases in diabetic patients. By contrast, duration of diabetes did not seem to influence the frequency of gallbladder Stone among diabetics.

الخلاصة:

الأشخاص الذين يعانون من مرض السكري هم أكثر عرضة لخطر أمراض المرارة بسبب تأثير مرض السكري على الأعصاب اللاإرادية التي تتحكم في حركة الأمعاء والمرارة. أيضا الأشخاص الذين يعانون من مرض السكري عادة ما يعانون من زيادة في الوزن، وترتبط السمنة بأمراض المرارة وخاصة حصاوي المرارة.

تهدف هذه الدراسة إلى تقييم أمراض المرارة لدي مرضى السكري. تم تسجيل 75 مريض سكري في هذه الدراسة (42 إناث و 33 ذكور)، وأعمارهم تتراوح بين 40-80 عاما. في مستشفى الحصاحيصا وتم اخضاعهم لفحص الموجات فوق الصوتية لتقييم تغيرات المرارة.

أظهرت نتائج هذه الدراسة أن من بين 75 حالة، كانت هناك 16 حالة من حصاوي المرارة (21.3٪)، (1) ورم (1.3٪)، 1 حمأة (1.3٪)، و 5 حالات التهاب المرارة (6.7٪)، و كانت 52 حالة طبيعية (69.3٪).

مرضى السكري الإناث بشكل ملحوظ أكثر تأثرا من الذكور وانتشار المرض مرتبط مع التقدم في السن. فترة الاصابة بمرض السكر لا يبدو أنها تؤثر في الاصابة بحصاوي المرارة.

Chapter one

1.1 Introduction:

The gallbladder is a pear-shaped sac that is adherent to the under surface of the right lobe of the liver attached to the common bile duct by the cystic duct .Bile which is important for the digestion of fat is storage in gallbladder, it is first produced by the liver and then secreted through the common bile duct, which leads to the small intestine (TRAVILL, 1977).

Diabetes Mellitus is a chronic disease and common endocrine disorder resulting from an inadequate action of insulin. It may also occur secondarily to generalize disease of the pancreas. It is characterized by abnormalities leading to complications.

People with diabetes are at greater risk of gallbladder diseases due to damage from diabetes to the involuntary nerves that control movement of bowel and gallbladder. Also people with diabetes are generally over weight, and obesity is linked to gallbladder diseases especially gallbladder stones (Alan et.al, 2000). Ultrasound is the best tool to detect the GB diseases, as it is safe, inexpensive, less time consuming and accurate.

Diabetes mellitus (DM) and gall bladder stones (GBS) are both common and costly diseases. In general, GBS are more frequent in females due to hormonal factors. Increasing age, overweight, family history of GBS and type 2 DM are all associated with an increased risk of gallstones (Jorgensen, 2005).

Several studies from across the world reported an increased prevalence of GBS in patients with DM (Hahm JS et.al, 1999). How diabetes predisposes to gallstones is not well understood. However, hypertriglyceridemia, autonomic neuropathy (leading to gallbladder hypomotility and biliary stasis) and hyperinsulinemia (Ruhl CE et.al, 2000) have been suggested as contributing factors to the increased risk of

GBS development in diabetics. An Italian study showed that the prevalence of gallstone disease is significantly higher in diabetic patients than in the general population. Another study from New Zeeland reported a GBS prevalence of 32.7% among diabetic patients as compared to 20.8% in controls. In this study, several gallbladder diseases have been highlighted in people with diabetes by using ultrasonography.

1.2 Problem of the study:

The diffusion of diabetes mellitus and asymptomatic of gallbladder diseases with many complications were neglected and cannot be considered. Early detection of gallbladder pathologies using ultrasound as reliable tool will aid in avoiding complications.

1.3 Objectives:

1.3.1 General objective

To evaluate the association between diabetes and gallbladder diseases.

1.3.2 Specific objective:

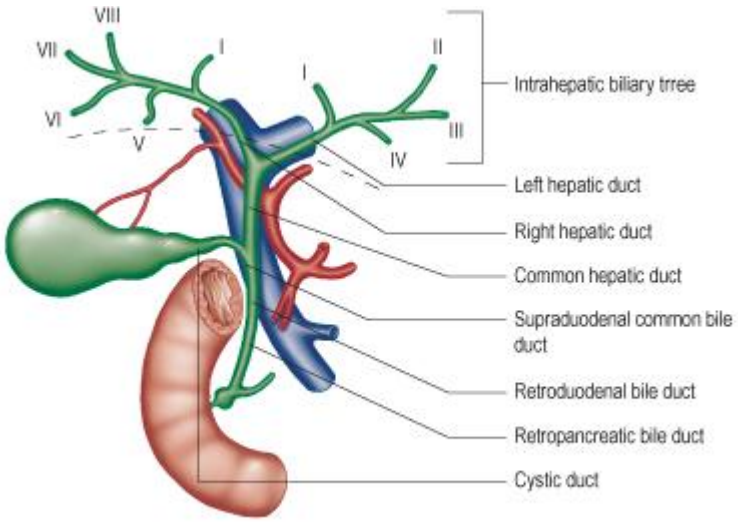
- To find whether there is a relation between the age of diabetic patients and gallbladder disease .
- To find the incidence of gallbladder pathologies in diabetic female compared with diabetic male.
- To correlate between the duration of diabetes and gallbladder diseases.

Chapter two

Literature review and theoretical background

2.1 Anatomy of Gallbladder and biliary tree:

The biliary tree consists of the system of vessels and ducts which collect and deliver bile from the liver parenchyma to the second part of the duodenum. It is conventionally divided into intrahepatic and extrahepatic biliary ducts. The intrahepatic ducts are formed from the larger bile canaliculi which come together to form segmental ducts. These fuse close to the porta hepatis into right and left hepatic ducts. The extrahepatic biliary tree consists of the right and left hepatic ducts, the common hepatic duct, the cystic duct and gallbladder and the common bile duct. (Gray's Anatomy.2008).



(Fig 2.1.1) Anatomy of GB and biliary trees

2.2 Gallbladder:

The gallbladder is a flask-shaped, blind-ending diverticulum attached to the common bile duct by the cystic duct. In life, and usually lies attached to the inferior surface of the right lobe of the liver by connective tissue. In the adult the gallbladder

is between 7 and 10 cm long with a capacity of up to 50 ml. It usually lies in a shallow fossa in the liver parenchyma covered by peritoneum continued from the liver surface. (Gray's Anatomy.2008).

The normally distended gallbladder (fasting state) has a thin wall (3 mm or less) and appears as a smooth echogenic line. In contrast, the contracted gallbladder (non fasting state) has a thicker wall which appears as a double walled hypoechoic structure (Burwin).

The gallbladder is described as having a fundus, body and neck. The neck lies at the medial end close to the porta hepatis, and almost always has a short peritoneal covered attachment to the liver (mesentery); this mesentery usually contains the cystic artery. The neck lies anterior to the second part of the duodenum.

The body of the gallbladder normally lies in contact with the liver surface. It lies anterior to the second part of the duodenum and the right end of the transverse colon. The fundus lies at the lateral end of the body and usually projects past the inferior border of the liver to a variable length. It often lies in contact with the anterior abdominal wall behind the ninth costal cartilage where the lateral edge of the right rectus abdominis crosses the costal margin. This is the location where enlargement of the gallbladder is best sought on clinical examination. The fundus commonly lies adjacent to the transverse colon. (Gray's Anatomy.2008).

The gallbladder varies in size and shape. The fundus may be elongated and highly mobile. Rarely the fundus of the gallbladder is folded back upon the body of the gallbladder, the so-called Phrygian cap. On ultrasound this may be wrongly interpreted as an apparent septum within an otherwise normal gallbladder. Rarely, the gallbladder may be bifid or completely duplicated, usually with a duplicated cystic duct.(Gray's Anatomy.2008).

The cystic artery, abranch of the right hepatic artery, supplies the GB. The cystic vein drains directly into the portal vein.

The lymph drains into acystic lymph node situated near the neck of the GB.

Sympathetic and parasympathetic vagal fibers form the celiac plexus. The GB contracts in response to the hormone cholecystokinin, which is produced by the mucus membrane of the duodenum on the arrival of fatty food from the stomach. (Richard S. Snell)

2.4 Cystic Duct:

The cystic duct is about 1.5in(3.8cm)long and connects the neck of the GB to the common hepatic duct to form the bile duct, it usually is what S-shaped and descend for avariable distance in right free margin of the lesser omentum. The mucus membrane of the cystic duct is raised to form aspiral fold that is continuous with asimilar fold in the neck of the GB. The fold is commonly known as "aspiral valve." The function of the spiral valve is to keep the lumen constantly open.(Richard S. Snell)

2.5 Physiology

Function of the biliary tree: Bile is important for fat digestion and absorption, Waste product removal from the blood. Bile salts help emulsify the large fat particles into minute particles that can be attacked by the lipase enzyme secreted in pancreatic juice. They also aid in the transport and absorption of the digested fat end products to and through the intestinal mucosal membrane.(Medical physiology).

Bile serves as a means for excretion of several important waste products from the blood, especially bilirubin, an end product of hemoglobin destruction, and excess cholesterol synthesize by the liver cells .(Medical physiology).

Bile is secreted in two stages by the liver:

The initial portion, which is secreted by liver hepatocytes, contains large amounts of bile acids, cholesterols, and other organic constituents. It is secreted into the minute bile canaliculi that lie between the hepatic cells.

A watery solution of sodium and bicarbonate ions is added to the bile as it flows through the bile ducts. This second secretion is stimulated by secrtin, causing increased quantities of bicarbonate ions that supplement pancreatic secretion for neutralization acid. (Medical physiology).

Bile is concentrated in the gallbladder. Active transport of sodium through the gallbladder epithelium is followed by secondary absorption of chloride ions, water, and most other soluble constituents. Cholecystokinin stimulates contraction of the gallbladder. Fatty foods that enter the duodenum cause cholecystokinin to be released from the local glands and causes rhythmical contractions of the GB and simultaneous relaxation of the sphincter of oddi, which guards the exiet of the common bile duct into the duodenum. When digestion is not taking place, the sphincter of odii remains closed and accumulates in the gall bladder. The gallbladder concentrates bile; store bile; selectively absorbs bile salts, keeping the acid; excretes cholesterol; and secretes mucus. To aid in these functions, the mucus membrane is thrown into permanent folds that unite with each other, giving the surface a honeycombed appearance.The columnar cells lining the surface have numerous micro villi on their free surface. Bile is delivered to the duodenum as the result of contraction and partial emptying of gallbladder. This mechanism is initiated by the entrance of fatty foods into the duodenum. The fat causes release of the hormone cholecystokinin from the mucus membrane of the duodenum; the hormone then enters the blood causing the gallbladder to contract. At the same, the smooth muscle around the distal end of the bile duct and the ampulla is relaxed,

thus allowing the passage of concentrated bile into the duodenum. The bile salts in the bile are important in emulsifying the fat in the intestine and in assisting with its digestion and absorption. (Medical physiology).

2.6 Pathology:

2.6.1 Diabetes Mellitus:

Diabetes mellitus (DM) is a multi system disease with both biochemical and structural consequence. It is a chronic disease carbohydrate, fat and protein metabolism, resulting from an inadequate action of hormone, insulin.

Two main types of primary diabetes mellitus are identified, mainly on clinical group; Type1diabetes (insulin dependent mellitus-IDDM, or juvenile – onset diabetes). Type2 diabetes (non – insulin dependent diabetes – NIDDM, or maturity – onset diabetes).(Alan Steven et.al, 1994).

Diabetes may also occur secondarily to generalize disease of the pancreas, e.g: chronic pancreatitis and haemochromatosis, or may be caused by the secretion of hormones which antagonize the effects of insulin, e.g.: in cushing's syndrome and acromegaly; such diabetes is called secondary diabetes mellitus.

Type2 diabetes: Is result of insulin resistance in peripheral tissues and it is four or five times more common than type 1 diabetes. Unlike type1 diabetes, where there is an absolute absence of insulin, in type2 diabetes the blood insulin levels are initially normal, or may even increase in early stages, before falling eventually to below normal. The defect in the type2 pattern is a combination of the effects of the relative deficiency of the insulin when compared to the need, and the phenomenon of the insulin resistance, in which the tissue are unable to respond to insulin. Insulin resistance is thought to be due to an impairment of the function of receptor for insulin on the surfaces of target cell, meaning that glucose dose not inters the

cell. Aportion called amylin is produce in the insulin – secreting cell of the pancreatic islets, this protein accumulates in excess around the pancreatic islet cells, producing an amorphous deposit of material with the characteristic of amyloid. It's role is not understood, but it may interfere with the subsequent secretion of insulin by the islet cells. (Alan Steven et.al, 1994).

Pathogenesis of type2 diabetes:

The precise pathogenesis in type2 diabetes are not known, although aetiology factors such as age, obesity and genetic predisposition are will recognized.

Diagnosis of diabetes millitus:

The diagnosis of diabetes millitus depend on finding hyperglcaemia. In general, a fasting venous blood level >7.8 mmol\1 or a random venous blood level > 11.1 mmol\1 is indicative of diabetes mellitus and impaired glucose tolerance in cases where fasting or random blood sugar levels are borderline. (Alan Steven et.al, 1994).

2.6.2 Diseases of the gallbladder:

2.6.3 Gall Stones:

Stones in the gallbladder and bile duct system (cholelithiasis) are the most common cause of diseases affecting the biliary tree. Stones form from the constituents of bile, the main components being variable proportions of cholesterol, calcium salts(phosphates, carbonates), and bilirubin(in the form of calcium bilirubinate).Although it is recognized that most stones have several constituents, two main types of stone have been defined according the major constituent: Cholesterol stone (80% of all stones) and pigment stones (20% of all stone). (Alan Steven et.al, 1994).

Cholesterol stones are predisposed by changing cholesterol solubility in bile:

Cholesterol stones occur in 20% of women and 8% of men, usually causing no

problem. They form when bile become super saturated with cholesterol, there being insufficient bile salt to keep the cholesterol in solution. In most cases the reasons for these changes are unclear.

The main risk factors asocial with cholesterol stone formation are:

Decrease bile acids in bile, caused by oestrogen or excessive loss from gut due to malabsorption in crohn's disease or cystic fibrosis.

Increase cholesterol in bile caused by obesity, female sex, increasing age. Cholesterol of the gallbladder occurs when the submucosa of the gallbladder is focally infiltrated by macrophages laden with cholesterol.This condition is frequently associated with development of cholesterol stones and is believed to be predisposed by the same conditions that cause decreased solubility of cholesterol in bile.Understanding of the pathogenesis of cholesterol stone formation has led to medical treatment of stones by oral therapy with bile salts dissolves stones. Pigment stones are predisposed by increased hepatic secretion of bilirubin. Several clinical situations are associated with the development of pigment stone, which are largely composed of calcium bilirubinate, with lesser amount of other calcium salt and mucoproteins. It is easy to understand why patients with abnormal red – cell breakdown, generating large amounts of conjugated bilirubin, develop pigments stones, but the association of pigment stones with cirrhosis, chronic biliary infection. Gallstones may be obstruct the biliary tract and predispose to development of carcinoma of the gallbladder. Over 70% of gallstone remains clinically silent. The main clinical complication of cholelithiasis arises from obstruction of the cystic duct or common bile duct by stone. (Alan Steven et.al, 1994).

The presence of stones in the biliary tract leads to muscle hypertrophy and thickening of the wall of the gallbladder (obstructive cholecytopathy). Stone

impacted in the cystic duct predisposed to inflammation of the gallbladder (cholecytitis), which may be acute or chronic, and those forming in the bile ducts (cholecholithiasis) predisposed to obstructive jaundice, cholangitis and acute pancreatitis. Stone in the gallbladder may cause dilated intrahepatic biliary tree (fig 2-2), and predisposed to the development of carcinoma of the gallbladder. (Alan Steven et.al, 1994).

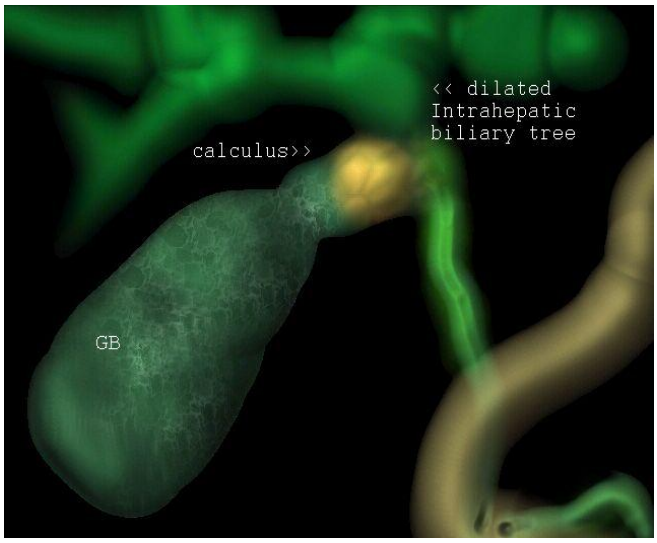


Figure (2.2) Gallbladder stone and dilated intra hepatic biliary tree

2.6.4 Acute calculus cholecystitis:

Acute inflammation of gallbladder (GB) secondary to calculus obstructing cystic duct. General Features: Impacted gallstone in cystic duct, gallbladder wall thickening, pericolecystic collection and positive sonographic Murphy sign, stone impacted in GB neck or cystic duct, distended GB (>5cm transverse diameter)

And more rounded in shape than normal "pear-shaped" configuration (Makela JT et al.2005).

.

2.6.4.1 Uncomplicated cholecystitis:

Gallstones impction in GB neck or cystic duct, Hazy delineation of GB wall, GB

wall lucency "halo sign", sonolucent middle layer(edema), positive sonographic Murphy sign, diffuse GB wall thickening(>4mm),striated wall thickening: several alternating irregular discontinuous lucenct and echogenic bands with GB wall, GB hydrops(distention with Ap diameter>5cm, sludge inside GB, clear pericholecystic fluid and crescent-shape(Makela JT et al.2005).

.

2.6.4.2 Complicated Cholecystitis:

Gallbladder perforation (pericholecystic abscess), gangrenous cholecystitis (asymmetric wall thickening, marked wall irregularities, intraluminal membrane), emphysematous cholecystitis (gas in GB wall -lumen), empyema of GB (highly reflective intraluminal echoes without shadowing, debris), gallstone ileus and bouveret syndrome(gallstone erodes into duodenum leading to duodenal obstruction).

Radiographic Findings: Calified stones in 15-20% of patients with cholecystitis

CT : GB wall thickening, pericholecystic fluid, GS inside GB neck or cystic duct, and asymmetric GB wall thickening.

Imaging recommendations:

Best imaging tool is US, in order to detect impacted or immobile calculus, the patient is best scanned in the left posterior oblique position; evaluate the region of the GB, its neck, cystic duct and adjacent soft tissues in multiple planes (Makela JT et al.2005).

2.6.5 Acute acalculus Cholecystitis:

Acute inflammation of GB not related to gallstone, usually secondary to ischemia.

General features: GB wall thickening without impacted GS and positive sonographic Murphy sign.

Ultrasound Finding: US features of acute a calculus cholecystitis are similar to

acute a cute calculus cholecystitis except for absence of impacted gallstone, GB wall thickening (>4mm-hypoechoic,layered appearances), GB distention (commonly filled with sludge, pericholecystic fluid collection and positive sonographic Murphy sign. (Pain and tenderness with transducer presser over the gallbladder).

Complication: Gangrenous cholecystitis(irregular GB wall thickening, intra luminal membrane and echogenic material due to sludge mucosa), GB perforation (collapsed GB; wall defect with adjacent hetrogenous hypoechoic fluid collection.

Color Doppler: Hyperemia within thickened-inflamed GB wall.

CT: Distended GB wall thickening

MRI: distended GB and high signal pericholecystic fat.(Barie PS et al.2003).

2.6.6 Chronic cholecystitis:

Thickening and fibrosis of GB wall due to chronic inflammation.

Ultrasonographic Findings: Diffuse GB wall thickening (Mean thickness ~5mm and smooth/irregular contour), Contracted GB, presence of gallstones in nearly all cases, absence of cholecystic inflammation.

Power Doppler: Lack of hyperemic changes within thickened GB wall.

Imaging Recommendations: Ultrasound is the initial and most sensitive imaging tool for diagnosis, ensure adequate fasting(>6 hours) prior to US examination to avoid false positive finding of thickened GB due to post-prandial status and examine patient in multiple planes to detect gallstone in a severely contracted GB.(Bortoff GA et al.2000).

2.6.7 Gallbladder cholesterol polyp:

Abnormal deposit of cholesterol ester producing a villus like structure covered with a single layer of epithelium and attached via a delicate stalk. Imaging Findings Multiple, small, non shadowing lesion attached to GB wall, located any

where to GB wall, most commonly in middle 1\3 of GB, usually 2_10mm in size. More than one half of all polypoidal gallbladder lesions are cholesterol polyps.

Polypoidal mass arising from GB wall, usually in the range of 2-10 mm in size, multiple lesion, medium to high level internal echoes, smooth in cotour, sometimes multi-lobulated outline, round or ovoid shape, broad-base with GB wall, does not cast posterior acoustic shadow, not mobile changing patients position, overlying GB wall is intact and normal, and no invasion of adjacent liver parenchyma or regional nodal metastases. Variation of U/S appearances: Large size, pedunculated and echogenic foci within larger lesions.

Power Doppler: A vascular or hypovascular on Doppler examination and larger lesion may have slight internal vasculaity.

CT: Small soft tissue density nodule on GBwall.

MRI: Small, round nodule in GB wall.

U/S:Protocol advice: Adequate fasting prior to U/S, scan in supine, decubitus and lateral positions to demonstrate immobility of GB polyp, and set depth of focal zone at level of GB mass maximize accuracy of mass characterization (Chattopadhyay D, et al.2005).

2.6.8 Thickened GB wall:

GB wall thickness>3mm.

Diffuse GB wall thickening(>3mm,especially over anterior wall), smooth contour, homogenous, heterogenous, hypoechoechoic thickening, diffuse hypoechoic region between two echogenic lines, and linear echogenic stiations within the hypoechoic area.

GB lumen obliterations in sever GB wall thickening, lack of invasion of adjacent structures in non neoplastic conditions.

Findings related to underlying causes:

Ascites in liver cirrhosis or hypo albuminaemia, change in hepatic parenchymal echogenicity in cirrhosis, hepatitis, gall stones, positive sonographic Murphy's sign in acute cholecystitis, liver invasion in malignancy.

Power Doppler:

A vascular if thickening due to systemic causes, hyperemic in acute choleycystitis.

CT: Homogeneous soft tissue thickening of GB.(Rubens DJ.2004).

2.6.9 Gallbladder Carcinoma with Diffuse Wall Infiltration:

Irregular wall thickening, tumor invasion of adjacent liver parenchyma, and Increased intra-tuoral vascularity.

General Features:Inflammatory conditions:Acute calculus/acalculus cholecystitis,chronic cholecystitis , AIDS-related cholangiopathy, acute hepatitis, perforated peptic ulcer, pancreatitis.

Systemic diseases: Congestive heart failure, renal failure, liver cirrhosis and hypoalbuminemia.

Neoplastic infiltration: Gallbladder carcinoma.(Rubens, et al.2004).

2.6.10 Porcelain Gallbladder:

) 2.6.10.1 Calcification of GB wall.

Ultrasound Finding: Degree and pattern of calcification determines the ultrasound appearance, thick diffuse GB wall calcification(echogenic curvilinear line in GB fossa and dense posterior acoustic shadowing) and segmental GB wall calcification.

Color Doppler: A vascular over-calcified GB wall.

Imaging Recommendations: US is the best imaging tool. Set focus at the level of GB to maximize depiction of high amplitude echoes and dense posterior acoustic shadowing, and pay attention to presence of associated GB soft tissue mass indicating presence of GB carcinoma.(Gore RM et al.2002).

2.6.11 Hyperplastic Cholecystosis:

Idiopathic non-neoplastic and non-inflammatory proliferative disorders resulting in GB wall thickening.

Adenomyomatosis: Mural GB wall thickening secondary to exaggeration of normal luminal epithelial folds in conjunction with smooth muscle proliferation.

Cholesterolosis: Deposition of foamy cholesterol-laden histiocytes in subepithelium of GB; numerous small accumulation or larger polypoid deposit(cholesterol polyp).(Secil M et al.2005).

Ultrasonographic Findings:

Cholesterolosis: Not related to serum cholesterol levels, multiple small GB polyps with no posterior acoustic shadowing or "comet-tail" artifact, usually ~5-10mm in size, well-defined, smooth margin and occasionally pedunculated, low to medium level of echoes.

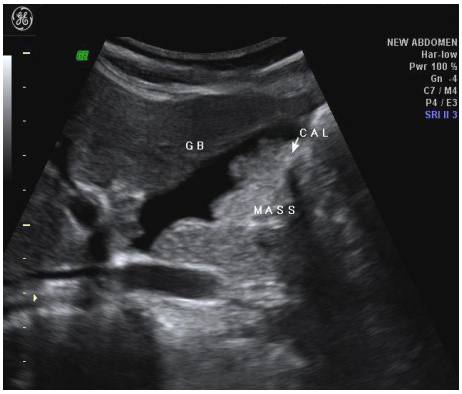
Adenomyomatosis is focal or diffuse GB wall thickening, tiny echogenic foci in GB wall producing "comet-tail" artifacts, presence of cystic spaces within GB wall, fundul adenomyoma and hourglass GB.

Usually a vascular GB wall thickening on CD and occasionally show increase color flow within thickened GB wall on color Doplor.

Protocol advice: Use high frequency transducer for best visualization of "comet-tail" artifacts and cystic spaces and absence of cystic spaces, echogenic foci, or presence of internal vascularity should prompt further investigation to rule out neoplasm. (Secil M et al.2005).

2.6.12 Gallbladder Carcinoma:

Malignant epithelial neoplasm arising from (GB) mucosa.



Fig(2-3) Ultrasonography of Gallbladder mass

Intraluminal moderately echogenic GB mass(>1cm), asymmetric GB wall thickening, destruction of GB wall, mass infiltrating GB fossa, gallstones, calcified GB wall, liver metastases and biliary diatation.

Color Doppler: Areas of increased vascularity within the mass.

Longitudinal and transverse ultrasound scan of GB fossa with gray scale and color Doppler and any polypoid mass of irregular shape within the GB lumen and every infiltrating lesion destroying GB wall is suspicious of GB carcinoma.(Enomoto T et al. 2003).

2.7 Biliary Ultrasound:

Patients are imaged in the supine position. Alongitudinal axis view of the GB the CBD present anterior to the PV. This approach to diagnose:

Gallstone(2-4) ,or sludge, or is acalculus cholecystitis in jaundiced patients, ductal dilatation, choledocholithiasis, features of acute cholecystitis (either calculus or not) such as sonographic Murphy sign in septic patients, GB wall thickening, pericholecystic fluid, and amechanical reason for jaundice.

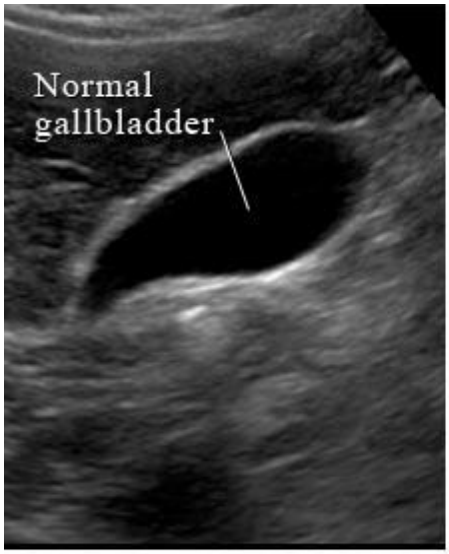


Figure 1

Figure 2

Fig (2 - 4) Ultrasonography of normal gallbladder-Fig (2.5) Ultrasonography of gallbladder stone

The sensitivity of ultrasound to establish the diagnosis has been questioned and it is often one of exclusion that is made after the GB has been percutaneously drained. There are features that are typically seen in patients with acalculus cholecystitis. The first is an enlarged GB, exceeding 90mm on longitudinal axis. Second the GB wall is thicker than 3mm.Next, sludge is invariable present in the lumen of the GB. Alternatively asonographic Murphs sign(pain in subcostal imaging) is rarely present.

Intra-or extra hepatic ductal dilation beyond 7mm is the sonographic hallmark or .biliary obstruction. Bile ducts are considered dilated if the same size or larger than the adjacent PV.

2.7.1Technique

The gallbladder should be examined in numerous patient positions: supine, left lateral decubitus, and the left posterior oblique position. In order to convincingly demonstrate stone mobility, scans may need to be performed in prone or erect

positions.

To show acoustic shadowing of calculi, it is essential to use the possible and to have the transducer focused in the region of the suspected calculi. The sound beam is directed through the most dependent portion of the gallbladder. In most supine patients this is the region of the gallbladder neck and cystic duct. In prone and erect positions the fundus is the most dependent region. Every study of the gallbladder should include an image demonstrating the gallbladder neck to prove or rule out the presence of a stone in this location.

Scanning with high-resolution high frequency curved linear or linear array transducers is mandatory in patients when gallstones are not detected. This minimizes missing tiny gallstones, especially in the fundus of superficial gallbladders.

The gallbladder should be examined in the fasting state to ensure optimal bile volume. A contracted, non fasted gallbladder can be difficult to visualize.

The standard measurement of GB wall thickness is made from the GB lumen to the liver parenchyma. This measurement includes the GB mucosa, smooth muscle of its wall, liver capsule, and any tissue between the liver and GB. The normal measurement is 3 mm or less.

Measurements are taken in the transverse rather than longitudinal plane to avoid any possibility of thickening due to measuring in an off-axis plane. The normal appearing wall is not routinely measured. (Burwin).

2.8 Previous Studies:

Agunloye, *et al*.(2012).From Nigeria Determined the prevalence of GS in both type 1and type 2 DM and elucidated the demographic and social factors associated with formation of GS in diabetic patients.400 diabetic patients aged between 15 and 82 years had abdominal ultrasound to diagnose or exclude the presence of GS.

The result a ppeare that GS was found in 70 (17.5%) of the 400 patients. Positive cases had a male to female ratio of 3:4 and 59 (51.92%) patients; smoking and alcohol intake were insignificantly implicated. Jaundice was recorded in 8 (11.4%) while abdominal pain was in 24 (34.3%) patients, and 52 (74.3%) patients of those with GSD had had diabetes for more than 4years.So GSD in DM is influenced significantly by age, and duration of the disease, while gender, social factors, and parity do not influence as strong associated factors.

Elmehdawi, et al, (2007). The study was to determine the frequency of GBS among Libyan diabetics in comparison to non diabetic outpatients and to evaluate the possible associated factors in this high risk group. Study was performed during 2007 at Benghazi Diabetes and endocrinology Center. The study involved 161 randomly selected type-2 diabetic patients under regular follow up at the center,, and 166 age and sex matched non-diabetic outpatients at the 7th of October teaching hospital. Real-time abdominal ultrasound was performed by two radiologists to examine the abdomen after an overnight fast. Results: About 40% of the diabetic cohort had gall bladder stones as compared to 17.5% of non-diabetic patients. Females were significantly more affected than males. Patients with gall bladder stones were significantly older and had a significantly higher body mass index than those without stone. So the prevalence of gallstones in Libyan diabetic patients is higher than the rates reported in other parts of the world. Libyan diabetic patients with gallstones tend to be older and more obese than those without gallstones. Duration of diabetes mellitus and type of treatment does not seem to influence the frequency of gall bladder stones among Libyan diabetics.

Bruce A. et.al (1996).Study was under taken to compare the prevalence of GS disease in308 diabetics and318 controls. There was a higher prevalence of (GSD) in diabetics (32.7%) compared to controls (20.8). Gender was taken into account,

the difference was only significant in females (diabetic 41.8% versus controls 23.1%).Analysis with type of diabetes revealed that subjects with non-insulin-dependent diabetes mellitus (NIDDM) had a higher prevalence of GSD than controls for both genders: males controls18.1%, NIDDM33.3%, IDDM15.6%. Females-controls 23.1%, NIDDM 48.6%, IDDM 36.3%. So in conclusion, there was a higher prevalence of GSD in diabetics compared to controls .However GSD is multifactorial and only in NIDDM females was diabetes an independent risk factor. The proportion of diabetes and controls with GSD who underwent cholecystectomy was equivalent.

STEVEN M et.al (1989).The study was to associate between non-insulin-dependent diabetes mellitus (NIDDM) and the prevalence of gallbladder disease remains controversial. The authors investigated this association in 1,250 men and 1,656 women from the San Antonio Heart Study (1984–1988) a population-based study of diabetes and cardiovascular disease. A total of 68% of the subjects were Mexican American, a population at high risk for both gallbladder disease and NIDDM. NIDDM was significantly associated with gallbladder disease in Mexican-American men and women and in non-Hispanic white women. Circumference, and ethnicity, using multiple logistic regressions, the odds of gallbladder disease in women was 1.6 times higher if NIDDM was present. Mexican-American women also had a significantly increased prevalence of gallbladder disease relative to non-Hispanic white women. In non diabetic women, fasting insulin was significantly related to prevalence of gallbladder disease. The authors conclude that women with diabetes have an increased prevalence of gallbladder disease relative to non diabetic women and that this association is not explained by the greater adiposity or unfavorable body fat distribution of the diabetic subjects.

CHAPTER THREE

Material and Method

3.1 Material:

3.1.1 Subjects: The data of this study collected 75 adult diabetic patients their ages ranging from 40 to 80 years . who came to Alhasaheasa hospital for follow up. Abdominal U/S was done for them.

3.1.2 Machine used

The machine used in this study were:

- SK-10 U/S machine, transabdominal curvilinear probe (3.5-5MH).
- Toshiba power vison6600(mobile 2004)(transabdominal curvilinear probe (3.5-5MH, and linear array transducers 7.5MH).

-WED-961(transabdominal curvilinear probe (3.5-5MH, and linear array transducers 7.5MH).

3.2 Method:

3.2.1 Technique used

The gallbladder be examined in patient positions: supine, and the left posterior oblique position. Scan with high-resolution high frequency curved linear array transducer and linear array transducer 7.5MH). Looking through the ribs, or subcostal view with patient rolled to left lateral decubitus, and rotate the probe to both longitudinal and short axis view.

3.2.2 data collection

The data were collected using a sheet for all patients in order to maintain consistency of information.

3-2.3 Design of the study: This cross-sectional based study.

3.2.4 Ethical consideration: permission of the patients at the area of the study was taken to do Abdominal U/S.

3-2.5 Study area and duration:

This study conducted in Alhasaheasa Teaching Hospital , Sudan –AlGazeara during the period from Desember 2015 to march 2016.

CHAPTER FOUR

RESULTS

Descriptive Statistics

Table 4-1 the mean and standard deviation of the variables used in the study

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age	75	40	80	61.53	10.108
Diabetes Duration	75	2	40	9.68	7.655

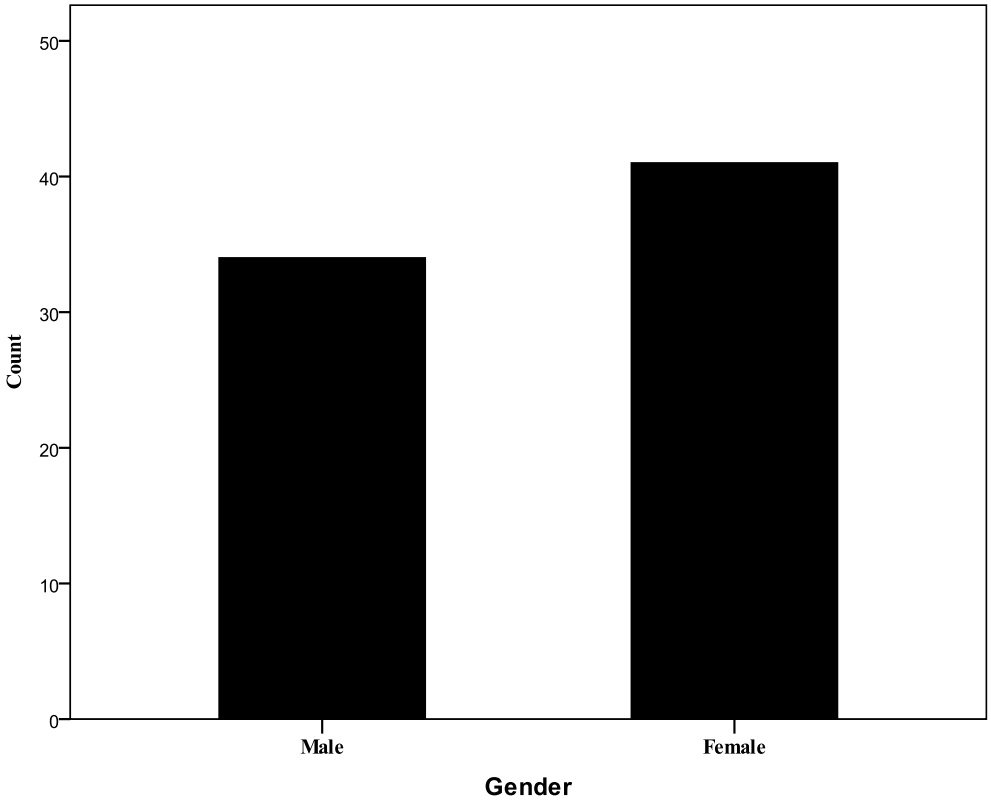


Fig (4-6) Gender distribution

Table 4-2 Frequencies and percentages of U/S findings

	Frequency	Percent
Gall stone	16	21.3
Polyps	1	1.3
Sludge	1	1.3
Cholecystitis	5	6.7
Normal	52	69.3
Total	75	100.0

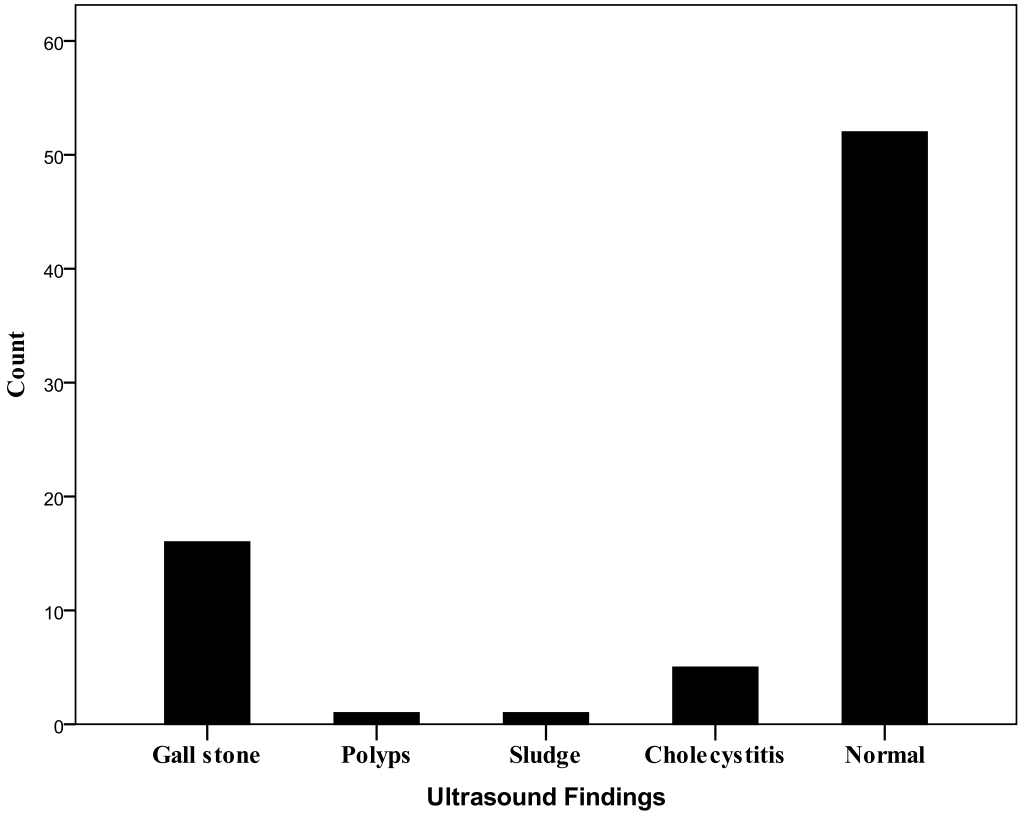


Fig (4-7) Ultrasound findings distribution

Table 4-3 Frequencies and percentages of **Diabetes Duration**

Diabetes Duration	Frequency	Percent	Valid Percent	Cumulative Percent
1 - 5	26	34.7	34.7	34.7
5 - 10	22	29.3	29.3	64.0
10 -15	11	14.7	14.7	78.7
15 -20	12	16.0	16.0	94.7
20 -25	1	1.3	1.3	96.0
25 -30	1	1.3	1.3	97.3
35 -40	2	2.7	2.7	100.0
Total	75	100.0	100.0	

Table 4-4 Diabetes Duration * Ultrasound Findings Crosstabulation

Diabetes Duration	Ultrasound Findings					Total
	Gall stone	Polyps	Sludge	Cholecystitis	Normal	
1 - 5	4	0	0	2	21	27
5 - 10	4	1	0	0	17	22
10 -15	2	0	1	2	7	12
15 -20	5	0	0	1	6	12
20 -25	0	0	0	0	1	1
25 -30	1	0	0	0	0	1
30-35	0	0	0	0	0	0
35 -40	1	0	0	0	1	2
Total	16	1	1	5	52	75

Table 4-5 Frequencies and percentages of **ages**

	Age	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	40-50	14	18.7	18.7	18.7
	51-60	23	30.7	30.7	49.3
	61-70	27	36.0	36.0	85.3
	71-80	11	14.7	14.7	100.0
	Total	75	100.0	100.0	

Table(4-6):The correlation between age and U/S finding

	FINDING					Total
	GS	Polyps	Sludge	Cholecystitis	NO U/S Findings	
40-50	4	0	0	1	8	13
51-60	2	0	0	1	19	22
61-70	8	0	1	1	19	29
71-80	2	1	0	2	6	11
Total	16	1	1	5	52	75

Table(4-7) The correlation between gender and U/S findings

Count

		GENDER			Total
		MALE	FEMALE		
FINDING	GS	4	12	0	16
	Polyps	1	0	0	1
	Sludge	0	1	0	1
	Cholecystitis	0	5	0	5
	NO U/S F	28	24	0	52
		0	0	78	78
Total		33	42	78	153

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1 Discussion:

This is a cross-sectional study aimed to assess the Gallbladder Diseases in diabetic patients. 75 diabetic patients were enrolled in the study (42 female and 33 male), their age ranging from 40 to 80 years; presented at Alhasahesa hospital.

The result of this study showed that out of 75 cases, there were 16 cases of Gall stone (21.3%), one was polyp (1.3%), one sludge (1.3%), 5 case presented with cholecystitis (6.7%), and 52 cases were normal (69.3%). This might reflect a higher risk of GBS among diabetic in general as a result of other contributing risk factors for GBD, such as genetic predisposition, obesity, multiparity and dietary habits.

Age also is a well recognized risk factor for the gallstones in diabetics. The prevalence of GBD in diabetics older than 40 years was higher than that in younger subjects. This result agreed with the study of (Liu et.al, 2004).

The correlation between duration of diabetes and U/S finding were investigated it showed that the duration of diabetes does not affect the incidence of GBD. This result was in line with the study of Libyan population (Elmehdawi et.al, 2008).

The findings indicate that diabetic patients are at increased risk of GBD, the GS is the most common disease that affects the GB. The occurrence of GBD in type two diabetic patients' influences by age, the prevalence of GS was higher in woman than men.

Conclusions

Diabetic patients had a significantly higher prevalence of GBD. Female diabetic patients were significantly more affected than males and the prevalence significantly increased with age particularly in males. Gender, was the most significant risk factors for GBD in diabetic patients. By contrast, duration of DM did not seem to influence the frequency of GB Stone among type 2 diabetics. Multiple GBS were the most common kind of GBS in diabetics.

Recommendations

The incidence of GSD in DM in this study was about 21.35 %, so U/S must be done routinely for diabetic patients.

Diabetic patients who have had the disease for long time also also should have routine U/S examination.

Proper abdominal U/S scan for diabetic patients to avoid any complications.

Proper U/S equipments should be available in all regions of Sudan to avoid any misdiagnosis.

Future studies must be done to look for the relation between stone diseases and the risk of developing type two DM.

This study can be extended and use large sample size to detect the prevalence of GSD in diabetic patients relative to controls.

REFERENCES

CHIANCONE, F. M. 2004. [Foods and drinks in a 19th century human physiology textbook]. Med Secoli, 16, 21-30.

Hahm JS, Park JY, Park KG. Gallbladder motility in diabetes mellitus using real time ultrasonography. Am J Gastroenterology 1996; 91:2391.

HU, Y. R., PAN, J. H., TONG, X. C., LI, K. Q., CHEN, S. R. & HUANG, Y. 2015. Efficacy and safety of B-mode ultrasound-guided percutaneous transhepatic gallbladder drainage combined with laparoscopic cholecystectomy for acute cholecystitis in elderly and high-risk patients. BMC Gastroenterology, 15, 81.

IBUKURO, K., FUKUDA, H., TOBE, K., AKITA, K. & TAKEGUCHI, T. 2016. The vascular anatomy of the ligaments of the liver: Gross anatomy, Imaging, and Clinical applications. Br J Radiol, 20150925.

Jorgensen T. Epidemiology and gallstones Ugeskr Laeger. 2005; 167(24):2610-3.

Liu CM, Tung TH, Liu JH, Lee WL, Chou P. A community-based epidemiologic study on gallstone disease among type 2 diabetics in Kinmen, Taiwan. Dig Dis. 2004; 22(1):87-91.

RUBENS, D. J. 2004. Hepatobiliary imaging and its pitfalls. Radiol Clin North Am, 42, 257-78

Ruhl CE, Everhart JE. Association of diabetes, serum insulin, and C-peptide with gallbladder disease. Hepatology 2000; 31:299.

TRAVILL, A. A. 1977. The anatomical basis of clinical practice: an anatomy learning programme. Med Edu, 11, 377-9.

YILDIZ, I., KOCA, Y. S. & BARUT, I. 2015. Overlap of Acute Cholecystitis with Gallstones and Squamous Cell Carcinoma of the Gallbladder in an Elderly Patient. Case Rep Surg, 2015, 767196.