

**PREVALENCE AND RISK FACTORS OF SYMPTOMATIC
GALLBLADDER STONE DISEASE USING ULTRASONOGRAPHY**

ERIC SAKA BOATENG

(10070339)

**THIS DISSERTATION IS SUBMITTED TO THE UNIVERSITY OF
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FOR THE AWARD OF MSc MEDICAL ULTRASONOGRAPHY DEGREE**

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DECLARATION

I, **ERIC SAKA BOATENG** do hereby declare that this thesis which is being submitted in fulfillment of the requirements for the degree of MSc Medical Ultrasonography is the result of my own research performed under supervision, and that except where otherwise other sources are acknowledged and duly referenced, this work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree

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Signed

Date.....

(Candidate ID.10070339)

Signed

Date.....

DR. VINCENT K. HEWLETT

Signed

Date.....

MR. LAWRENCE ARTHUR

Signed

Date.....

DR. S.Y. OPOKU (Head of Department)

DEDICATION

The work is dedicated to God who granted me knowledge, strength, understanding and wisdom to do this work for purposes of preserving the world till He who died and rose on the third day will manifest to receive His own. Amen.

Consequently dedication of this work is extended to my lovely wife Mrs. Deborah Nakour Saka and our three children Desmond Saka Boateng, Abigail Agyeiwaa Saka and Nyhira Yeboah Saka for their prayers and encouragement.

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LIST OF ABBREVIATIONS

AC	Acute Cholecystitis
BMI	Body Mass Index
CBD	Common Bile Duct
CI	Confidence Interval
ERCP	Endoscopic retrograde cholangiopancreaticography
ESWL	Extracorporeal Shockwave Lithotripsy
GBD	Gallbladder disease
GBS	Gallbladder stones
GST	Gallstones
HDL	High Density Lipoprotein
HMGLOA	Hydroxylmethylglutaryl Coenzyme A
KBTH	Korle-Bu Teaching Hospital
LC	Laparoscopic cholecystectomy
LDL	Low Density Lipoprotein
MC	Minilaparotomy cholecystectomy
MPC	Mamprobi Polyclinic
MRCP	Magnetic resonance cholangiopancreaticography
NSAID	Non-Steroidal Anti-inflammatory Drug
OC	Open cholecystectomy
OR	Odds Ratio
UPC	Ussher Polyclinic
USG	Ultrasonography

ABSTRACT

Background: Diseases of the gallbladder are common and its management is costly. The best epidemiological screening method to accurately determine point prevalence of gallstones disease is ultrasonography. Symptomatic gallstones present with characteristic right upper quadrant discomfort or pain (biliary colic). Many risk factors for cholesterol gallstones formation are not modifiable such as ethnic background, increasing age, female gender and family history or genetics. Conversely, the modifiable risks for cholesterol gallstones are obesity, rapid weight loss and a sedentary lifestyle. The rising epidemic of obesity and the metabolic syndrome predicts an escalation of cholesterol gallstones frequency. Worldwide risk factors for biliary sludge include pregnancy, drugs like ceftiaxone, octreotide and thiazide diuretics, and total parenteral nutrition or fasting. Diseases like cirrhosis, chronic hemolysis and ileal Crohn's disease have been identified worldwide as risk for black pigment stones. The risk factors associated with gallstones in the Ghanaian context is however yet to be determined.

Aim: The aim of this research study was to determine the prevalence and risk factors of symptomatic gallstones among Ghanaian patients in three hospitals in Accra.

Methods: Using a quantitative cross sectional method, 100 patients aged more than 20 years were enrolled by convenient sampling method in April 2014. They answered questionnaire pertaining to symptoms of gallstones, diet and environmental factors. Subsequently ultrasonography was performed in all the 100 participants with right upper quadrant abdominal pains using Toshiba Aplio 300 ultrasound scanner with a curvilinear transducer of frequency 5.0 MHz, 2005 make. The data was analyzed using SPSS version 13.

Results: Ultrasonography revealed a 42% prevalence of gallstones at the selected hospitals. Chi-square test revealed a significantly increased risk of gallstones in females aged between 20-30years, 60-70years with multiparity status and a clinical history of right upper quadrant abdominal pains. An increased risk was revealed in diabetic males who drank unpurified water.

Conclusion: A strong association was discovered between high cholesterol diet intake and gallstones disease. The study further revealed high prevalence of gallstones in females (47.2%) than males (28.6%). This finding is agreeable with most published literature which indicated female: male ratio of almost 2:1.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

The gallbladder is a small organ located on the right side of the abdomen, just below the liver. The gallbladder's main function is to store bile (made by the liver) and secrete it into the small intestine to help digestion. Bile is made of water, cholesterol, fats, bile salts (natural detergents that break up fat), and a pigment called bilirubin. Gallstones are crystal-like masses that typically form in the gallbladder if the bile contains too much cholesterol, bile salts, or bilirubin. Gallstones vary in size and could be as large as a golf ball and may develop any number and size of stones (Schirmer *et al.*, 2005). They are more common in women and older persons, as well as overweight persons (Shaffer, 2006). In the United States, 20% of people over the age of 65 have gallstones, but most never experience symptoms. However, complications from gallstones can be serious if symptomatic stones are left untreated (Friedman, 1993). Gallstones remain a serious health concern affecting millions throughout the world (Kern, 1983). Its prevalence is about 25% in industrialized societies but are uncommon in underdeveloped and developing societies (Diehl *et al.*, 1995)

It is reported in the literature of increasing medical understanding of how gallstones develop. In particular, it is believed that gallstones may be caused by a combination of factors including heredity, obesity, and the ability of the gallbladder to contract (motility). Gallstones are categorized into *cholesterol stones* that are mostly hardened cholesterol and account for approximately 80% of the calculi, and *pigment stones* made of bilirubin that account for the

remainder of 20%. Pigment stones are further categorized into black and brown pigment stones. Cholesterol gallstones form when there's too much cholesterol in the bile and not enough bile salts. Problems with the gallbladder's motility may cause the bile to become too concentrated and lead to stone formation. The cause of pigment stones is uncertain. They tend to develop in people with pre-existing conditions such as cirrhosis, biliary tract infections, and hereditary blood disorders such as sickle cell anaemia (Ali & Siddiqui, 2013).

Diseases of the gallbladder commonly manifest as gallstones and gallbladder cancer. Several epidemiology studies have been directed to investigate gallstone prevalence. However studies employing necropsy surveys or healthcare databases carry biases by their implicit nature which is either in postmortem or requiring biliary symptoms/complications, respectively (Kratzer *et al.*, 1999). Another potential measure of disease burden, indicated as the frequency of cholecystectomy, is a limited marker for the prevalence of gallstones, as the perceived threshold for surgery and patient access to care differ greatly (Pederson & Hoem, 2002). Some epidemiological studies have been confounded by inadequate sample size or selection bias. Small sample sizes are open to a beta-II type statistical error: a failure to accurately identify a true difference (i.e., a false negative result) and selection biases may lead to spurious differences (i.e., a false positive result). More reliable epidemiological studies now use transabdominal ultrasound to screen robust numbers in defined asymptomatic populations. Ultrasonography, a non-invasive and safe imaging technique can accurately detect the point prevalence of gallstones in a defined symptomatic population as well as quantify the frequency of gallstone disease (Kratzer *et al.*, 1999).

People with calculi in their gallbladder, kidney or urinary tract may experience intractable pains, however calculi in the kidney or urinary tract can be flushed out with medicines and taking copious amount of water which is not so with the gallbladder except by cholecystectomy. Gallstones formation occurs because certain substances in bile are present in concentrations that approach the limits of their solubility. When bile is concentrated in the gallbladder, it can become supersaturated with these substances, which then precipitate from solution as microscopic crystals. The crystals are trapped in gallbladder mucous, producing gallbladder sludge. Overtime, the crystals grow, aggregate and fuse to form macroscopic stones. Occlusion of the ducts by sludge and stones produces the complications of gallstone disease (Lawrence, 2006). Presence of stones in the gallbladder is referred to as cholelithiasis.

Cholelithiasis, a condition that results in the migration of gallstones into the ducts of the biliary tract, and sometimes stones from mineral accretions and rocklike clumps of cholesterol or other digestion substances form within the gallbladder and are collectively known as gallstones. The constitution and chemical composition of the bile content in the gallbladder determines to a large extent the chances of the formation of the gallstones (Shaffer, 2006). They can range in size from miniscule sizes like the head of a pin or grow as big as a golf ball.

A diet rich in sugars and fats as well as one having low-fiber content, is the most likely contributing factor to the formation of gallstones. The presence of gallstones in the gallbladder may lead to acute cholecystitis, an inflammatory condition characterized by retention of bile in the gallbladder and often secondary infection by intestinal microorganism, predominantly *Escherichia coli* and bactericides species, obstruction of the flow by a stone at this critical point may lead to abdominal pain and jaundice (Erben *et al.*, 2011). Stagnant bile above an

obstruction bile duct stone after becoming infected and bacteria can spread rapidly back up the ductal system into the liver to produce a life threatening infection called ascending cholangitis. Gallstones in the gallbladder may also cause progressive fibrosis and loss of function of the gallbladder a condition known as chronic cholecystitis. In particular, chronic cholecystitis predisposes to gallbladder cancer. In a survey from government hospital in India, out of 1065 data of stone cases consisting of gallstones, urinary stones, renal stones collected in the three consecutive years, i.e., 2008 -2011, gallstones were found in 716 cases or 67.2% prevalent. Geographically, gallstones occur commonly in the western hemisphere (Kratzer *et al.*, 1998) and are mostly asymptomatic.

Generally, gallstone diseases contribute substantially to health care costs, and its complications are sometimes life threatening. Shafer (2005) reported that more than 700,000 cholecystectomies are performed each year in the U.S. Hospitalization due to gallstone disease and its resulting complications costs more than five billion dollar, each year in the US only. The prevalence of the disease differs between countries, ethnic groups, age and gender.

It is well documented that other mechanisms also influence the cholecystectomy rates since there is a weak correlation to prevalence. Other possible explanations are differences in health care organization, non-operative options and surgeons' attitude towards indications for surgery, especially regarding patients with mild or moderate pain (Pederson *et al.*, 2002). Cholecystectomy rates in Scandinavia are in the range of 0.7-1.4/1000 inhabitants per year (Mjalaw *et al.*, 1998).

In Sweden, approximately 10 000 cholecystectomies are performed each year, making it one of the most common surgical procedures. According to Ahlberg *et al.*, (1978), rates as high as 4/1000 inhabitants/year were reported in the past. After the introduction of laparoscopic cholecystectomy (LC) and day-care surgery in the late 1980s several studies revealed an increase in cholecystectomy rates of approximately 20%. As a consequence, even small changes in indications for cholecystectomy have a major impact on health care costs (Escarse *et al.*, 1915). Since the introduction of LC, many studies have discussed and high-lighted the importance of adequate surgical technique in order to improve the outcome of the operation and timing of surgery. Comparisons to open cholecystectomy, with or without minimal incision, have also been high-lighted (Harjuj *et al.*, 2000).

Most patients with symptomatic gallstone disease benefit from cholecystectomy (Peterli *et al.*, 2000). However, pain persists in a considerable number of cases and it is therefore important to identify such patients in order to avoid the so called post cholecystectomy syndrome. Moreover, complications resulting from gallstone disease, such as gallstone related pancreatitis, cholecystitis, jaundice and/or cholangitis due to obstruction of the common bile duct (CBD) contribute substantially to morbidity and mortality, as well as health care costs. Identifying those at risk of developing such complications is therefore of critical importance

The incidence of gallstones has a specific geographic and ethnic variation (Randi *et al.*, 2006). The highest incidence rates of gallbladder cancer in the world are 21.5/100 000 in females in India, 13.8/100 000 in Pakistan and 12.9 /100 000 in Quito (Randi *et al.*, 2006). In a review of worldwide incidence, the female-to-male ratio was reported between 2 and 3 (Randi *et al.*, 2006). Gallstones is said to play a major role (Zatoski *et al.*, 1997) in the causation of gallbladder

cancer. Other risk factors are obesity, multiparity and chronic infections (Randi *et al*, 2006). Gallstones are twice as high in women as in men and are the leading cause of digestive cancer in women in northern Indian cities (Dhir & Mohandas, 1999).

Gallstone disease remains one of the most common medical problems leading to surgical intervention. Cholelithiasis is the presence of one or more gallstones (calculi) in the gallbladder. In developed countries, about 10% of adults and 20% of people aged > 65years have gallstones which generally tend to be asymptomatic. The most common symptom is biliary colic. Though it does not cause dyspepsia or fatty food intolerance, it however presents more serious complications including cholecystitis, biliary tract obstruction (by stones in the bile ducts (choledocholithiasis) sometimes with infection (cholangitis) and gallstone pancreatitis.

Diagnosis is usually by ultrasonography. However, if cholelithiasis causes symptoms or complications, cholecystectomy is necessary. A study of the natural history of cholelithiasis demonstrates that approximately 35% of patients initially diagnosed with having, but not treated for gallstones, later developed complications or recurrent symptoms leading to cholecystectomy (Schimer *et al.*, 2005). Risk factors for gallstones include female gender, obesity, increased age, American Indian ethnicity, a western diet, rapid weight loss, and a family history. The increasing detection of symptomatic gallstones leads to difficult decisions for surgeons and patients regarding surgical or expectant management of the stones. Gallstones may present as biliary pain, acute cholecystitis, biliary obstruction or pancreatitis, but it is unclear who develops symptoms and what the commonest initial symptoms are. Studies of the natural history of silent gallstones suggest that a large majority of patients with such stones will remain asymptomatic. (Attili *et al.*, 1995). However, diabetics are at increased risk as are patients whose

stones are detected initially at laparotomy. Incidental cholecystectomy is usually safe, and preoperative detection by ultrasonic screening is an advantage in planning the operation. Prophylactic cholecystectomy is not indicated to prevent gallbladder carcinoma (except in cases of porcelain gallbladder) and there is conflicting evidence about whether cholecystectomy predisposes to colorectal carcinoma.

1.2 PROBLEM STATEMENT

It has been observed that patients are increasingly reporting to radiology departments for abdominal ultrasound and most of their clinical histories indicate right flank pain. Even though this pain could result from several pathologies associated with the liver, gallbladder, right kidney, right ureter and ascending colon, the organ which is mostly found to be the cause is the gallbladder. Evidence from the literature (Caroli-Bosc *et al.*, 2000) has shown that cholelithiasis is a major cause of right flank pains which eventually ends up in cholecystectomies.

Rather unexpectedly, the prevalence of gallstones in Ghana is unknown. According to the Ghana Statistical Board (2013), there has been an increasing trend of cholecystectomies performed at the major teaching hospitals in Ghana between 2000 and 2012. The major cause of these increasing surgical intervention is however unclear and this might be a contributor to the increasing health problems in Ghana. Additionally, several risk factors like gender, age, ethnicity, diet, and life-style have been identified as contributing factors to gallstones around the world. The risk factors associated with gallstones in the Ghanaian context is however yet to be determined. Until these risk factors as well as the prevalence of gallstones are determined, the general public may likely be at the verge of falling victims to this health problem.

1.3 SIGNIFICANCE OF THE STUDY

Gallstones, amongst other numerous causes, stands as the highest recognized cause of cholecystectomy and constitutes a significant health problem (gallbladder diseases) in some countries, affecting 10% to 15% of the adult population (Schirmer, Winters & Edlich, 2005). In Ghana, a study like this is necessary to ascertain whether or not gallstones form part of the increasing number of health problems witnessed in the country currently. An investigation and identification of the risk factors associated with GB stones would further inform our policy makers in the health sector to either maintain or amend existing health policies and create awareness for Ghanaians to adopt healthy eating habits and lifestyle that will prevent gallstone formation.

1.4 AIM

The aim of the study was to determine the prevalence and risk factors of symptomatic gallstones among Ghanaian patients in three hospitals in Accra.

1.5 OBJECTIVES

The specific objectives of the study were:

- 1) To identify the prevalence of symptomatic gallstones amongst Ghanaians in Accra
- 2) To identify the risk factors associated with symptomatic gallstones amongst Ghanaians.
- 3) To determine the most common predisposing factor to symptomatic gallstones formation in Ghana

CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION

The review of this study was reported in several sections. First, the prevalence of gallbladder diseases from other studies was reviewed. Also, reviews of risk factors of gallstones were discussed. Further the identification of gallbladder stone disease by the use of ultrasound as been studied was reviewed.

2.1.1 ANATOMY OF THE GALLBLADDER

The gallbladder is located under the surface of the liver, bound by vessels, connective tissue, and lymphatics. It has four regions: the fundus, body, infundibulum, and the neck. The gallbladder terminates in the cystic duct and then enters the extra hepatic biliary tree. The fundus is the round, blind edge of the organ. It is composed of fibrotic tissue and projects just beyond the right lobe of the liver. The fundus leads to the body of the gallbladder, the largest part. The superior surface of the body is attached to the visceral surface of the liver, unless a mesentery is present.

This close relationship allows for the direct spread of inflammation, infection, or neoplasia into the liver parenchyma. The infundibulum is the tapering area of the gallbladder between the body and neck. This portion and the free surface of the body of the gallbladder lies close to the first and second portions of the duodenum, and in close proximity to the hepatic flexure and right third of the transverse colon. The infundibulum is attached to the right transverse colon surface of the second part of the duodenum by the cholecystoduodenal ligament. The neck of the

gallbladder is 5–7 mm in diameter and often forms an S-shaped curve. It is superior and to the left, narrowing into a constriction at the junction with the cystic duct

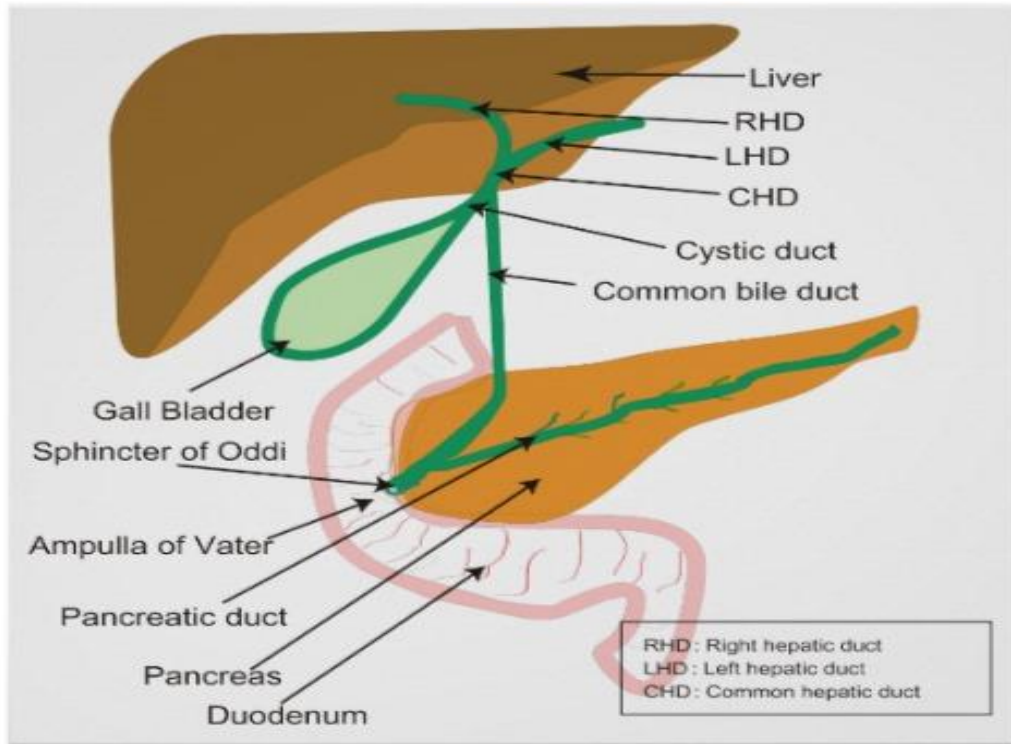


Fig.2.1: Anatomy of the biliary system. Source: Zazzle Art, San Jose CA

The right and left hepatic ducts unite in an extra hepatic position in most cases. The length of the hepatic lobar duct varies from 0.5–1.5 cm. usually a short extra hepatic right lobar duct joins a longer left duct at the base of the right branch of the portal vein at differing angles. The common hepatic duct is formed by the merger of right and left hepatic ducts. In a minority of cases, a right segmental duct joining a left hepatic duct forms a third duct. There may be numerous variations in the left ductal system. Twenty percent of the population has accessory hepatic ducts. In these individuals, the aberrant duct joins the common hepatic duct at various locations along its course.

In rare instances this aberrant duct may join the cystic duct or a duct in the opposite lobe. Usually, however, these aberrant ducts are on the right side. The hepatocyte-cholangiocyte level is the beginning of the biliary drainage system and where portions of the hepatocyte membrane form the canaliculi (small channels). Bile drains from this level into intrahepatic ducts.

The canaliculi and proximal ductal system converge in the canal of Hering. Smaller ducts combine to form the segmental bile duct. Segmental ducts within the liver form the right and left hepatic ducts. Union of ducts from hepatic segments II, III, and IV form the left lobar duct. The right hepatic duct drains segments V, VI, VII, and VIII. Lining the intrahepatic ducts are cholangiocytes (epithelial cells). The cholangiocytes line complex networks of interconnecting tubes involved in secretory and absorptive processes. Cholangiocytes may be cuboidal in smaller ductal structures. They are columnar in larger structures and contain microvillus increasing surface area. These cells are believed to play a role in transport functions (protein from lymph or plasma into the bile). It is also probable that they are involved in the transport and metabolism of bile acids. Actually, it is likely these cells are hormone responsive. The hepatic artery arises from the celiac axis and courses through the upper portion of the pancreas toward the liver. The hepatic artery gives rise to the gastro duodenal artery posterior and superior to the duodenum. It divides to right and left branches and then into smaller branches. In many cases, a third artery supplies portions of segment IV and the right lobe of the liver.

The right, middle, and left hepatic veins drain most of the hepatic flow and empty into the inferior vena cava. Each has a short extrahepatic segment. The largest vein, the right hepatic, drains the right lobe of the liver. The middle vein drains the medial segment of the left lobe and

some of the anterior segment of the right. The middle hepatic vein joins the left hepatic vein with variability in the juncture site. The left hepatic vein drains the left lateral segment of the liver.

The portal venous system extends from the intestinal capillaries to the hepatic sinusoids. This venous system carries the blood from the abdominal gastrointestinal tract, the pancreas, gallbladder, and spleen back to the heart (coursing through the liver). The largest vessel in this system is the portal vein, which is formed by the union of the splenic vein and superior mesenteric veins. The left gastric and right gastric veins and the posterior superior pancreaticoduodenal vein drain directly into the portal vein. The portal vein runs posterior to the pancreas, and its extrahepatic length may be anywhere from 5–9 cm. At the porta hepatis, it divides into the right and left portal veins within the liver, and the cystic vein typically drains into the right hepatic branch. The portal vein supplies 70% of the blood flow to the liver, but only 40% of the liver oxygen supply. The remainder of the blood comes from the hepatic artery and Blood from both of these vessels mixes in the sinusoids.

2.1.2 Gallstone development and pathophysiology

Depending on their composition, gallstones are often divided into three major types: cholesterol-, black pigment- and brown pigment stones. Black pigment stones are more common among patients with haemolytic diseases (hereditary spherocytosis, sickle cell anaemia, and Thalassaemia) and liver cirrhosis (Aydogdu *et al.*, 2001, Benvegnu, *et al.*, 2001, Fernandes, *et al.*, 2000). Brown stones are often caused by stasis and infection in the biliary system. In the Western world, the major constituent of gallstones is cholesterol, which comprises 50-98 % of the dried substance of the stone. Other constituents may include fatty acids, triglycerides, proteins, polysaccharides, as well as calcium bilirubinate, calcium carbonate and calcium bicarbonate.

Gallstones vary in size from less than a millimeter up to a few centimeters in diameter. Most patients only harbour stones in the gallbladder, but in 10-15 % the stones have migrated into the common bile duct (Tazumah *et al.*, 2006). Important factors in the development of cholesterol stones are super saturation of cholesterol in bile, nucleation and growth of crystals in the gallbladder and gallbladder dysmotility resulting in impaired emptying. The gallbladder stores and concentrates bile during fasting. After gastric emptying, especially after a fatty meal, and mediated by the hormone cholecystinin, the gallbladder contracts simultaneously with relaxation of the sphincter Oddi, resulting in an extrusion of concentrated bile which mixes with food in the duodenum (Everson, 1991).

Biliary colic is considered to be caused by the impaction of one or more stones in the neck of the gallbladder. The raised intraluminal pressure, contraction and distension of the gallbladder give rise to biliary pain (colic).

2.2 PREVALANCE OF GALLSTONES WORLDWIDE

As mentioned, gallstones are common in the Western world. The prevalence among adults is approximately 10-15% for men and 20% for women in Europe and North America (Caucasians) (Schimer *et al.*, 2005) American Indians and Mexican Americans have higher prevalence in comparison to Afro-Americans. Pima Indians in southern Arizona account for the highest recorded prevalence of gallstone disease, with figures of above 70% in women aged 25 years or more (Sampliner, *et al.*, 1970). Scandinavian studies on selected adult age groups show prevalence figures for gallstone disease of 13-18% in men and 15-25% in women (Borch *et al.*, 1998). Similar to other studies, these studies show that age increases prevalence and that there is

preponderance among women. The prevalence of gallstone disease in Sweden has previously mainly been investigated in autopsy series (Lindstrom, 1977) and in vivo in selected age groups (Muhrbeck *et al.*, 1995).

The prevalence of gallstones in a Danish population was examined by Jørgensen (1987) after randomly sampling 4,807 participants aged between 30 to 60 years. Each participant had his or her gallbladder examined by ultrasonography. The overall prevalence of gallstone disease (cases with stones and cholecystectomized cases) in males aged 30, 40, 50, and 60 years was 1.8%, 1.5%, 6.7%, and 12.9%, respectively with a corresponding prevalence of 4.8%, 6.1%, 14.4%, and 22.4%, respectively in females indicating significant differences according to sex. Furthermore, differences between the 40- and 50-year and 50- and 60-year age groups were significant in both sexes.

Bainton *et al.*, (1976) examined a weighted random sample of a population of a South Wales industrial town, for gallstones by cholecystography. The overall prevalence rates were 6.2 per cent for men 45 to 69 years of age and 12.1 per cent for women of the same ages. There was no marked increase in prevalence with age in either sex. More so, symptoms of dyspepsia suggestive of gallstones were found with approximately equal frequency in those with and without gallbladder disease.

Heaton *et al.*, (1991) determined the prevalence of gall stone disease among a sample of 1896 British adults using real time ultrasound. A prevalence rate of 72.2% was indicated. The results showed that the prevalence rose with age (60-69 years, 22-24% of women and 11.5% of men had gall stones or had undergone cholecystectomy) except in women of 40-49 years. The cholecystectomy rate of people with gallstone disease was higher in women than in men. The

study concluded that either gallstones are especially prone to cause symptoms in younger people or that there are two kinds of cholelithiasis – symptomatic and silent.

Ultrasonography was carried out on 1104 by Khuroo, *et al.*, (1989) to detect gall stones disease. Gall stones were detected in 49 adults. The prevalence of gall stones in adult population was 6.12% (men 3.07% and women 9.6%). The prevalence of gall stones rose with age in males and females, however, there was no correlation with obesity, diet, or socioeconomic status. The study concluded that prevalence increases progressively to reach a peak in the sixth decade and the rate is significantly higher in multiparous women.

A Swedish retrospective study from 1986 determined the incidence of symptomatic gallstone disease among patients with abdominal complaints (Norrby *et al.*, 1986). Cholecystography was used as the routine examination for the detection of gallstones in the study. The study concluded that the incidence of gallstone disease decreased since the proportion of cholecystographies showing gallstones decreased over time.

Everhart *et al.*, (1999) conducted a study on prevalence and ethnic differences in gallbladder disease in the United States. The study incorporated national population-based survey to determine the age, sex, and ethnic distribution of gallbladder disease in the United States. Gallbladder ultrasonography was performed among a representative U.S. sample of more than 14,000 persons. Diagnosis of gallbladder disease involved the detection of gallstones or cholecystectomy. The results indicated an estimated 6.3 million men and 14.2 million women aged 20–74 years had gallbladder disease.

Age-standardized prevalence was similar for non-Hispanic white (8.6%) and Mexican American (8.9%) men, and both were higher than non-Hispanic black men (5.3%). Among women, age-adjusted prevalence was highest for Mexican Americans (26.7%) followed by non-Hispanic whites (16.6%) and non-Hispanic blacks (13.9%). Among women, multivariate adjustment reduced the risk of gallbladder disease for both Mexican Americans and non-Hispanic blacks compared with non-Hispanic whites. The study concluded that more than 20 million persons have gallbladder disease in the United States. Ethnic differences in gallbladder disease prevalence differed according to sex and were accounted for by known risk factors. In Asia, Rajani *et al.*, (2012) analysed different risk factors associated with gallstones in a survey conducted at Jharkhand, India. The study purported that cholesterol rich diet especially non vegetarian consumption (68% of patients were non vegetarian) and age are the major risk factors. The study also revealed that gallstones are found more frequently in women than men. The ratio of male to female gallstone patients was about 1: 3. Furthermore, 72.6% of cases were in the age of 21-50. The study concluded that the incidence of gallstone increases with age while genetics, diabetes and smoking are not much related to gallstone formation. A very high and increasing prevalence have been reported in the northern states (Sarin, *et al.*, 1995; Tandon, *et al.*, 1996; Sharma, *et al.*, 1990; Khuroo, *et al.*, 1989; Kapoor, *et al.*, 2003).

Ultrasonography was used to determine the prevalence of gallstone disease in the population of the town of Sirmione, Italy by Barbara, *et al.*, (1987). Prevalence of 6.7% in men and 14.6% in women, ranging from 18 to 65 years of age (overall prevalence of 11%) were reported. Furthermore, the prevalence of cholelithiasis in the same age span was 6.9% (4.5% in men and 8.9% in women). Prevalence of cholelithiasis increased with age in both sexes. Prevalence of

gallstone disease was also found to be higher in obese and hypertriglyceridemic subjects and to increase with the number of pregnancies.

The prevalence of gallstones and gallbladder disease was studied in a rural Caucasian (aged between 15 to 50 years) population by Williams and Johnston (1980). Diagnosis of gallstones and bladder disease was established by cholecystography. The study reported a prevalence of gallstones of 167/1000. Also, discriminant analysis showed that skin fold thickness and range of daily energy intake or all measures of obesity together correctly separated the persons with gallstones from those without.

Barker, *et al.*, (1979) conducted a prospective study of the prevalence of gall stones at necropsy in nine towns in England and Wales. Age- and gender-standardised prevalence ranged from 20.6% in Ipswich to 9.2% in Wakefield. The distribution of gall stones differed from that of all-cause mortality and was negatively correlated with that of mortality from ischaemic heart disease. The study further reported that socioeconomic influences related to affluence do not appear to be major determinants of the distribution of gall stones.

Another prospective study on the prevalence of gall stone disease at necropsy was undertaken by Bates, *et al.*, (1992) over a 10 year period. The study revealed that in women, the prevalence of gall stone disease remained static. However, in men aged 50-59 years it rose from 7% (n = 148) in the first three years to 18% (n = 138) in the last three years (p less than 0.01) and in men aged 60-69 it rose from 12% (n = 370) to 20% (n = 366, p less than 0.01). The study further reported that men with gallstones were less likely to have had a cholecystectomy than women, and overall 88% of gall stones remained in situ.

Gallbladder diseases commonly manifest as gallstones (cholelithiasis), polyps, sludge, cholecystitis, choledocolithiasis, cholesterolosis, and gallbladder cancer. Amongst these numerous gallbladder diseases, gallstones appears to be the most prevalent in American Indians (60-70%), but less prevalent in Hispanics of mixed Indian origin and further reduces amongst Black Americans (Shaffer, 2006; Afdhal, 1999; Kratz, Mason, & Kachele, 1999). In United States alone, more that 30 million people develop this problem and nearly one million new patients annually are found to have gallstones, of which half undergo surgery (Salam *et al.*, 2003). Different disorders do contribute to the formation of gallstones in the human body.

By analysis of their chemical compositions, gallstones can be categorized into three main types: cholesterol, black pigment stones and brown pigment stones (Conte *et al.*, 2011). The black pigment stones are derived from the precipitation of calcium hydrogen bilirubinate where pigment super saturation and deposition of inorganic salts, phosphate and calcium bicarbonate accelerate the nucleation as reported in the study of Conte *et al.*, (2011). Cholesterol gallstones on the other hand form by unphysiological biliary super saturation from hypersecretion of cholesterol, gallbladder hypo motility and the accumulation of mucin gel (Carey, 1993). The explanation given by Conte *et al.*, (2011) further illustrates that the brown pigment stones are formed in the ducts due to bile stasis, parasites, uncompleted polymerization of calcium hydrogen bilirubinate, saturated fatty acids and bacterial infection with enzymatic hydrolysis of biliary lipids. As the incidence of gallstone disease escalates, there is a concomitant increase in complications like gallstone-related pancreatitis (Lindkvist *et al.*, 2004).

Previous work done in Saudi Arabia shows that cholesterol stones were predominant compared to mixed and pigment stones, while 57% of the gallstones were of cholesterol variety (Diehl *et al.*, 1995). The result is in conformity with the studies carried out in Korea, Germany, United States and Singapore (Diehl, *et al.*, 1995). It means that in Saudi Arabia like western and other developing countries, the incidence of cholesterol stones is high. Factors that predispose to cholesterol hyper secretion are obesity, aging, diabetes mellitus and use of drugs like thiazide and oral conceptions. Estrogenic influences including oral contraception's and pregnancy increase the expression of hepatic lipoprotein receptors and stimulate hydroxymethylglutaryl Coenzyme A (HMGCOA) reductase activity. Thus both cholesterol level and biosynthesis are increased. From the above observations, it seems that the increases incidence of cholesterol stones in Saudi Arabia may be due to high fat diet, Again the custom of multiple marriages, multiple pregnancies and the use of oral contraception by the females may be responsible for the increased occurrence of gall stones in females three and half times more as compared to males.

Cholecystectomy is the most common major general surgical operation performed in North America and Europe (Vogt, 2002). The clinical conditions resulting from cholelithiasis have a marked geographical distribution and are not common problems facing African surgeons. This may change, as diet, activity and longevity change with development. Knowledge of the surgical approach to the gallbladder and biliary ducts is a fundamental skill of general surgery. Moreover, there is enormous pressure to introduce laparoscopic cholecystectomy in low-income countries.

Gallstones remain a serious health concern affecting millions throughout the world (Salam *et al.*, 2003) and it exhibits prevalence rates of about 25% in developed societies but are uncommon in developing or underdeveloped societies (Kern, 1983). In gallstone disease, the obstruction may

be an obvious evidence of cholesterol or pigmented stone in the cystic duct. Formation of gallstones in vivo takes years and it is quite difficult to monitor from nucleation to consolidation (Swidsinski *et al.*, 1998). Biliary pain may however result when there is an increased intraluminal pressure as the gallbladder contracts against the obstructed outlet. According to Lonborg *et al.*, (1995), gallstone diseases may be symptomatic or asymptomatic and for that matter, very much essential to define exactly which symptoms are caused by gallstones. It can be deduced from their explanation that symptomatic gallstones are revealed by true biliary pain and/or complications, and nonspecific abdominal complaints including dyspepsia. Gallstone-associated pain seems to follow a certain pattern in most patients (Vetthus, *et al.*, 2006). Some consensus groups, over the years, have also attempted to establish criteria for biliary pain relative to defined characteristics (Ruhl & Everhart, 2011). And they concluded that some characteristics associated with such condition may include episodic, steady, severe pain located in the upper abdomen and lasting more than 30 minutes and some accompanying features (e.g., nocturnal onset; nausea and vomiting; radiating through to the back (Ruhl & Everhart, 2011). Their explanation depicts the importance for clarifying what constitutes true biliary pain so as to better predict relief following cholecystectomy.

Current research however shows that cholecystectomy, unlike previously, no longer relieves biliary pain in about 10%-33% of the population of people with documented gallstones (Barhane, *et al.*, 2005). Even though the confusion of gallstone related pain with other functional gut disorders like irritable bowel syndrome (IBS) and dyspepsia will not provide a favorable outcome from cholecystectomy the avoidance of an unnecessary cholecystectomy becomes critically germane in an era of escalating rates of surgery (Thistle *et al.*, 2011).

2.3 PREVALENCE OF GALLBLADDER STONE DISEASE IN AFRICA

Historically, Becker and Chatgidaki (1952) reported an incidence of 2% (six stones per year) in a study of 4,494 autopsies over a 15-year period in South Africa. In all 92 stones were found. Also, a review of disease pattern by Bremner (1971) at Baragwaneth Hospital in South Africa indicated a four-fold increase of cholecystectomy from 1959 to 1969. Another 5-year review by Ajao (1982) among 835 patients in Ibadan indicated an average of seven per year. Patients were operated on for inflammatory disease of the gallbladder. In another similar 3-year review conducted by Ajao (1982), 19 cases were reported between 1974 and 1977.

Ganiyu (2004) determined the prevalence of cholelithiasis and cholecystitis in a Nigerian population over a five-year period (1997-2001) in an urban teaching hospital. Only participants who had a surgical operation and histological confirmation of cholelithiasis and cholecystitis was included in the study. The results indicated that in the first three years, 18 (39.1%) cases were seen, but in the next two years 28 (60.9%) patients had cholecystectomy. Also, the male: female ratio was 1:4.8. Only four (8.7%) of these patients were obese. Thirty-two (69.6%) were multiparous. Only four (8.7%) of the patients had pigmented stones, the majority of which were mixed stones. The study concluded that gallbladder disease is increasing in the African population as a result of changing dietary habits.

Elmehdawi, *et al.*, (2009) investigated the prevalence of gallbladder stones among type 2 diabetic patients in Benghazi Libya. A case-control study design was used to compare 161 (107 females and 54 males) randomly selected type-2 diabetic patients with 166 age and sex matched non diabetic patients (109 females and 57 males) recruited from subjects attending the medical outpatient department of 7th of October teaching hospital for checkup. Two radiologists

employed real-time ultrasound to examine the abdomen after an overnight fast. Gallstones were observed in 39.75% of the diabetic cohort and in 17.5% of the control. The prevalence was significantly higher in female diabetics than in male diabetics (47% vs.26%, $p = 0.01$). The study concluded that Libyan diabetic patients had a significantly higher prevalence of gallstones than non-diabetics (~2.3 times). Female diabetic patients were significantly more affected than males and the prevalence significantly increased with age particularly in males. Older age (>41 years in females and >53 years in males), high BMI (>24 kg/m²), female gender, and parity were the most significant risk factors for gallstones in Libyan diabetic patients.

2.4 PREVALENCE OF GALLBLADDER STONE DISEASES BY ULTRA SOUND

Historically a wide variety of tests have been used to detect gallbladder function and stones. Today the transabdominal ultrasound US is the gold standard for diagnosis of cholelithiasis (Portincasa *et al.*, 1920).

In a large Danish study published in 1991, an age and sex stratified random population sample (ages 30, 40, 50 and 60 years) of Danish origin was followed up with ultrasonography after five years (Jensen, 1991). Re-screening was done on 82.8% (2987/3608). The five year incidence of gallstones in each age group was 0.3, 2.9, 2.5 and 3.3% among men and 1.4, 3.6, 3.1 and 3.7% among women. The overall annual incidence was 0.93 %. The study also showed that gallstones could have disappeared due to dissolution or spontaneous passage in 4.5 % of the patients over a 5-year period. The incidence was related to age and gender, although the difference between women and men decreased with increasing age.

Glabek, *et al.*, (1987) screened a population of 2464 persons (between 20 and 70 years) in a study designed for establishing gallstone prevalence rates. An ultrasonic examination was used to establish the diagnosis of gallstones. The results from the study indicated a prevalence rate of 21.9%. The prevalence rates with respect to gender were 17.7% in men and 21.2% in women. From age group 20–29 years to age group 60–69 years the prevalence rates increased from 4.9% to 37.0% in men and from 6.0% to 41.3% in women. Jorgensen, (1989) analysed the presence of gallstones diagnosed by ultrasonography in relation to relative weight, weight change since age 25, slimming treatment, physical activity, smoking, consumption of coffee, and diabetes mellitus in a cross sectional study. A random sample of 4581 men and women of Danish origin (aged 30, 40, 50, and 60 years). The study established a significant association in women with high body mass index, history of slimming treatment, and weight gain since the age of 25 of more than 5 body mass index units with gall stones. In men, history of slimming treatment and smoking were significantly associated with gallstones.

A total sample of 2,584 residents in the Yaeyama District of Okinawa, Japan, were investigated in 1984 to determine the prevalence of gallstone disease and its associated factors by Nomura, *et al.*, (1987). Diagnosis of gallstone disease was established by ultrasonography. An overall prevalence of 3.2% was established. Prevalence increased with age from 0% under 19 years of age to 11.4% over 70 years of age and was higher in females (4.0%) than in males (2.5%). The results further indicated that age and fatty liver were significant predictors of gallstone disease.

Kratzer, *et al.*, (1998) examined A study population of 1116 blood donors (656 men, age 38.0 ± 12.0 years; 460 women, age 34.1 ± 11.2 years) at the Central Blood Bank of the German Red Cross, Ulm. Subjects were assigned to one of four groups based on age (18-30, 31-40, 41-50, and

51-65 years). Following a structured interview of each study subject, an ultrasound examination was carried out and a blood sample obtained for laboratory study. The results from the study showed that 6.0% of all study subjects (5.8% of the men and 6.3% of the women) exhibited evidence of current or past gallbladder disease (cholelithiasis or history of cholecystectomy). The prevalence of gallbladder disease correlated positively with age, reaching a maximum of 13.7% (9.5-20.0) in the 51- to 65-year-old age group, and also correlated as with body mass index (BMI).

The GREPCO group (Angelico *et al.*, 1997) studied the natural history of gallstones and the incidence of gallstones in a 10-year ultrasonographic follow-up study of 253 (59.4%) out of 426 initially examined women aged 20-69 years at baseline. The overall incidence of gallstones was 6.3% (16 subjects), including 0.8% (2 subjects) without stones at baseline. The incidence was positively related to age. Moreover, BMI and parity were positively related to gallstone development.

2.5 RISK FACTORS

Risk factors for symptomatic gallstones were assessed by Malcolm-Maclure, *et al.*, 1980 in 88,837 women. A Nurses' Health Study cohorts were followed for four years after completing a detailed questionnaire about food and alcohol intake in 1980. In all, 433 cholecystectomies and 179 cases of newly symptomatic, unremoved gallstones, diagnosed by ultrasonographic examination or x-ray films, were reported during the four-year follow-up. The age-adjusted relative risk for very obese women, who had a Quetelet index of relative weight greater than 32 kg per square meter, was 6.0 as compared with women whose relative weight was less than 20 kg per square meter. For slightly overweight women the relative risk was 1.7. The results from

the study depicted a roughly linear relationship between relative weight and the risk of gallstones. Also, high energy intake, as compared with a low energy intake was associated with an increased incidence of symptomatic gallstones and an alcohol intake of at least 5 g per day was associated with a decreased incidence as compared with abstinence. Parity did not appear to be an important risk factor. The study concluded that there is a strong association between obesity and symptomatic gallstones

Risk of symptomatic gallstones in women with severe obesity was quantified by Stampfer, *et al.*, (1992). The study established a monotonic increase in gall stones disease risk with obesity. Women with a body mass index (BMI) $> 45 \text{ kg/m}^2$ had a sevenfold excess risk compared with those with a BMI $< 24 \text{ kg/m}^2$. Also, women with a BMI $> 30 \text{ kg/m}^2$ had a yearly gall stone incidence of $> 1\%$ and those with a BMI $> 45 \text{ kg/m}^2$ had an incidence of approximately 2% per year.

Prevalence of gallbladder disease and associated risk factors among American Indian populations using ultrasonography of the gallbladder and standardized diagnostic criteria was established by Everhart, *et al.*, (2002). Participants included individuals aged 47 years and older, of 13 American Indian tribes or communities in Arizona, Oklahoma, and South and North Dakota. Gall bladder disease was the sum of gallstones (determined by ultrasound examination) and cholecystectomy (determined by ultrasound and self-report). A total of 3,296 participants were examined at three sites. The results showed that among women, 17.8% had gallstones, and 46.3% had evidence of a cholecystectomy (total of 64.1% with gall bladder disease). Among men, 17.4% had gallstones, and 12.1% had evidence of a cholecystectomy (a total of 29.5% had gall bladder disease). Also, American Indian heritage, and waist circumference were associated

with gall bladder disease among men. Age, American Indian heritage, diabetes, and parity were associated with gall bladder disease among women. Body mass index was not independently associated with gall bladder disease in either sex.

To assess the prevalence and risk factors of gallstone disease (GSD) in Taiwan. A prospective ultrasonographic study of GSD was conducted in 3647 Chinese subjects who received a paid hospital physical check-up by Chen, *et al.*, (1998). With a comparison of their demographic characteristics and biochemical parameters, ultrasonography was done. The study diagnosis revealed 2946 (M/F: 1838/1108) with normal gallbladder, 286 (M/F: 196/90) with gallstones, 100 (M/F: 56/44) with previous cholecystectomy for gallstones, 243 (M/F: 174/69) with gallbladder polyps, 17 (M/F: 10/7) with mixed gallstones/polyps and 35 as 'miscellaneous'. They found out that the overall prevalence of GSD in the studied group was 10.7% with risk factors being age ($p < 0.05$), high body mass index ($p < 0.05$), diabetes mellitus (adjusted odds ratio: 1.998; $p < 0.05$) and glucose intolerance (adjusted odds ratio: 2.056; $p < 0.05$)

In an epidemiological survey to determine the prevalence and risk factors of gallstone disease (GSD) in an adult population of Taiwan, by Chen *et al.* 2006, 3333 Chinese adults (aged $>$ or $=$ 18 years) underwent ultrasonography. A questionnaire on personal history was completed to ascertain whether the removed gallbladder contained stones in all cholecystectomized subjects, the dietary habits (vegetarian/non-vegetarian diet), the history of GSD in the participant's first-degree relatives, the history of gastrointestinal surgery (vagotomy, gastrectomy for peptic ulcer disease, or ileal resection), parity, and use of oral contraceptives. The study found out that The overall prevalence of GSD was 5.0% (4.6% in men, 5.4% in women) with no significant sex

differences (men/women).The study concluded that age and fatty liver in both sexes were risk factors for GSD in the study population.

Risk factor of gall diseases has been studied in high altitude population. Abu-Esha *et al.* ,(2007)studied the prevalence of gallstone disease and related risk factors in a Saudi Arabian population in a cross-sectional community-based study made of 291 people, with a structured interview collected background data and upper abdominal ultrasonography to detect gallstones, participants were examined and results revealed that prevalence of gallstone disease was 11.7% with logistic regression multivariate analysis of risk factors, the study found out that female sex, family history of gallstone disease and past history of pancreatitis were risk factors of gall bladder stone disease.

Jørgensen, (1989) examined the relationship between occurrence of gallstone disease diagnosed by ultrasonography and complaints about abdominal pain and discomfort. A total of 3608 participated in the investigation. The results of the study indicated low (0 to 25%) predictive values of various complaints about pain and discomfort, in particular, pain was not associated with size, number or motility of the stones. The study concluded that in a random population it is difficult to define the symptoms specific for gallstones and thereby to distinguish between symptomatic and asymptomatic gallstones.

Zatonski *et al.*, (1997) determined possible new risk factors for gallbladder cancer a case-control study of cancer of the gallbladder was investigated in five centers located in Australia (Adelaide), Canada (Montreal and Toronto), The Netherlands (Utrecht), and Poland (Opole) from 1983 to 1988. Cancer diagnosis was confirmed by either biopsy, cholecystectomy, or at the

time of autopsy. There were 196 cases and 1515 controls. About 98% of participants were whites. A history of gallbladder symptoms requiring medical attention (e.g., reduced bile secretion from the gallbladder into the small intestine due to obstructions of the common bile or cystic ducts) was the major risk factor associated with gall bladder cancer. Furthermore, elevated body mass index, high total energy intake, high carbohydrate intake (after adjustment for total energy intake), and chronic diarrhea were also found to be associated with gallbladder cancer. The study concluded that the findings are consistent with a major role of gallstones, or risk factors for gallstones, in the cause of gallbladder cancer.

Most studies document an elevated risk associated with childbearing and parity (Novacek, 2006; Angelico *et al.*, 1997; Jorgensen 1988). However, with regard to pregnancy two large studies, one in Germany and one in France could not verify these findings (Walcher *et al.*, 2005; Caroli-Bosc *et al.*, 1999).

Geography and particularly ethnicity play an enormous role in the prevalence of gallstone disease and also the type of stone that forms: cholesterol gallstones predominate in the developed countries of the Western world; brown pigment stones in the bile ducts are more common in Asia (Salam *et al.*, 2003). Prevalence is inordinately high in American Indians and their admixtures, and also Northern Europeans; somewhat lower in European and American whites (Everhart *et al.*, 2002). Mexican Americans are also at heightened risk when compared to White Americans; however, this risk is directly related to the degree of Amerindian admixture (Everhart, 2001).

Intermediate prevalence rates occur in Asian populations (Singh *et al.*, 2001) and Black Americans (Everhart, 2001). The lowest frequencies (<5%) occur in sub-Saharan Black Africans

(Bagi *et al.*, 1991). The majority of gallstones in developed countries consist predominantly of cholesterol (>85%), where as the remainder constitutes black pigment stones composed of calcium bilirubinate (Tazuma, 2006). The situation differs in East Asia where brown pigment stones are located in bile ducts, predominately associated with parasitic infestation.

In developed countries, however, these bile duct stones arise in association with the inflammation and infection that result from biliary strictures and malignancies (Tazuma, 2006). The frequency of hepatolithiasis, as a proportion of all bile duct stones, is as high as 20% in China and Taiwan, yet as low at 2% to 3% in Japan, Singapore, and Hong Kong (Shod, Tanaka, Sagar, 2003). The stone type curiously has recently shifted in developing Asian countries from pigment to cholesterol stones. The basis for this change may reflect a decreased rate of chronic biliary infections and consumption of a more Westernized diet (Shaffer, 2005).

2.5.1 Family history & genetics

Genetic susceptibility is a key factor in gallstone formation (Ammert & Matern, 2005). Familial studies reveal an increased frequency: a nearly 5 times elevated risk in the relatives of gallstone patients. These rates are even higher in monozygotic twins at 12% and dizygotic twins at 6% (Gilat *et al.*, 1983). Yet spouses of affected patients do not have any increased risk, thereby eliminating a shared environment as the basis - i.e., similar dietary and other common habits among family members as the explanation for this apparent association (Van der linden & Westlin, 1996). In a Swedish twin study, genetic effects accounted for 25%, shared environmental influences for 13% and unique environmental effects for 62% of the phenotypic variance (Grjibovski *et al.*, 1998).

No mode of simple Mendelian pattern of inheritance can account for the majority of cases with gallstone disease. In fact, stone formation is a complex interaction of genes and environmental factors, particularly diet-gene interactions (Rudkowska & Jones, 2008). Several genes have been associated with gallstone disease (Stinton *et al.*, 2010). Identified so far have been: the apolipoproteins E (*APOE*) and B (*APOB*) (Mittal & Mittal, 2002), cholesterol ester transporting protein (*CETP*), cholesterol 7 α -hydroxylase (Pullinger *et al.*, 2002), cholecystokinin receptor A (*CCKAR*) (Amer *et al.*, 2003), the LDL receptor (*LDLR*) (Feng *et al.*, 1998) and the *CETP* (Savoki *et al.*, 1995). Genome-wide association analysis has revealed that variants for the hepatic cholesterol secretion (*ABCG8 19H* and *ABCB4*) represent a susceptibility factor for human gallstones (Schafmayer, Volzke, *et al.*, 2007).

2.5.2 Age

A study by Einarsson *et al.*, (1985) revealed that the frequency of gallstones increases with age, escalating markedly after age 40 to become 4-10 times more likely in older individuals. The stone type also changes with age: initially being composed predominantly of cholesterol (corresponding to an increased cholesterol secretion into and saturation of bile) but in late life tending to be black pigment stones. Further, symptoms and complications increase with age, leading to more frequent cholecystectomies (Volzke *et al.*, 2005).

2.5.3 Gender and female sex hormones

Even though one of the major risk factors for developing gallstones is gender (i.e. common in women than in men), other risk factors such as race, age, genes, ethnicity, diet, and life-style are also contributors to this condition (Fornari *et al.*, 1990). Worldwide prevalence of gallstones in females based on ultrasonographic surveys varies (Everhart *et al.*, 2002). According to Shaffer

(2005) North American Indians for instance have the highest reported rates of cholelithiasis, afflicting 64.1% of women and 29.5% of men. The aboriginal populations of South America also have an exceedingly high prevalence of gallstones: 49.4% of native Mapuche Indians of Chile women and 12.6% of men harbor gallstones (Miquel *et al.*, 1998). In contrast White Americans have an overall prevalence of 16.6% in women and 8.6% in men (Everhart, 2001). The explanation to the above facts is that the female gender has a most compelling association with gallstone disease, especially during the fertile years.

Women are almost twice as likely as men to form gallstones; the gap narrows following menopause after which men begin to catch up (Einarsson *et al.*, 1985). Etminamm, *et al.*, (2011) have attributed the difference in female and male to female sex hormones, parity, oral contraceptive use and estrogen replacement therapy as established risk factors for cholesterol gallstone formation. Female sex hormones adversely influence hepatic bile secretion and gallbladder function. Estrogens increase cholesterol secretion and diminish bile salt secretion, while progestins act by reducing bile salt secretion and impairing gallbladder emptying leading to stasis. A new 4th generation progestin, drospirenone, used in some oral contraceptives may further heighten the risk of gallstone disease and cholecystectomy; however, the increased risk is quite modest and not likely to be clinically meaningful (Etminamm, *et al.*, 2011).

During pregnancy when female sex hormones are endogenously raised, biliary sludge (particulate material that is composed of cholesterol, calcium bilirubinate, and mucin) appears in 5% to 30% of women. Resolution frequently transpires during the post-partum period: sludge disappears in two-thirds; small (<1 cm) gallstones (microlithiasis) vanish in one-third, but definitive gallstones become established in ~5% (Maringhini, *et al.*, 2007). Additional risk

factors for stone formation during pregnancy include obesity (prior to the pregnancy), reduced high density lipoprotein (HDL) cholesterol and the metabolic syndrome (Kocw, *et al.*, 2008).

2.5.4 Obesity

Several studies identify obesity as a major risk factor for developing gallstones (Shaffer 2005; Angelico *et al.*, 1997; Jorgensen 1988; Attili *et al.*, 1997; Kodama *et al.*, 1999; Torgoson *et al.*, 2003; Vecchia *et al.*, 1991) gender disregarded, although the relationship is usually stronger in women than in men. Biliary hyper secretion of cholesterol, which is an important determinant in gallstone formation, is profoundly exacerbated by obesity. Rapid weight loss is also associated with an increased risk of developing gallstones (Torgerson *et al.*, 2003). After bariatric surgery such as Roux-en-Y gastric bypass (but not gastric banding) with rapid weight loss, approximately 40% of the patients form stones. This could justify prophylactic cholecystectomy in these patients.

The exploding prevalence of obesity now reaches epidemic levels in both developed and developing nations like China (Ogden *et al.*, 2007). Obesity, particularly abdominal or centripetal obesity, is a well-established risk factor for gallstone disease (Shaffer, 2005; Erliner, 2000; Tsai, *et al.*, 2004). At least 25% of morbidly obese individuals have evidence of gallstone disease (Ulido, *et al.*, 2009). Obesity in the late teenage years carries the greatest risk, whereas thinness protects against cholelithiasis (Shaffer, 2005; Maclure, *et al.*, 1989). Females with obesity have an even increased risk of stones formation. Women with severe obesity (body mass index [BMI] $>32 \text{ kg/m}^2$) show an age-adjusted relative risk of 6.0 for the development of gallstones compared with non-obese controls; their annual incidence of developing gallstones is 2% (Maclure, *et al.*, 1989). Obesity is associated with an increased activity of the rate-limiting

step in cholesterol synthesis, the hepatic enzyme, 3-hydroxyl-3-methyl-glutaryl co-enzyme A (HMG-CoA) reductase, leading to increased cholesterol synthesis in the liver and its heightened secretion into bile (Erlinger, 2000; Lambou-Gianoukos, *et al.*, 1977).

2.5.5 Heredity

Most (Kratzer *et al.*, 1998; Chapman *et al.*, 2000; Attili *et al.*, 2005) but not all studies (GREPCO 1984) show a relationship of gallstone occurrence with a family history of the disease. Unless such studies are based on screening for gallstones among relatives, the results are highly unreliable since most gallstones are asymptomatic and non-operated. The high prevalence among PIMA Indians is most probably due to heredity (Sampliner *et al.*, 1995, Friedman *et al.*, 1966). However, when studying these populations, other predisposing factors are also over represented, for instance, the female/male ratio is higher as well as the frequency of obesity and parity. In some ethnical groups in South America the prevalence of gallstones is high. A study from Chile showed that cholesterol lithogenic genes are widely spread among Chilean Indians and Hispanics.

2.5.6 Sickling

Rennels *et al.*, (1984) performed sonographic tests on 65 patients with major sickle hemoglobinopathies. Cholelithiasis was found in 26% of the 42 patients with hemoglobin SS, in 20% of the 15 with Hb SC, and in 12.5% of the 8 with Hb S- β -thalassemia. Another study by Lachman, *et al.*, (1979) ascertained the prevalence of Cholelithiasis among sickle cell disease patients. An Overall prevalence of gallstones was found to be 29%. Walker *et al.*, (2000) also investigated the prevalence, incidence, risk factors, clinical associations, and morbidity of gallstones among 311 patients with homozygous sickle cell disease and 167 patients with sickle

cell-hemoglobin C disease in a cohort study from birth. The study reported that gallstones developed in 96 patients with homozygous sickle cell disease and 18 patients with sickle cell-hemoglobin C disease. Sarnaik *et al.*, (2000) reported a gallstone prevalence rate of 27% among patients with sickle cell hemoglobinopathy. Bond *et al.*, (1987) studied the prevalence of gallstones by abdominal ultrasound examination in 131 patients with sickle cell disease. 58% had gallstones. Gall stones were present in 17% of patients with haemoglobin S + C disease and 17% with haemoglobin S beta thalassaemia.

2.5.7 Occupation

Occupation/education is sometimes used as a measurement of socioeconomic status or Life-style. In the Italian MICOL study, a higher risk of gallstone disease was found among housewives and in men with higher education (Attili *et al.*, 1997). The opposite was noticed in a British study which showed a relationship between gallstone disease and low social Class (Murray *et al.*, 1994). An American study investigated differences between Mexican Americans and non-Hispanic whites and found that the prevalence of gallstone disease was twice as high among Mexican American women. These ethnic differences persisted after stratifications for age, parity and BMI. Interestingly, after controlling for age, parity, BMI and ethnicity, the prevalence among women was inversely related to level of education, income, occupation and habitat, all measurements of socioeconomic status (Diehl *et al.*, 1985).

2.5.8 Smoking

Data in the literature is conflicting as to whether smoking is predisposing or protective. It has been suggested that smokers are protected against the development of gallstones through a mechanism which leads to a decrease in prostaglandin synthesis and mucus production in the

gallbladder epithelium (Rhodes & Venables, 1991). Another study by Stampfer *et al.*, (1992) came to the opposite conclusion when they found smoking to be an independent risk factor in women smoking heavily (>35 cigarettes/day) (Stampfer *et al.*, 1992). In a large British cohort study, smoking was identified as an important risk factor for developing symptomatic gallstone disease (Murray *et al.*, 1994). In a study from Australia, a risk of mis-estimating the risk in case-control studies was shown, since even first exposure to smoking among women was associated with an increased risk. Late occurring cases seem to have a different relation to the exposure factor than do the early (Mc Micheal *et al.*, 1992).

2.5.9 Dyslipidemia, diabetes mellitus and the metabolic syndrome

A study to compare the prevalence of gallstone disease in 308 diabetics and 318 controls was undertaken by Chapman, *et al.*, (1996). The study established a higher prevalence of gallstone disease in diabetics (32.7%) compared to controls (20.8%; $p < 0.001$ chi-squared test). Gender difference was only significant in females (diabetics 41.8% versus controls 23.1%; $p < 0.001$). The study concluded that there was a higher prevalence of gallstone disease in diabetics compared to controls.

Cholesterol gallstone disease is a metabolic problem, which correlates with lipid abnormalities, diabetes mellitus and adiposity. A low HDL cholesterol (Petitti, *et al.*, 1981) and hypertriglyceridemia (Ahlberg, 1979; Barbara, *et al.*, 1987) carry an increased risk of developing stones. In contrast, there is no definite association with hypercholesterolemia (Shaffer, 2005; Thijs, *et al.*, 1990). High homocysteine levels also may correlate with gallstone disease (Sakuter & Suzuki, 2005). The metabolic syndrome is defined by the presence of at least 3 features out of abdominal obesity, high blood pressure, high fasting glucose, increased triglyceride levels and

reduced HDL levels (Eckel, *et al.*, 2005). Both the metabolic syndrome and diabetes mellitus are risk factors for gallstone disease (Mendez-Sauche, *et al.*, 2005). The metabolic syndrome has also been associated with stone complications (Ata, *et al.*, 2011). Hepatic insulin resistance may act by enhancing hepatic cholesterol secretion, depressing bile salt synthesis and/or impairing gallbladder motility (Biddinger, *et al.*, 2008; Nakeeb, *et al.*, 2006).

It has been suggested that gallstone development is associated with common metabolic disorders such as, obesity, diabetes mellitus and dyslipidemia which supports the hypothesis that gallstone disease is part of the metabolic syndrome (Ruhl, *et al.*, 2002; Mendez-Sachez *et al.*, 2005). Another pathophysiological link between insulin resistance and gallstone development is the increase of cholesterol saturation in gallbladder bile. This is related to an increase in body cholesterol synthesis and hypersecretion of biliary cholesterol as observed in obesity (Shaffer 2005, Attili *et al.*, 1997). This idea was supported by the findings in epidemiological studies (Attili *et al.*, 1997; Chapman *et al.*, 1996; Pagliarulo *et al.*, 2004; De Sautis *et al.*, 1997; Cheu *et al.*, 2006) but the matter is controversial since other studies found no such correlation (Meudez-Saudez *et al.*, 2005; Perssou & Thulin, 1991; Kono *et al.*, 1992).

2.5.10 Non-Steroidal Anti-inflammatory Drug (NSAID)

In a study carried out twenty years ago it was suggested that gallstone formation could be prevented by the intake of NSAID (Hood *et al.*, 1988). This could not be verified in a large randomized study on aspirin usage of more than 1g/daily (Kurata *et al.*, 1991) or in an experimental study on hamsters (Borch *et al.*, 1994).

2.5.11 Chrons disease

The pathogenesis of the association between Chrons disease and gallstone disease is unclear. Previously it was believed to be attributable to bile acid malabsorption in the diseased or resected ileum segment, causing hepatic excretion of cholesterol supersaturated bile. This explanation was not supported in a study showing that bile cholesterol saturation is significantly lower in patients with Chrons disease than in controls. A correlation between gallstone disease and Chrons disease was found in a large study which also showed an association of gallstone disease to the site of Chrons disease at diagnosis, as well as to the number and site of bowel resections (Fraquelli *et al.*, 2001).

It is surprising, however, that the incidence of cholecystectomies is not increased among patients with Chrons disease and that after ileal resection few patients require cholecystectomy (Chew, 2003). Hence, simultaneous or prophylactic cholecystectomy is not justified.

2.5.12 Alcohol

Alcohol consumption has been shown to be associated with a lower prevalence of symptomatic (Friedman *et al.*, 1966, Maclure *et al.*, 2001) as well as asymptomatic, gallstone disease (La Vecchia *et al.*, 1991; Stampfer *et al.*, 1992; Volzke *et al.*, 2005; La Vecchia *et al.*, 2005). The intake of alcoholic beverages was also inversely related to the risk of cholecystectomy (Leitzmann *et al.*, 1999). A large prospective study in men showed an inverse relation of alcohol beverage to symptomatic gallstone disease, but interestingly, the association was not present when consumption was less than 1-2 days a week (Leitzmann *et al.*, 1999). In contrast, a large study from Germany found no relation to alcohol consumption (Leitzmann *et al.*, 1997).

2.5.13 Physical activity

The exact role that physical activity plays in preventing the formation of gallstones is unknown. One suggested mechanism behind the protective effect of physical activity is a reduced colonic transit time associated with a reduced intestinal bile salt dehydroxylation and increased gallbladder motility (Lammart, Sauerbruch, 2005). Most of the epidemiological studies found no such correlation, gender disregarded (Friedman *et al.*, 1996; Jorgensen *et al.*, 1990; Komo *et al.*, 1995; GREPCO, 1998). Leitzman *et al.*, (1998) however, found a significant inverse relation between physical activity and gallstone disease among men. These authors also performed a larger study on more than 60 000 women and showed recreational physical activity to be associated with a decreased risk of cholecystectomy (Leitzman *et al.*, 1998). This association was independent of other risk factors, such as obesity and recent weight loss.

2.5.14 Rapid weight loss

Low caloric diets and bariatric surgery with rapid weight loss are associated with gallstones developing in 30% to 71% of such individuals (Everhart, 1993; Wright, *et al.*, 2002). Weight loss that exceeds 1.5 kg/week following bariatric surgery increases the risk for stone formation; these stones are most likely to become apparent during the first 6 weeks after surgery when weight loss is most profound (Weinsien, *et al.*, 1995; Shaffer *et al.*, 2001). Weight loss-associated gallstones are typically asymptomatic, only 7% to 16% develop symptoms, best predicted by a postoperative weight loss exceeding 25% of the body weight (Ulindo & Fajuwak, 2009). Even less extreme weight fluctuations create a risk for stone formation (Syngal & Colditz, 1999), as is a history of dieting (Jorgensen & Jorgensen, 1989).

2.5.15 Diet and Total Parental Nutrition

Other than a high caloric intake that leads to obesity, any importance of the dietary content is unclear and difficult to analyze (Mendez-Sanchez, *et al.*, 2007; Tseng, *et al.*, 1999). Diets specifically high in cholesterol, fatty acids, (Tsai, *et al.*, 2008) carbohydrates (Scragg, *et al.*, 1984; Leitzmann, *et al.*, 2005) or legumes (Covarrubias, *et al.*, 1989) seem to increase the risk of cholelithiasis. In contrast, unsaturated fats, coffee, fiber (Leitzmann, *et al.*, 2004; Leitzmann, *et al.*, 1999; Ann, *et al.*, 2003; Attili, *et al.*, 1998), ascorbic acid (vitamin C) and calcium (Hudes, 2003; Simon & Hudes, 1998; Cuevas, *et al.*, 2004) and moderate consumption of alcohol (Scragg, *et al.*, 1984; Leitzman, *et al.*, 2003; Hann, *et al.*, 1999) reduce the risk. Certainly, the shift to a more Western diet, high in refined carbohydrates and fat (triglycerides) and low in fiber, best explains the profound increase in cholesterol gallstones amongst American Indians and in European countries following World War II. This dietary change also might account for the shift from pigment to cholesterol stones in Asian countries (Kameda, *et al.*, 1984). Genetic variations, especially in the genes that control cholesterol metabolism, might underscore why some respond to dietary change by developing cholesterol gallstones (Kany, *et al.*, 1999; Rudkowska *et al.*, 2008).

2.5.16 Lifestyle factors and socioeconomic status

The exact role of socioeconomic status and gallstones is controversial (Shaffer, 2005). A previous cross-sectional study of non-Hispanic Whites and Mexican Americans, found gallbladder disease inversely related to socioeconomic status (Diehl, *et al.*, 1985). Socioeconomic status, however, may merely be an indirect marker for other risk factors like obesity and chronic medical conditions. The role of smoking in cholelithiasis is unclear (Paffenberger, *et al.*, 1998). Reduced physical activity heightens the risk of gallstone disease whereas increased physical

activity helps prevent cholelithiasis, independent of its role in weight loss (Leitzmann, *et al*, 1999; Leitzmann, *et al*, 1999). Increased endurance exercise (to 30 minutes 5 times a week) may avert symptomatic gallstones developing in men (Luben, *et al*. 2010).

CHAPTER THREE

STUDY DESIGN AND METHODS

3.1 INTRODUCTION

This Chapter describes the research design used in the study, the study area, the target population, the sampling method used and the statistical analysis.

3.2 STUDY DESIGN

A quantitative, cross-sectional design was adopted for the study. A Cross-sectional design was appropriate because it allowed for the study to be carried out over a short period of time. The cross-sectional design had the advantage of being useful in estimating the prevalence of an outcome of interest (in this case, gallstone) for a given population, commonly for the purposes of public health planning (Bland, 2001). This design also made it possible to collect data on individual characteristics, including exposure to risk factors, alongside information about the outcome (Bland, 2001). In this approach, the study design provided a 'snapshot' of the outcome and the characteristics associated with it, at the time of this study (Bland, 2001).

A questionnaire was thus initially used to collect background data from participants and was later followed by an ultrasound scan procedure to identify the presence or absence of gallstones in consented participants. Information was elicited concerning socioeconomic status, educational level, marital status, reproductive factors, and occupation, tobacco and alcohol habits. Details of the dietary habits were also collected. Symptoms ascertained for gallbladder disease were:

jaundice, pain right upper abdomen after taking food or fatty food, acidity, gases, vomiting, loss of appetite and loss of weight. Participants presenting with these symptoms were considered 'symptomatic'.

3.3 STUDY SITES

The chosen study sites for this study were the Radiology Departments of the Korle-Bu Teaching Hospital, Mamprobi Polyclinic and the Ussher Polyclinic. These are hospitals with patient population of diverse socioeconomic backgrounds. The KBTH is a 2,000 bed capacity hospital that serves the capital city of Ghana; Accra. It also serves as the main referral hospital for the regional and district hospitals. The hospital is the teaching center for the various Schools under the College of Health Sciences, which includes the School of Allied Health Sciences.

The Radiology Department of the KBTH consists of seven units where various radiological investigations are performed by the radiologists and sonographers with the assistance of nurses. The various ultrasound cases referred to the ultrasound laboratory include abdominal, abdominopelvic, obstetrics, pelvic, breast and thyroid, scrotal and Doppler studies.

The Mamprobi Polyclinic is a 50 bed capacity hospital which serves the Mamprobi community and its environs. The majority of the indigenous people in Mamprobi are fishermen and traders. The Radiology Department of the MPC consists of a general radiography unit and an ultrasound laboratory where various ultrasound procedures are performed by sonographers and medical doctors with the assistance of nurses. The various ultrasound cases referred to the ultrasound laboratory include abdominal, abdominopelvic, obstetrics, pelvic, breast, and thyroid, scrotal and Doppler studies.

The Ussher Polyclinic is a 40 bed capacity hospital that serves the James town community and its environs. The majority of the indigenous people in James town are fishermen and fisherwomen. The Radiology Department of the UPC consists of a general radiography unit and an ultrasound laboratory where various ultrasound procedures are performed by sonographers, and medical doctors with the assistance of nurses. The various ultrasound cases referred to the ultrasound laboratory include abdominal, abdominopelvic, obstetrics, pelvic, breast and thyroid, scrotal and Doppler studies. Table 3.1 depicts the number of patients reporting to the radiology department for abdominal ultrasound scan related to right upper quadrant pain of the aforementioned hospitals on daily, weekly and monthly basis.

Table 3.1: Retrospective data on patients reporting for abdominal ultrasound

Frequency	KBTH		Ussher		Mamprobi	
	No.	Percent, %	No.	Percent, %	No.	Percent, %
Daily	10		5		7	
Weekly (5 days)	50		25		35	
Monthly	200		80		100	
Total	260	100.0	110	100.0	142	100.0

3.4 STUDY POPULATION AND SAMPLE SIZE

A sample size of 100 was utilized and this was informed by the retrospective data on the number of patients reporting to the three hospitals for abdominal ultrasound on accounts of right upper

quadrant pain. The convenient sampling technique was adopted to achieve this. This implies that the participants of the study were recruited at the convenience of the researcher.

3.5 INCLUSION AND EXCLUSION CRITERIA

3.5.1 Inclusion Criteria

The study population included all patients referred to the three selected hospitals within the stipulated period of study for abdominal ultrasound scan on account of right upper quadrant (RUQ) pain.

3.5.2 Exclusion Criteria

Patients that presented with cholecystectomy, seriously ill patients, bed ridden patients, patients below 20yrs, mentally retarded and all patients who decided to opt out during the study were excluded. This is because cholecystectomy patients do not have gallbladder whiles bed ridden patients pose difficulty in weight and height measurement. Subjects diagnosed of gallstones without symptoms which usually occur as an incidental finding during an examination for another indication (asymptomatic gallstones) were also excluded. The elimination of patients presenting with asymptomatic gallstones was achieved through the clinical history on the request forms and by a preliminary interview of patients who presented for an abdominal ultrasound scan.

3.6 PROCEDURE FOR DATA COLLECTION

Data collection proceeded with an initial completion of a consent form. A structured questionnaire was also used to solicit information on the socioeconomic status, educational level, marital status, reproductive factors, occupation, life-styles (tobacco and alcohol habits),

ethnicity, diet, gender, age, genetics, obesity and weight loss, period of pain (Pre or post-prandial of fatty food) and acidity of participants. The complexion of respondents was determined using a modified Fitzpatrick (Type VI) scale ranging from fair to dark. The short fat questionnaire was employed to measure participant's fat intake- it is a self-administered and self-coded scale with a high criterion validity ($r=0.55$) and test-retest reliability ($r=0.85$) values.

3.6.1 Pre-Piloting and Piloting of Structured Questionnaires

The nature of the study and the lack of adequate literature on the topic in Africa demanded that the interview questionnaires be structured clearly and simply in order to receive the appropriate responses for the required data. Parahoo (1997) and Hungler (1999) have therefore suggested the use of pre-piloting as a means of streamlining the structure of questionnaires. For this reason, a pre-piloting of the study was conducted.

3.6.1.1 Pre-piloting

Twenty-five questionnaires with 30-items were submitted to the supervisor of the project for pre-piloting for the purposes of testing the reliability of the questionnaire, and also to reduce the risk of bias from incorrect interpretation of words. After pre-piloting, the questionnaire was modified into 27 items.

3.6.1.2 Piloting

Twenty-five of the modified Twenty-five of the modified questionnaires were distributed to patients at the Radiology Department, KBTH, MPC and UPC. This helped reframed some questions before giving them out for the study

3.6.2 Physical Examination of Study Participants

Participants were then examined physically to observe any signs of jaundice and to determine their complexion. With respect to the fat content in their diet, questions were asked on their favorite diet and type/size of meat intake. With respect to alcoholism and smoking, participants were asked rate and duration of alcohol and tobacco intake.

Weight and height measurements were taken in a private area in the ultrasound lab. Weight was measured to the nearest 0.1 kg with subjects in the erect position, using standard weight scale with all accessory items such as shoes, jackets and other heavy objects removed. Height was measured with a portable stadiometer to the nearest 0.1 centimeter. Each participant stood upright on a base plate bare footed with the back straight, feet together and heels touching the back of the plate. The head was adjusted and the head plate of the height measuring tool was lowered to touch the vertex of the head and height recorded. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m²).

This was followed by an abdominal ultrasound scan to ascertain the cause of the right upper quadrant pain. This further helped in determining if gallstones were correlated to any of the above mentioned risk factors.

3.6.3 Abdominal Ultrasound Procedure/Protocol

Tran abdominal ultrasound procedure was explained to participants. The examinations were done in the morning following an overnight fast without sedation. Fasting prevents the contraction of the gallbladder for easy visibility. In accordance with patient management techniques and professional ethics, participants were professionally prepared by changing into

clean gowns and helped onto the sonography couch for the examination. Patients were laid supine with thighs straighten to patient comfort. The ultrasound search was focused on the contents of the gallbladder and the surrounding tissues using convex probe of frequency between 3.5-5.0 MHz Longitudinal and transverse scans of the right upper quadrant was done in both the supine and left lateral positions.

3.6.4 Assessment of Reliability of the Measurement

Sonographically, all the assessed gallbladders were expected to be normally distended. Gallstones were then assessed by their echogenic appearances and by their posterior acoustic shadows. Positional variations during performance of scan were also used to assess mobility of gallstones and to differentiate them from polyps. Since the focus of the study was to determine the presence and not sizes of gallstones, no measurements were taken in this respect.

All sonographic images were then assessed independently by a practicing consultant radiologist at KBTH and a senior sonographer at Ussher and Mamprobi polyclinics. Only those with an unequivocal mass lesion, liver parenchymal involvement or metastasis were diagnosed with gallbladder cancer.

3.7 INSTRUMENTATION

Ultrasound Scan Equipment Toshiba Aplio 300, manufactured in 2005 with linear probe (5.0-11.0) MHz and convex probe (3.5-5.0) MHz, Ultrasound thermal paper, ultrasound gel, weight scale and height measuring tool were used for collecting data. Scalable and versatile, the Toshiba Aplio 300 provides superior image quality with outstanding depth and detail along with enhanced ergonomics and automated features that elevate efficiency to an entirely new level. The

Aplio 300 platinum system is ideal for all routine ultrasound examinations, including general imaging, women's imaging and shared service.

Based on over 40 years of industry-leading experience, Aplio 300 overcomes the challenges of conventional ultrasound with Toshiba's revolutionary High-density Beamformer architecture. Incorporating advanced signal processing capabilities and an array of unique imaging technologies, it quickly and consistently delivers images with exceptional resolution and detail that improves accuracy and increase confidence in clinical decision making. Precision imaging enhances the definition of structures and sharpens borders to separate clinical information from clutter and noise for a more accurate representation of patient anatomy.

Differential Tissue Harmonics (D-THI) overcomes the limitations of conventional Tissue Harmonic imaging by providing improved visualization and definition of lesions, stones, cyst and subtle tissue characteristics while scanning at increased depth and on difficult-to image patients. Toshiba's exclusive Advanced Dynamic flow (ADF) feature employs sophisticated high- resolution, color-flow technology to display the smallest blood vessels and complex blood flow with amazing accuracy.

3.8 DATA MANAGEMENT PLAN

All procedures were conducted with strict adherence to standard protocols. Cross checking of data entries to ensure data capture for accurate analysis adhered to. Research participant were given codes for identification. Data obtained from the study were stored on data collection sheets and transferred unto electronic storage devices in the Department of Radiography (DoR) for easy retrieval in the future by other researchers.

3.9 STATISTICAL ANALYSIS

The data was analyzed using SPSS version 13.0. Double data entry was made to check the consistency. Standard of living index (SLI) was calculated by the weighted sum of consumer durables.

Prevalence was determined for gallstones diseases by considering symptoms, gender and site of study. The association between male and female prevalence was tested using logistic analysis and normal test for proportion (large sample test). Multivariate analysis was performed by logistic regression using all variables which are significant in bi-variate analysis. Chi-square test, as an estimate of relative risk, of GBD and GST, together with their 95% confidence intervals (CI) was obtained by unconditional multiple logistic regression analysis. Models were fitted separately for GBD by gender. All models included specific variables for identifying risk factors for GBD. In logistic analysis, only those variables that are not highly correlated with other independent variables were considered taking into account the importance of the variable.

Data were analyzed separately for males and females, and for symptomatic individuals. Prevalence was determined for GBD, which includes GST, cholecystitis, polyps and GBC. In this mass screening study, ultrasonography findings was treated as standard as histological confirmation was not possible.

3.10 ETHICS

Ethical approval was sought from SAHS (currently School of Biomedical and Allied Health Sciences, SBAHS) Ethics and Protocol Review Committee of the College of Health Sciences,

University of Ghana, Legon. Patient consent was sought prior to the study and it was made clear to patients that they had the right to withdraw at any stage of the study. Permission was sought from the three selected hospitals for the use of their Radiology Departments for the data collection.

3.11 DISSEMINATION OF RESULTS

Results from the study will be disseminated by publication, conference and seminar presentations. Hard copies of the dissertation will be delivered to Department of Radiography, SBAHS library and soft copies on search engines like pub med.

CHAPTER FOUR

RESULTS

4.1 INTRODUCTION

This Chapter presents the results of the study conducted to determine the prevalence and risk factors of gallstones in patients presenting with right upper quadrant abdominal pain. The results are presented in accordance with the stated objectives of the study and include key aspects such as demographics characteristics, parity, risk factors and gallstones.

4.2 DEMOGRAPHIC CHARACTERISTICS

4.2.1 Response Rate

One hundred patients reporting to the three study sites and presenting with abdominal ultrasound related to right upper quadrant pain were recruited for the study (Table 3.1). All of them consented to participation following compliance with participation protocols and ethics. Hence a 100% response rate was achieved for the study.

The age, gender and marital demographics of the participants are presented in Table 4.1. In Table 4.1, the ages of the respondents ranged from 20 – 69 years with a mean age of 20.88 ± 4.33 years. Majority ($n=46$, 46%) of the respondents were aged 20 – 29 years, while the 50-59 years group were least ($n=10$, 10%) represented.

4.2.2 Age, Gender and Marital Demographics

Table 4.1: Distributions for demographic characteristics of respondents

		Frequency	Percent
Demographic variable	Group		
Age (yrs)	20-29	46	46.0
	30-39	15	15.0
	40-49	12	12.0
	50-59	10	10.0
	60-69	17	17.0
	Total	100	100
Mean age: 20.88 ± 4.33			
Gender	Male	28	28.0
	Female	72	72.0
	Total	100	100.0
Marital status	Single	40	40.0
	Married	60	60.0
	Total	100	100

There were more females (72%) in the study compared to males (28%), and most (60%) of the respondents were married.

The educational demographics are shown in Table 4.2. The educational level of majority of the respondents was low. In particular, 85% ($n=85$) had studied up to the SSS level, while a fewer number had gained tertiary education up to the BSc ($n=14$, 14%) and MSc ($n=1$, 1%) levels respectively.

Table 4.2: Distributions for demographic characteristics of respondents

Demographic variable	Group	Frequency	Percent, %
Education	Primary	2	2.0
	JSS	43	43.0
	SSS	40	40.0
	Tertiary-undergraduate	14	14.0
	Tertiary-postgraduate	1	1.0
	Total	100	100.0
Occupation	Formal	19	19.0
	Informal	59	59.0
	Unemployed	22	22.0
	Total	100	100.0
Ethnicity	Akan	39	39.0
	Ga	24	24.0
	Mole-Dagbon	19	19.0
	Ewe	18	18.0
	Total	100	100.0

The results further showed that more respondents ($n=59$, 59%) worked in the informal sector while 22% were unemployed. On the basis of ethnicity, more than a third ($n=39$, 39%) of the respondents were Akans and 24% were Gas. The least represented of the four ethnic groups were Ewes ($n=18$, 18%).

4.2.3 Distributions for respondents Parity

The histogram of Figure 4.1 shows the parity distribution of respondents. Most of the respondents 43% had no child, 33% had 1-3 children while only 2% had more than 9 children.

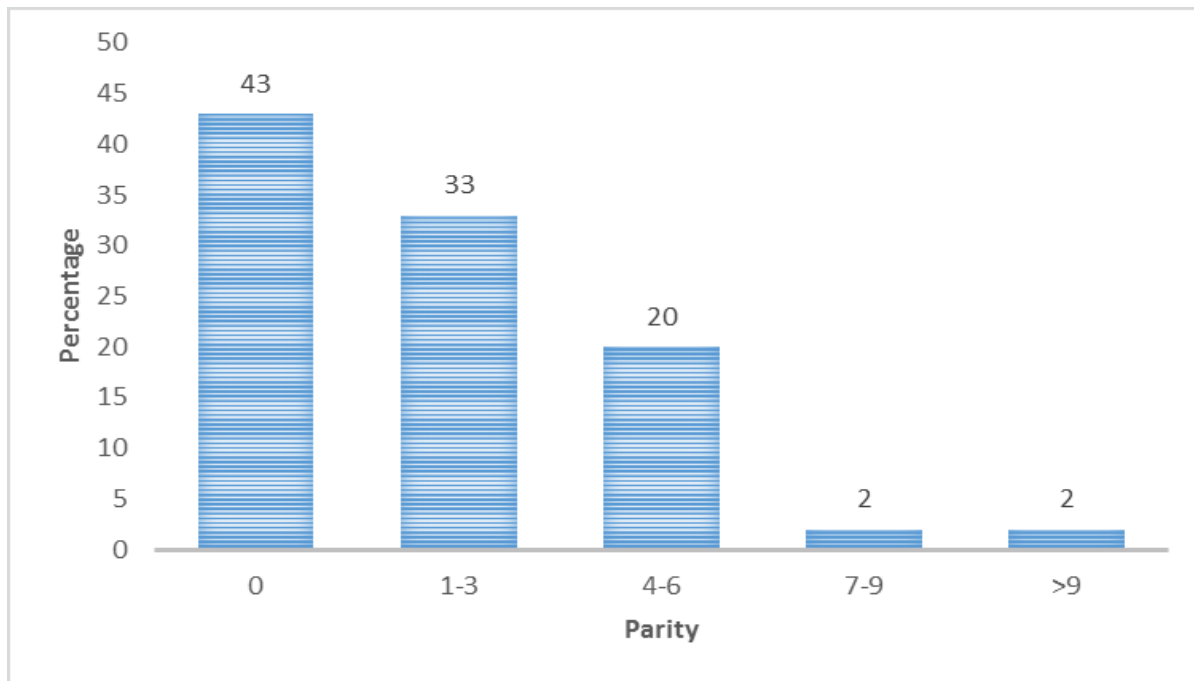


Fig. 4.1: Parity distribution of respondents

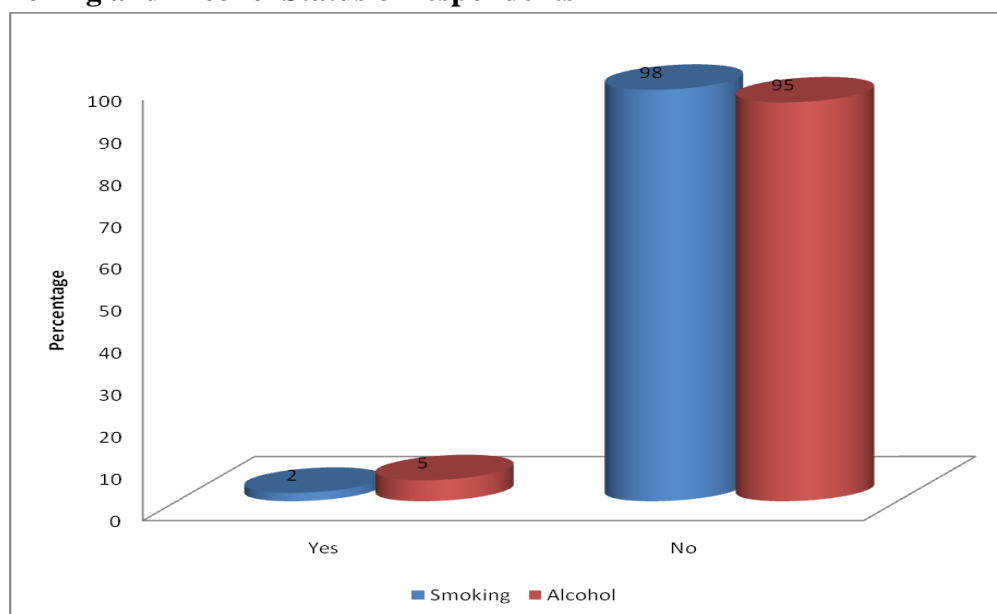
4.3 RISK FACTORS OF GALLSTONES

The distributions of risk factors associated with GSD are presented in Table 4.3. The results of Table 4.3 indicated that more than half of the respondents, ($n=56$, 56%) were on moderate fat diet and 32% on high fat diet. Majority of the respondents ($n=67$, 67%) drank purified water while an appreciable number ($n=22$, 22%) indicated drinking both pipe born and purified water. With respect to the diabetic status of the patients, only 11% were diabetic while the greater majority ($n=89$, 89%) were non-diabetic. The results of the sickling survey established that 67% presented with AA sickling status while 3 (3%) were SC. About half (48%) of the respondents were fair skinned.

Table 4.3: Distribution for risk factors of Gallstones

Risk Factors	Frequency, (%)	Frequency, (%)	Frequency, (%)	Total	
Diet	Low fat 12, (12.0)	Moderate fat 56, (56.0)	High fat 12, (12.0)	100	
Source of Water	Pipe borne 11, (11.0)	Purified 67 (67.0)	Pipe born and purified 22, (22.0)	100	
Diabetic Status	Diabetic 11, (11.0)	Non-diabetic 89, (89.0)		100	
Sickling Status	AA 67 (67.0)	AS 25, (25.0)	SC 3 (3.0)	SS 5, (5.0)	100
Complexion	Fair 48, (48.0)	Dark 29, (29.0)	Chocolate 23, (23.0)	100	

4.3.1 Smoking and Alcohol Status of respondents

**Figure 4.2: Drinking and smoking status of respondents**

A relatively small number of the respondents either drank alcohol ($n=5$, 5%) or smoked ($n=2$, 2%). The distribution is illustrated in Fig.4.2.

4.3.2 Body Mass Index

Table 4.4: Distributions for BMI categories of respondents

	Classification	BMI (kg/m ²)	Percent
	Underweight	< 18.5	23.0
BMI (kg/m ²)	Normal	18.5 - 24.9	61.0
	Overweight	25.0 - 29.9	14.0
	Obese	> 30.0	2.0
Average BMI (kg/m ²)	28.52 ±3.48		

The BMI of respondents were classified using the WHO standard of classification. Underweights were respondents with weight < 18.5 kg/m²; normal is 18.5-24.9 kg/m²; overweight is 25-29.9 kg/m² and obese is 30 kg/m² and above. The literature indicates that overweight was a pre-cursor to gallbladder stone disease. Majority of the respondents 61% had a normal weight, 23% were underweight while only 2% were obese. This is shown in Table 4.4.

4.4 PREVALENCE OF GALLSTONES

Table 4.5 shows the distributions of respondents on various aspects of Gallstones. The study shows a high prevalence of Gallstones of 42% among the respondents. Also 16% had single stones while 26% had multiple stones. More than half of the respondents, 57% have had pain for 5-9 weeks and 7% have had it for 15-19 weeks. All the stones 42 (100%) were hyperechoic. None of the respondents ($n=0$, 0%) had gallbladder cancer though 1 (1%) had renal stones.

Table 4.5: Distribution for the various aspects of gallstones

Gallstones		Frequency	Percent
Presence of stones	Yes	42	42.0
	No	58	58.0
	Total	100	100.0
Number of stones	Single	16	38.0
	Multiple	26	62.0
	Total	42	100.0
Duration of pain	1 - 4 weeks	25	25.0
	5 - 9 weeks	57	57.0
	10 – 14 weeks	11	11.0
	15 - 19 weeks	7	7.0
	Total	100	100
Echogenecity	Hyperechoic	42	42.0
	N/A	58	58.0
	Total	100	100
Gallbladder disease	Acalculus Cholecystitis	2	2.0
	Cholecystitis	4	4.0
	Gallbladder Polyp	2	2.0
	N/A	92	92.0
	Total	100	100
Gallbladder cancer	Yes	0	0.0
	No	100	100
	Total	100	100
Renal stones	Yes	1	1.0
	No	99	99.0
	Total	100	100
Symptomatic	Yes	100	100.0
	No	0	0.0
	Total	100	100

4.5 COMPARISON OF PREVALENCE OF GALLSTONES AMONG THE VARIOUS SITES

Table 4.6: Association between site of the study and presence of gallstones

Site	Gallstones			χ^2	<i>p</i> -value
	Yes	No	Total		
Usher	17 (56.7)	13 (43.3)	30 (100)	3.913	0.142
MPC	10 (33.3)	20 (66.7)	30 (100)		
KBTH	15 (37.5)	25 (62.5)	40 (100)		
Total	42 (42.0)	58 (58.0)	100 (100)		

*Significant at 5%

There was no association between the site of the study (Usher, MPC and KBTH and the presence of gallstones ($p=0.142$). However, usher polyclinic reported the highest prevalence of gallstones ($n=17, 56.7$), KBTH had 37.5 while MPC had the least 33.3% prevalence.

Table 4.7: Association between duration of pain and presence of gallstones

Duration of Pain weeks	Gallstones			χ^2	<i>p</i> -value
	Yes	No	Total		
1-4	4 (16.0)	21 (84.0)	25 (100)	28.9	0.001*
5-9	21 (36.8)	36 (63.2)	57 (100)		
10-14	10 (90.9)	1 (9.1)	11 (100)		
15-19	7 (100.0)	0 (0.0)	7 (100)		
Total	42 (42.0)	58 (58.0)	100 (100)		

*Significant at 5%

The study showed a significant association between the duration of pain and gallstones ($p=0.001$). There was a steady increase in the presence of gallstones with a corresponding increase in duration of pain. All 7 (100%) those who have experienced pain for 15-19 weeks had gallstones, 10 (90%) for those with pain for 10-14 weeks, 21 (36.8%) for those with pain for 5-9 weeks while the least gallstones ($n=4$, 16%) was found in those with duration of pain of 1-4 weeks.

Table 4.8: Association between BMI classification and presence of gallstones

BMI Classification	Gallstones		Total	χ^2	<i>p</i> -value
	Yes	No			
Underweight	8 (34.8)	15 (65.2)	23 (100)		
Normal	28 (45.9)	33 (54.1)	61 (100)	2.326	0.508
Overweight	6 (42.9)	8 (57.1)	14 (100)		
Obese	0 (0.0)	2 (100)	2 (100)		
Total	42 (100)	58 (100)			

*Significant at 5%

There was no association between BMI classification of respondents and the presence of gallstones ($p=0.508$). However, most respondents with gallstones ($n=28$, 45.2%) had normal BMI and none of those who were obese had gallstones. Also, 42.9% of those overweight had gallstones while 34.8% of those underweight had gallstones.

From Table 4.9, There was a significant association between the sickling status of respondents and the presence of gallstones ($p=0.042$). The prevalence was high ($n=4$, 80%) among those with genotype SS while none 0% was reported among those with genotype SC.

Table 4.9: Association between sickling status classification and presence of gallstones

Sickling status	Presence of gallstones			χ^2	<i>p</i> -value
	Yes	No	Total		
AA	24 (35.8)	43 (64.2)	67 (100)		
AS	14 (56.0)	11 (44.0)	25 (100)		
SC	0 (0.0)	3 (100)	3 (100)	8.198	0.042*
SS	4 (80.0)	1 (20.0)	5 (100)		
Total	42 (42.0)	58 (58.0)	100 (100)		

*Significant at 5%

More than half of the respondents 56% with AS genotype had gallstones while 35.8% of respondents with AA genotype had gallstones.

Table 4.10: Association between diabetic status classification and presence of gallstones

Diabetic Status	Presence of gallstones			χ^2	<i>p</i> -value
	Yes	No	Total		
Diabetic	8 (72.7)	3 (27.3)	11 (100)		
Non Diabetic	34 (38.2)	55 (61.8)	89 (100)	4.97	0.032*
Total	42 (42.0)	58 (58.0)	100 (100)		

*Significant at 5%

There was a significant association between diabetic status of respondents and presence of gall bladder stones ($p=0.032$). The prevalence was higher ($n=8$, 72%) among persons living with

diabetes compared with those without diabetes 38.2%. Persons living with diabetes had 4 times risk of developing gallstones compared with persons without diabetes (OR=4.31).

4.6 GENDER DISTRIBUTION OF GALLSTONES

Table 4.11: Association between Gender and Gallstones

Gender	Yes	No	Total	χ^2	<i>p</i> -value
Male	8 (28.6)	20 (71.4)	28 (100.0)		
Female	34 (47.2)	38 (52.8)	72 (100)	2.879	0.090
Total	42 (42.0)	58 (58.0)	100 (100.0)		

*Significant at 5%

In this study, 28.6% of the males had gallstones compared with 47.2% of the females. This seems to suggest that females have more gallstones compared with males. However, there was no significant association between sex of the respondents and gallstones ($\chi^2 = 2.879$; $p=0.090$).

4.7 AGE DISTRIBUTION OF GALLSTONES

Table 4.12: Association between Age Group and Gallstones

Age group	Yes	No	Total	χ^2	<i>p</i> -value
20-29	20 (43.5)	26 (56.5)	46 (100)		
30-39	8 (53.3)	7 (46.7)	15 (100)		
40-49	3 (25.0)	9 (75.0)	12 (100)	2.277	0.685
50-59	4 (40.0)	6 (60.0)	10 (100)		
60-69	7 (41.2)	10 (58.8)	17 (100)		
Total	42 (42.0)	58 (58.0)	100 (100)		

*Significant at 5%

In this study, there was no association between presence of gallstones and age of respondents. However, more than half of the respondents 53.3% in age group 30-39 years had gallstones, 43.5% of respondents in age group 20-29 years also had gallstones. Only a quarter of respondents in age group 40-49 had gallstones while 41.2% of respondents in age group 60-69 years had gallstones. However, there was no significant association between age of the respondents and gallstones ($\chi^2= 2.277$; $p=0.685$).

4.8 FAT INTAKE, SMOKING AND ALCOHOL DISTRIBUTION OF GALLSTONES

Table 4.13: Association between Fat intake, smoking, alcohol and Gallstones

Alcohol Intake	Gallstones			χ^2	p-value
	Yes	No	Total		
Yes	2 (40.0)	3 (60.0)	5 (100)	0.009	0.926
No	40 (42.1)	55 (57.9)	95 (100)		
Total	42 (42.0)	58 (58.0)	100 (100)		
	Smoking Status				
Yes	2 (100.0)	0 (0.0)	2 (100)	2.818	0.093
No	40 (40.8)	58 (59.2)	98 (100)		
Total	42 (42.0)	58 (58.0)	100 (100)		
	Fat Intake				
Low	3 (25.0)	9 (75.0)	12 (100)	3.219	0.200
Moderate	22 (39.3)	34 (60.7)	56 (100)		
High	17 (53.1)	15 (46.9)	32 (100)		
Total	42 (42.0)	58 (58.0)	100 (100)		

*Significant at 5%

There was no significant association between respondents alcohol intake, smoking status, fat intake and presence of gallstones ($p >0.05$). Forty percent (40%) of the respondents who take alcohol had gallstones while 42.1% of respondents who do not take alcohol had gallstones. Also,

all respondents who smoke (100%) had gallstones while 40.8% of those who do not smoke had gallstones. The study also showed that respondent who smoked had 2.4 times risk of developing gallstones. There was a steady rise in the proportion of respondents who have gallstones and level of fat intake. More than half of respondents 53.1% with high fat intake had gallstones while only a quarter of those with low fat intake had gallstones. This is shown in Table 4.12.

CHAPTER FIVE

DISCUSSION

5.1 INTRODUCTION

This Chapter discusses the findings of the study in relation to literature reviewed on a study to determine the prevalence and risk factors associated with symptomatic gallstones. The findings are discussed in accordance with stated aim and objectives of the study. The study sought to determine the prevalence of symptomatic gallstones amongst Ghanaians in Accra; identify risk factors associated with gallstones and determine the most common predisposing factors to gallstones.

5.2 DESCRIPTIVE CHARACTERISTICS OF THE STUDY

All the stones detected ultrasonographically in this study were hyper echoic in nature. Most respondents had experienced the pain more than 5 weeks. Most of the respondents ($n=46$, 46%) were in the early youthful age group of 20-29 years and quite a few of them ($n=17$, 17%) were over 60 years. The least proportion 10% was found among the 50-59 years age group. The age distribution of those reporting for gallstones investigation was not in agreement with most studies because older age is identified as a risk factor to gallstones prevalence. Most respondents (60%) in this study were married.

However, the educational level of respondents in this study was generally poor as only 14% had first degree while 83% had SSS and JSS level education. More than half of the respondents 59%

worked in the informal sector though 22% were unemployed. This may also be attributed to the level of education of respondents as formal sector employment is mainly based on the educational level of respondents. Ethnicity among the respondents was evenly represented in the study though most of the respondents were Akans and Gas, the general ethnic distribution of the nation shows that the most common and populous ethnic group is Akan. The distribution of the Gas may be due to the fact that the study was conducted in the Greater Accra Region which is predominantly a Ga community. A large proportion of the respondents ($n=43$, 43%) had 1-3 children and 43% ($n=43$, 43%) had no child. According to 2010 census most Ghanaian families are small in size (GSS, 2011). The large proportion of respondents without children could also be attributed to the young age distribution of the respondents in the study. Eleven percent (11%) prevalence of diabetes observed in this study is quite high compared to the national prevalence of 6.4% as indicated by Amoah *et al.* (2002), 9% Addo *et al.* (2009) 8% as reported by Cook-Huynh *et al.* (2012). Most of the respondents 67% were also AA in terms of sickling status and only a small proportion 35% were SC. In terms of complexion, approximately 48% of the respondents were fair. The proportion of respondents taking alcohol and those smoking was low in this study. Only 5% and 2% of the respondents drank alcohol and smoke respectively.

5.3 RISK FACTORS OF GALLSTONES

In this study, 56 % ($n=56$, 56%) of the respondent in the study were predominantly on moderate fat diet and 32% were on high fat diet. Also, 67 % ($n=67$, 67%) of the respondents drank purified water while 22% drank untreated water. In this study, diabetes was significantly associated with gall bladder stones ($p=0.032$). Diabetes was found to be significantly associated with gallstones. The prevalence of 72% gallstones was very high among persons living with diabetes with a risk 4 times compared with those without diabetes. This finding has been suggested by some

researchers. Gallstone development is associated with common metabolic disorders such as, obesity, diabetes mellitus and dyslipidemia which supports the hypothesis that gallstone disease is part of the metabolic syndrome (Ruhl, Everhart, 2002; Mendez-Sanchez *et al*, 2005). The association between diabetes mellitus and gallstones may be explained by the pathophysiological link between insulin resistance and gallstone development, the increase of cholesterol saturation in gallbladder bile further relate to an increase in body cholesterol synthesis and hypersecretion of biliary cholesterol as observed in obesity (Shaffer 2005; Attili *et al*, 1997). The current finding is also supported by several epidemiological studies (Attili *et al*, 1997; Chapman *et al*, 1996; Pagliarulo *et al*, 2004; De Sautis *et al*, 1997; Cheu *et al*, 2006). However, the finding is still in contention since other studies found no association between gallstones and diabetes mellitus (Meudez- Saudez *et al*, 2005; Perssou & Thulin, 1991; Kono *et al*, 1992).

Further, the study did not find any association between alcohol and smoking. The literature has conflicting reports regarding smoking as a predisposing factor. It has been suggested that smokers are protected against the development of gallstones through a mechanism which leads to a decrease in prostaglandin synthesis and mucus production in the gallbladder epithelium (Rhodes & Venables, 1991) while another study by Stampfer *et al*. (1992) concluded that smoking was an independent risk factor in women who heavily engage in it (>35 cigarettes/day). In a large British cohort study, smoking was identified as an important risk factor for developing symptomatic gallstone disease (Murray *et al* 1994). Late occurring cases seem to have a different relation to the exposure factor than early cases (Mc-Michael *et al* 1992). Again, alcohol consumption has been shown to be associated with a lower prevalence of symptomatic gall bladder stones (Friedman *et al*, 1966; Maclure *et al*, 2001) as well as asymptomatic gallstone

disease (La Vecchia *et al*, 1991; Stampfer *et al*, 1992; Volzke *et al*, 2005; La Vecchia *et al*, 2005) and the intake of alcoholic beverages was inversely related to the risk of cholecystectomy (Leitzmann *et al*, 1999). A large prospective study in men showed an inverse relation of alcohol beverage to symptomatic gallstone disease, but interestingly, the association was not present when consumption was less than 1-2 days a week (Leitzmann *et al*, 1999). Another large study from Germany found no relation to alcohol consumption (Leitzmann *et al*, 1997). The study did not find any association between the prevalence of gallstones and the three sites of study.

Leitzmann *et al*, (1997) also established a significant association between duration of pain and gallstones. The prevalence of gallstones was higher in respondents who had experienced pain for longer periods however; the BMI of respondents was not associated with the presence of gallstones (Leitzmann *et al*, 1997). Contrary to other findings, gallstones were more prevalent in respondents with normal BMI in the current study.

Several studies identify obesity as a major risk factor for developing gallstones (Shaffer, 2005; Angelico *et al* 1997, Jorgensen 1988, Attili *et al*,1997; Kodama *et al*, 1999; Torgerson *et al*, 2003; La Vecchia *et al*, 1991). Rapid weight loss is also associated with an increased risk of developing gallstones (Torgerson *et al*, 2003).

Sickling status of respondents showed an association between gallstones and their status. It was higher in respondents who had SS sickling status while none was found in those who were SC. This finding is consistent with other studies: Rennels *et al* (1984) performed sonographic tests on 65 patients with major sickle hemoglobinopathies. Cholelithiasis was found in 26% of patients with hemoglobin SS, in 20% with Hb SC, and in 12.5% of patients with Hb S- β -thalassemia.

Another study by Lachman, et al (1979) ascertained the prevalence of Cholelithiasis among sickle cell disease patients. An Overall prevalence of gallstones was found to be 29%. Sarnaik *et al* (2000) reported a gallstone prevalence rate of 27% among patients with sickle cell hemoglobinopathy. Bond *et al* (1987) studied the prevalence of gall stones by abdominal ultrasound examination in 131 patients with sickle cell disease. 58% had gallstones. Gall stones were present in 17% of patients with haemoglobin S + C disease and 17% with haemoglobin S beta thalassaemia.

Regarding gender, there was no significant association with gallstones however the results depicted that 28.6% of male participants had gallstones while 47.2% of female participants had gallstones. Worldwide prevalence of gallstones in females based on ultrasonographic surveys varies (Everhart *et al.*, 2002, Shaffer, 2005, Miquel *et al.*, 1998). In contrast, White Americans have an overall prevalence of 16.6% in women and 8.6% in men (Everhart, 2001). The explanation to the above facts is that the female gender has a most compelling association with gallstone disease, especially during the fertile years.

Women are almost twice as likely as men to form stones; the gap narrows following menopause after which men begin to catch up (Einarsson *et al.*, 1985). Etminamm, *et al.*, (2011) have attributed the difference in female and male to female sex hormones, parity, oral contraceptive use and estrogen replacement therapy as established risk factors for cholesterol gallstone formation. Female sex hormones adversely influence hepatic bile secretion and gallbladder function. Estrogens increase cholesterol secretion and diminish bile salt secretion, while progestins act by reducing bile salt secretion and impairing gallbladder emptying leading to stasis. Again, a new 4th generation progestin, drospirenone, used in some oral contraceptives

may further heighten the risk of gallstone disease and cholecystectomy; however, the increased risk is quite modest and not likely to be clinically meaningful (Etminamm, *et al.*, 2011). In all, the most common predisposing factor to gallstones formation was high cholesterol diet intake.

5.4 PREVALENCE OF GALLSTONES

The study showed high prevalence (42%) of gallstones among respondents of which 60% were multiple stones. According to some studies (Shaffer, 2006; Afdhal, 1999; Kratz, Mason, & Kachele, 1999) gallstones appeared to be most prevalent among American Indians (60-70%), but lower in Hispanics of mixed Indian origin and much lower amongst African Americans. Contrary to the findings of this study, Diel (1991) purported a prevalence of approximately 10-15% and 20% among Men and women in Europe and North America (Caucasians). Borch *et al.*, (1998) also reported high prevalence of gallstones in Scandinavia and other Northern European countries, but low in sub-Saharan Africa and Asia (Massarat, 2001). In addition, the assertion of Massarat (2001) that the prevalence in sub-Saharan Africa and Asia were lower is contrary to the findings of this study. The high prevalence rate in Ghana (sub-Saharan Africa, 42%) compared to the prevalence rates in other sub-Saharan African countries could be due to the rapid change in dietary pattern, and increase use of contraceptives in the sub-region. Hence, more rigorous investigations should be conducted to identify the major risk factors associated with gallstones in Ghana.

CHAPTER SIX

CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS

6.1 INTRODUCTION

This Chapter summarizes all the findings and presents the conclusion, recommendation as well as the limitations of the study.

6.2 CONCLUSION

In these three selected hospitals study, the prevalence of gallstone disease was 47.2% among females and 28.6 % among males. The total prevalence of gallstones was 42%.The prevalence rose with increasing age and was higher among females. There was a positive relation of fat intake to gallstone development. Furthermore, there was an inverse association between alcohol and tobacco consumption to gallstone prevalence. There was a strong association between the duration of right upper quadrant abdominal pain to gallstone development. Sickling status of respondents showed an association between gallstones and their status. It was higher in respondents who had SS sickling status while none was found in those who were SC. Most of the subjects with gallstones were fair in complexion.

6.3 RECOMMENDATIONS

Considering the aim of the study, this is to determine the prevalence and risk factors of symptomatic gallstones among Ghanaian patients in three hospitals in the Greater Accra region, it is recommended that:

1. A nationwide screening program for gallstones should be designed and implemented for the early identification and detection of the disease.
2. Health policy makers/officials, government and all stake holders aid in the education and sensitization of the public on predisposing/risk factors such as obesity, sickling, diabetes, gender, age, high cholesterol diet etc
3. Future studies should focus on the prevalence of gallstone disease in remote regions in Ghana, asymptomatic patients to provide a more comprehensive data on gallstone disease among Ghanaians.
4. Patients with gallstones should have pre-operative bilirubin and liver function tests including alkaline phosphate and GGT
5. Asymptomatic patients with gallstones should be observed for the development of right upper quadrant pains (symptoms)

6.4 LIMITATIONS

The main limitation encountered was inadequate literature from Ghana; most of the literature was thus obtained from studies conducted in the United States, Scandinavia and other developed countries. There is little work done on the study in Ghana. Limited resources and time were other constraints that could not allow for larger study sample than what was used. Finally most of the eligible respondents were bedridden so could not answer to weight and other demographic questions and so was excluded from the study. In spite of these limitations, the study although an exploratory one, has helped to bring to the fore, the prevalence and risk factors to gallbladder stone development.

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APPENDIX I

INFORMATION SHEET

PREVALENCE AND RISK FACTORS OF SYMPTOMATIC GALLSTONES

USING ULTRASONOGRAPHY

Purpose of the study

The purpose of the study is to assess the prevalence and risk factors of gallstones among Ghanaians in the greater Accra metropolis. This will help Ghanaians identify the diets and other lifestyle that could pose as risk to the development of gallstones so as to avoid them.

Study procedure

Patients referred for abdominal ultrasound scan with respect to right flank pain at KBTH, Ussher polyclinic and mamprobi polyclinic will be recruited for the study. A questionnaire will be given to them by the investigator to fill their demographic data after which ultrasound scan of the upper abdomen will be done to ascertain the cause of the right flank pain. Patients will have to fast for at least 2 hours before ultrasound scan of the gallbladder.

Risk to the patient

The procedure may cause thermal burns but these rarely occur. There is however, no documented long term effect to the patient. Thermal risk can be prevented by using optimum scan time by adhering to the principles of ALARA (As low as Reasonably Achievable)

Patient's right

The patient has the right to withdraw from the study at any time. The patient will receive the normal treatment as other patients at the department. The patient will not pay for the examination throughout the period of the study. Any ethical violation by the investigator can be reported to the SAHS Ethical and protocol review Committee, College of Health Sciences, University of Ghana. Hereafter you will be known by a code. If you have any concerns about this study and wish to contact someone independently, you may contact the under-listed members of the Dissertation Advisory Team (DAT):

Dr. V.K. Hewlett, 0274649759.

Mr. L. Arthur, 0233510104.

School of Allied Health Sciences, College of Health Sciences

University of Ghana, P.O.Box KB 14 Korle Bu. Accra.

APPENDIX II

INFORMED CONSENT FORM

DEPARTMENT OF RADIOGRAPHY
SCHOOL OF ALLIED HEALTH SCIENCES
COLLEGE OF HEALTH SCIENCES
UNIVERSITY OF GHANA

Title of Project: **PREVALENCE AND RISK FACTORS OF GALLBLADER STONES
USING ULTRASONOGRAPHY.**

Name of Researcher: **ERIC SAKA BOATENG**

Confidentiality: All data will be confidentially and anonymously handled. At any stage of the research you have right to opt out.

Iconsent to participate in the above named research project. The purposes of the research have been explained and I understand also that my participation is entirely voluntary and that there is no personal benefit to me via my participation.

Signature/ thumb print of participant

Witnessed by-----

Signature of investigator-----

Date-----

APPENDIX III**DATA COLLECTING SHEET (QUESTIONNAIRE)****Section A: Demographics**

Patient Code Number	-----
Age	-----Yrs
Sex (Male/Female)	-----
Marital Status	Single/married
Parity	-----
Educational Background	-----
Occupation	-----
Favorite Diet	-----
Water Consumption	Pipe born Water/Purified Water
Weight	-----Kg
Height	-----
Body Mass Index	-----kg ----- Meters
Diabetic Status-Diabetic/Non Diabetic	
Ethnicity	-----
Sickling Status	AA / AS/ SS/ Sc

Alcoholic Beverage intake

Yes/No

If yes, for how long

Physical Observation

COMPLEXION

PAIN DURATION

Section B: Gallbladder Ultrasound

Stone Presence Yes/No

If Yes Single/Multiple

Echogenicity of Stone

Symptomatic/Asymptomatic

Other Gallbladder Disease

Gall Bladder Cancer

Other stones (Renal /ureteric)

APPENDIX IV

SONOGRAPHIC IMAGES OF THE GALL BLADDER

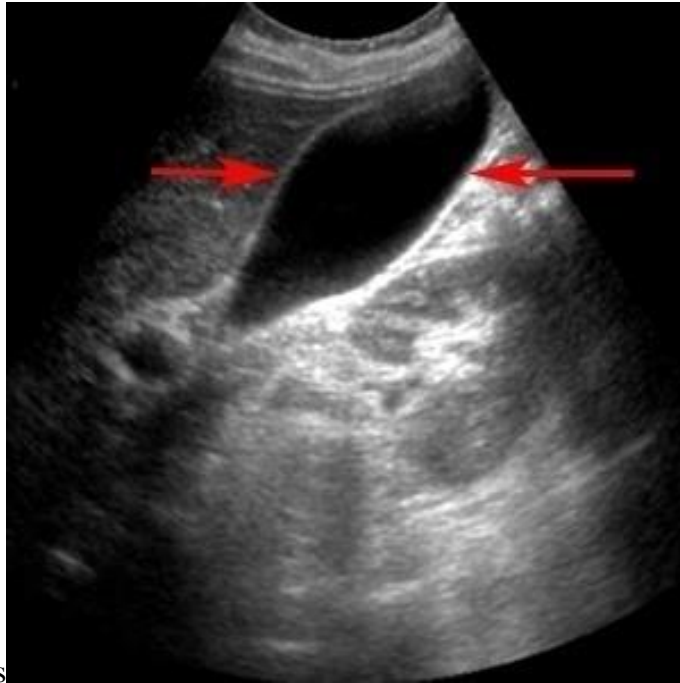


Fig. 1: Normal appearing gallbladder indicated between arrows. Source: Emergency ultrasound, university of virgina, 2003

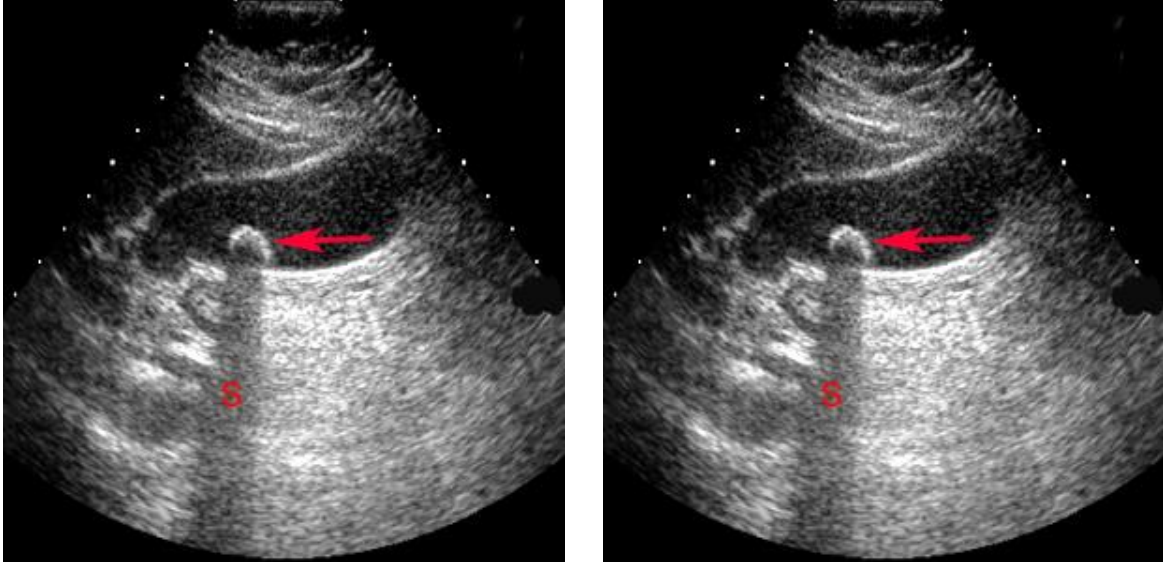


Fig.2: Gallstone (red arrow) within the gallbladder produces a bright surface echo and causes a dark acoustic shadow (S).

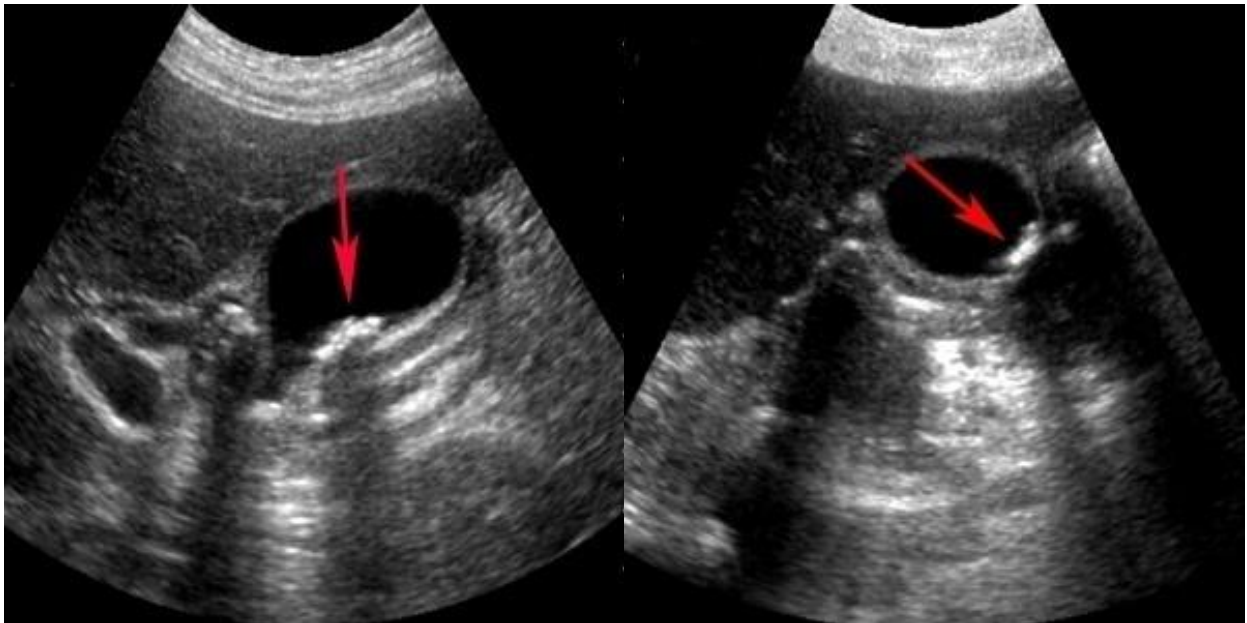


Fig. 3: Rolling stone sign - movement of gallstones with GB with position change
Source: Emergency ultrasound, university of virgina, 2003



Fig. 4: Image through the long axis of the GB (GB) demonstrate the gallbladder neck (red arrow) GB wall thickness is measured between the gallbladder lumen and the hepatic Parenchyma (arrowheads) with normal thickness. Source: Emergency ultrasound, university of virgina, 2003

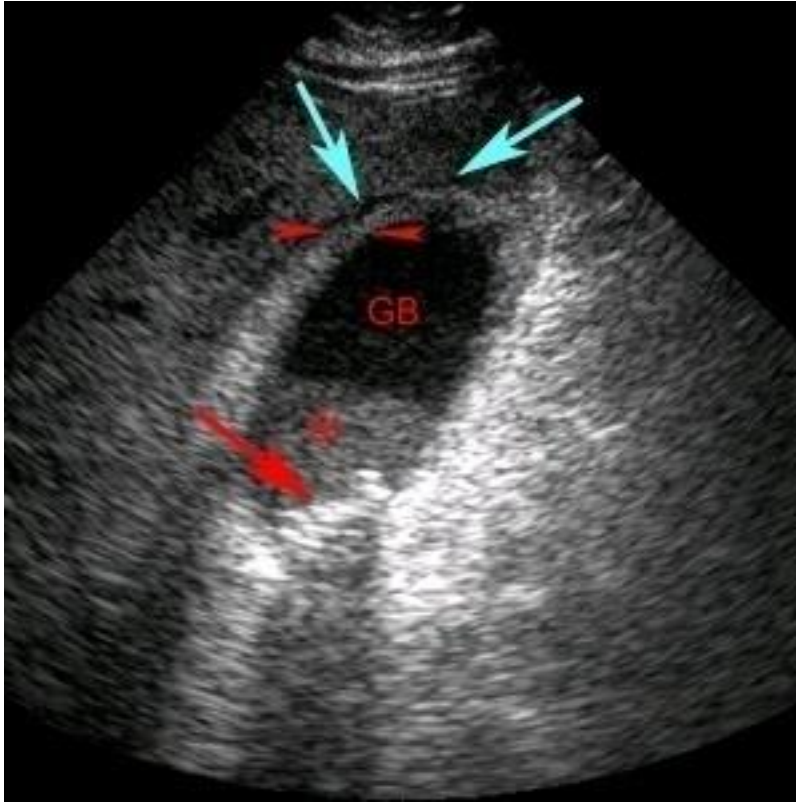


Fig.5: The gall bladder (GB) is filled with echogenic sludge (SI) and a gallstone (red arrow) is impacted in the gallbladder neck. The gallbladder wall (red arrow heads) is markedly thickened indicative of wall edema and there are pericholecystic fluid (blue arrow) pockets surrounding the gallbladder. Source: Emergency ultrasound, university of virgina, 2003

APPENDIX V-ETHICAL CLEARANCE

**SCHOOL OF ALLIED HEALTH SCIENCES
COLLEGE OF HEALTH SCIENCES
UNIVERSITY OF GHANA
ACADEMIC AFFAIRS**

**Phone: +233-0302-687974/5
Fax: +233-0302-688291**

**My Ref. No. SAHS/ 10070339
Your Ref. No.**



P. O .Box KB 143
Korle Bu
Accra
Ghana

2nd April, 2014.

Mr. Eric Saka Boateng,
Dept. of Radiography,
SAHS,
Korle Bu.

Dear Mr. Boateng,

ETHICS CLEARANCE

Ethics Identification Number: SAHS – ET. /10070339/AA/2A/2013-2014.

Following a meeting of the Ethics and Protocol Review Committee of the School of Allied Health Sciences held on Monday 24th March, 2014, I write on behalf of the Committee to approve your research proposal as follows:

TITLE OF RESEARCH PROPOSAL: "Prevalence and Risk Factors of Gallbladder Stone Disease Using Ultrasonography"

This approval requires that you submit six-monthly review reports of the protocol to the Committee and a final full review to the Committee on completion of the research. The Committee may observe the procedures and records of the research during and after implementation.

Please note that any significant modification of the research must be submitted to the Committee for review and approval before its implementation.

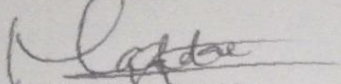
You are required to report all serious adverse events related to this research to the Committee within seven (7) days verbally and fourteen (14) days in writing.

As part of the review process, it is the Committee's duty to review the ethical aspects of any manuscript that may be produced from this research. You will therefore, be required to furnish the Committee with any manuscript for publication.

Please always quote the ethical identification number in all future correspondence in relation to this protocol.

Thank you.

Yours sincerely,



Dr. Michael Mark Addae
(Chairman, Ethics and Protocol Review Committee)

cc Dean
 Co-ordinator/HoD, Dept. of Radiography
 Senior Assistant Registrar

APPENDIX VI-IMAGES FROM THE FIELDWORK



Source: Field work



Source: Field work



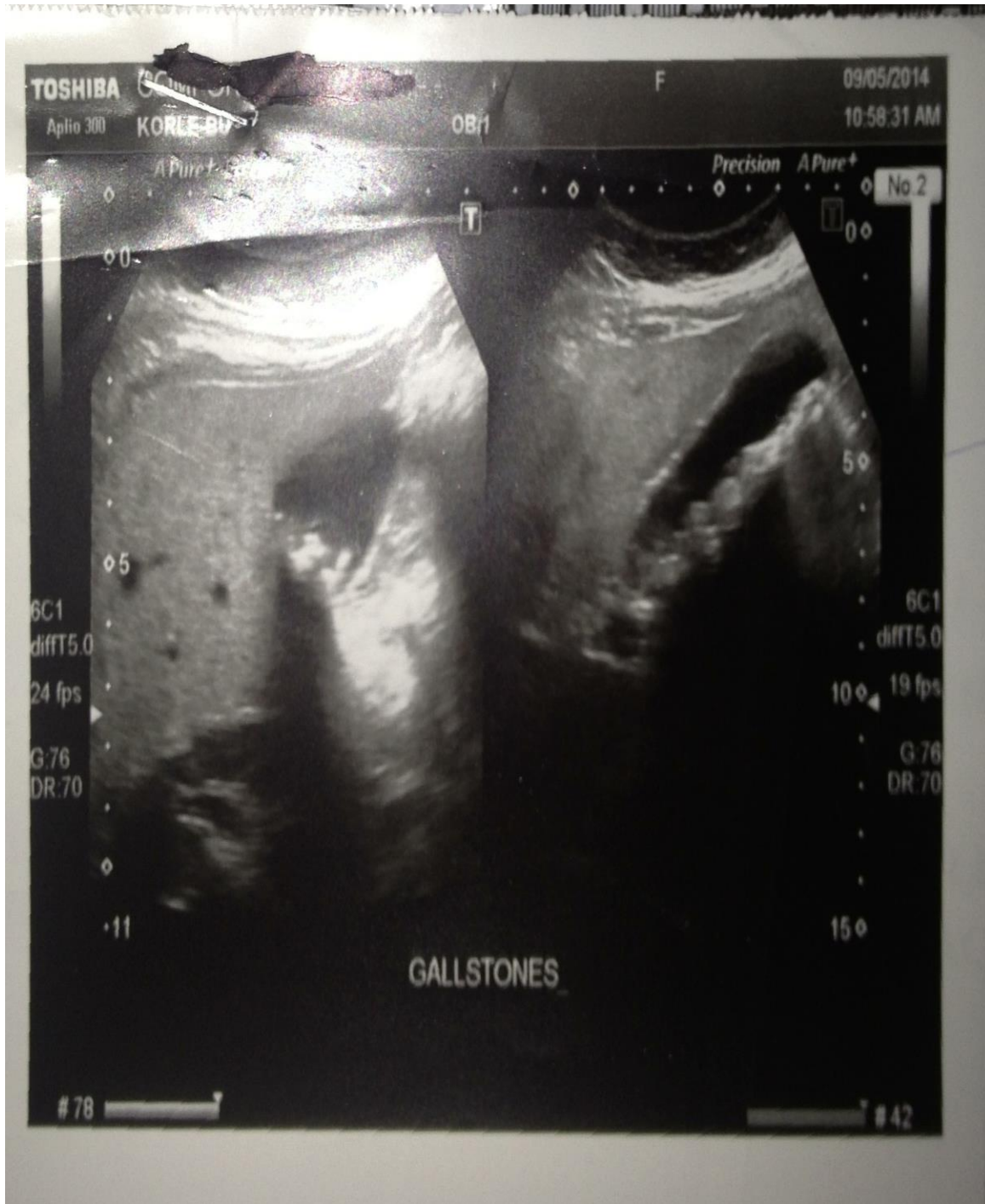
Source: Field Work



Source: Fieldwork



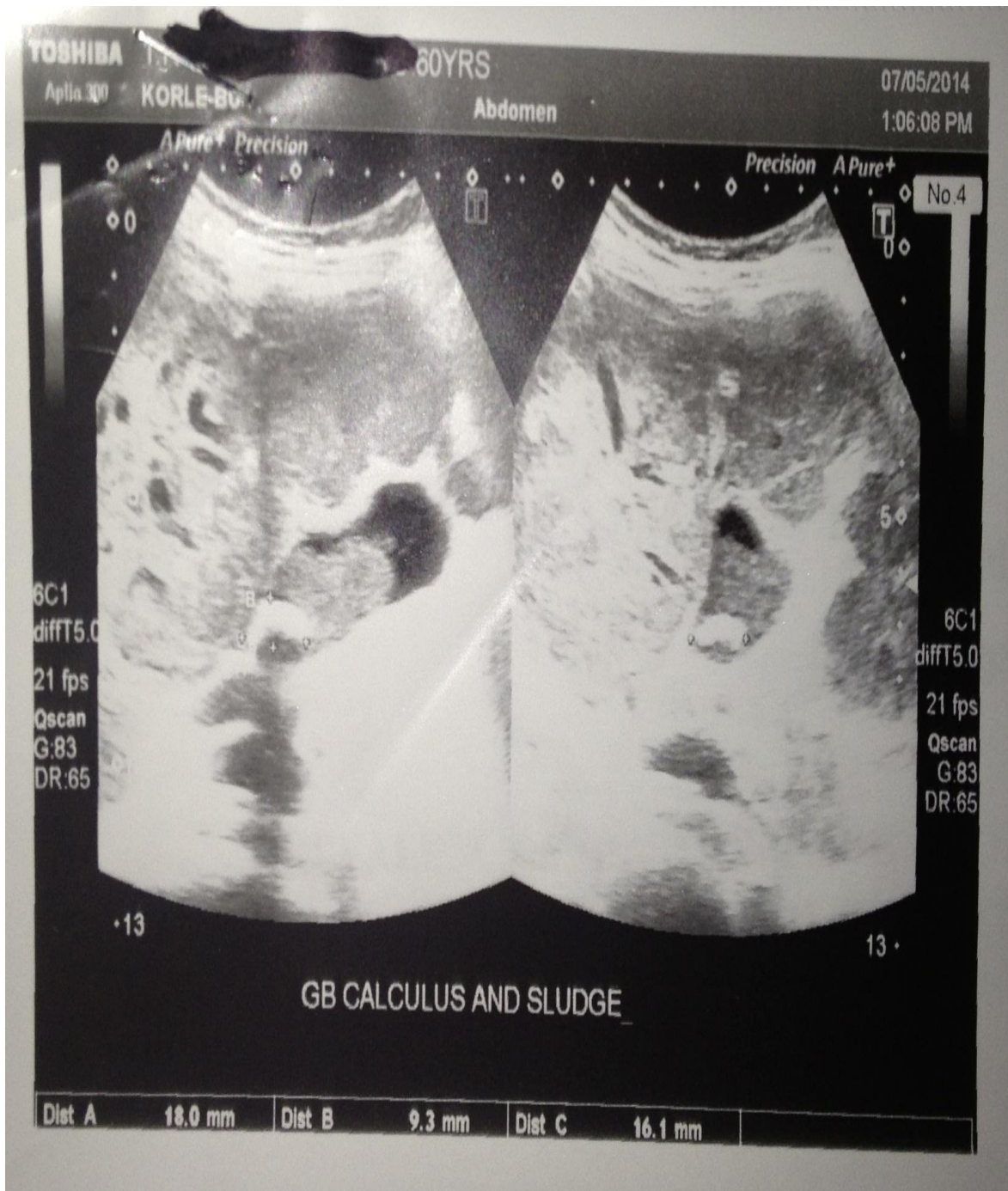
Source: Field Work



Source: Field Work



Source: Field Work



Source: Field work