



ADDIS ABABA UNIVERSITY  
COLLEGE OF HEALTH SCIENCES  
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DEPARTMENT OF ANATOMY

Assessment of the prevalence of gallstone disease and associated risk factors among patients who visited the surgical department of DebreBirhan comprehensive specialized hospital: an institution based cross-sectional study.

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January, 2024

Debre Birhan, Ethiopia

Assessment of the prevalence of gallstone disease and associated risk factors among patients who visited the surgical department of DebreBirhan comprehensive specialized hospital: an institution based cross-sectional study.

By

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MSc Thesis Submitted to Graduate Studies, Addis Ababa University, College of Health Sciences, School of Medicine, Department of Anatomy, for partial fulfillment of the requirement of a Master of Science degree in Human Anatomy.

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January, 2024

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### **Declaration form**

This is to certify that the thesis prepared by Natnael Yikeber, entitled: assessment of the prevalence of gallstone disease and associated risk factors among patients who visited the surgical department of DebreBirhan comprehensive specialized hospital, Debre Birhan, Ethiopia, January, 2024 and submitted in partial fulfillment of the requirements for the Degree of Masters of Science in Human Anatomy complies with the regulations of the university and meets the accepted standards with respect to originality and quality. This thesis has not been presented for a degree in any other university, and that all sources of materials used for the thesis have been duly acknowledged.

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## List of acronyms and abbreviations:

AOR	Adjusted odds ratio
BMI	Body mass index
CI	Confidence interval
COR	Crude odds ratio
DBCOSH	Debre birhan comprehensive specialized hospital
GI	Gastro intestinal
GS	Gallstone
GSD	Gallstone disease
HMIS	Health management information system
LUQ	Left upper quadrant
NGO	Nongovernmental organizations
ODK	Open data kit
RUQ	Right upper quadrant
SD	Standard deviation
SPHMC	St. Paulos hospital Millennium Medical College
SPSS	Statistical package for the social science
TASH	Tikur Anbessa Specialized Hosspital
USA	United States of America

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## Abstract

**Background:** Gallstones are bile salt deposits that occur in the gallbladder through cholelithiasis or bile ducts by choledocholithiasis. The majority of patients with gallstones are asymptomatic. Gallstones can be generically classified as cholesterol or pigment and an intermediate mixed cholesterol gallstone. In areas where gallstone illness frequency was previously low, it has continuously increased. There are several risk factors associated with gallstone disease.

**Objectives:** To assess the prevalence of gallstone disease and associated risk factors among patients who visited the surgical department of DebreBirhan comprehensive specialized hospital.

**Methodology:** The study was conducted at DebreBirhan comprehensive specialized hospital's surgical department using a retrospective institutional-based cross-sectional design. A total of 169 patients were selected using a simple random sampling method between the periods of January 2020 and December 2022. Data was collected using a structured checklist and the Open Data Kit. Descriptive statistics and binary logistic regression analyses with two or more variables were performed after each completed form was checked for completeness.

**Results:** The study had a total of 165 participants, with 86 (52.1%) males and 79 (47.9%) females, resulting in male to female ratio of 1.17:1. The mean age of the participants was  $41.58 \pm 16.185$  years. The overall prevalence of gallstone disease was 7.9%, with a higher prevalence observed in women (15.2%) than men (1.2%). The prevalence of gallstone disease was found to be highest (61.3%) among participants aged between 26 and 45 years, with a decrease in prevalence after the age of 65 years. The majority of the participants were asymptomatic, with vomiting and abdominal pain being the most common symptoms. The multivariate logistic regression analysis revealed that female gender (OR=6.88), alcohol intake for more than five years (OR =4.27), and history of gastrointestinal surgery (OR=6.5) were significantly associated with gallstone disease. Further analysis in females showed that parity (OR=8.5) and, after adjusting for alcohol intake, diabetes (OR=4.6) and hypertension (OR=1.37) were significantly associated with gallstone disease.

**Conclusion:** in conclusion, the prevalence of gallstone disease was 7.9%, and fairly common in our study area. Female gender, alcohol intake for more than five years, and a history of gastrointestinal surgery were strongly associated with the occurrence of gallstone diseases. Whereas age and family history of gallstone disease were not significantly associated.

**Keywords:** Gallstone disease, cholelithiasis, prevalence, risk factors, Ethiopia.

# 1. Introduction

## 1.1 Background of the study

Gallstones (GS) are bile salt deposits that occur in the gallbladder or bile ducts. They are created from calcium ions, bile pigments, and excess concentrations of cholesterol (1). The biliary tract consists of bile ducts inside and outside the liver. The biliary tree transports, stores, and concentrates bile. Intrahepatic bile ducts merge into larger ducts, the common hepatic duct at porta hepatitis, which becomes the bile duct ( choledochus ) after merging with the cystic duct. The common bile duct reaches down to the back wall of the duodenum, where it empties together with the pancreatic duct through the ampulla Vateri at the major duodenal papilla (2). Gallstones form in the bile duct by choledocholithiasis as opposed to the gallbladder through cholelithiasis (1).

Gallstones are recognized when symptoms or difficulties emerge that are brought on by gallstones in the gallbladder and/or bile duct. One of the most common gastrointestinal (GI) conditions, gallstone disease (GSD) frequently necessitates emergency abdominal surgery and hospitalization (3).

The majority of individuals had multiple gallstones rather than only a single stone. Although the majority of asymptomatic stones were discovered incidentally on X-ray & ultrasound taken during a routine medical examination or when testing for an existing medical condition. Others are palpated during laparotomies and some are on oral cholecystograms (4,5).

Individuals who had minor symptoms initially experienced serious consequences such as acute cholecystitis, obstructive jaundice, biliary pancreatitis, gangrenous gallbladder, duodenal fistula, gallbladder cancer, and cholecystectomy. After 5, 10, 15, and 20 years, those with asymptomatic stones tended to have lower cumulative probabilities of events (severe complications) than those with symptomatic (5).

A cohort study that tracked patients for 11 to 24 years found that the incidence of new-onset biliary colic in asymptomatic GSD increased by 2% per year during the first five years, reaching 15% at ten years and 18% at twenty years. Only 2% of patients experienced problems (6). The complication rate after an average of 8.7 years was 2.9% for individuals who had not previously experienced symptoms and thereafter developed symptoms, 8.5% and 9.2% for patients who had moderate and severe symptoms at enrollment, respectively (7).

According to their primary chemical components, gallstones can be generically classified as cholesterol, pigment stones and mixed cholesterol GS. Each form of gallstone may have a unique pathophysiology and etiology, which are poorly understood. A complex interplay of genetic and environmental factors leads to gallstones (8).

Cholesterol or cholesterol-predominant (mixed) stones, develop when bile becomes excessively saturated with cholesterol (3). Common risk factors for oversaturation include being female due to the effects of estrogen, being overweight with a high body mass index, being fertile or having children, being older than forty, and finally having a family history or genetics (9). Reduced gallbladder motility also helps stone formation (3).

Patients with cirrhosis, sickle cell disease, congenital spherocytosis, and thalassemia are at a higher risk of developing black pigment stones, which are composed of 70% calcium bilirubin. The intrahepatic and extrahepatic bile ducts, as well as the gall bladder, are the sites where brown pigment stones develop. They develop as a result of infection and stasis in the biliary system, typically in the presence of *Escherichia coli* and *Klebsiella* spp. The creation of these stones, which are widespread in South East Asia, has been linked to *Ascarislumbricoides* and *Opisthorchissenensis*, respectively (10).

The frequency of GSD has consistently grown in regions where it was previously low. Owing to the rapid urbanization and ongoing adoption of a westernized diet, which alters risk variables other than age. There are several risk factors, some of which cannot be changed, such as race, genetics, age, and female gender, while others can, such as obesity, parity, diet, oral contraceptives, and clofibrate, as well as conditions such as diabetes, hyperlipidemia, ileal diseases, hemolytic anemia, and biliary infections (11). The quantity of cholesterol absorbed from the gut and released into the bile and the amount of bile salts created and released into the bile all grow with age. Reduced blood flow and contraction accompany the aging process that causes the gallbladder to stop functioning properly (12).

Conception, hormone replacement therapy, a history of using estrogen above 50 mcg, and unrestricted family planning increase the risk of developing GSD among women in the reproductive age group (13). Women had a two fold increased chance of developing GS due to the influence of sex hormones (progesterone and estrogen) during the reproductive age. In multiparous women, the likelihood of having GS increased by several parties, abortion, and prolonged fertility eras (14).

## 1.2 Statement of the problem

The GSD is increasingly burdening healthcare systems worldwide. Due to rapid urbanization and changing to a westernized diet, the prevalence of GSD has increased steadily globally (15). Nowadays, gallstone disease is a widespread issue in developed nations and appears to be increasing in developing countries. Gallstone disease posing a significant health burden that drives up the frequency of hospital admissions, surgeries, and health care costs (16,17).

In larger sonographic epidemiologic surveys conducted in Europe, the median gallstone prevalence rate ranged from 5.9% to 21.9%. Cholelithiasis has a mean prevalence rate of 10-12% in European populations, compared to 3-4% in Asian people (18).

Gallstones, which are the most prevalent form of biliary system disease in adults and the main reason for hospital admissions for digestive (GIT) issues, are thought to affect 20–25 million adults in the United States (USA) (19). The number of cholecystectomies carried out annually in the USA ranges between 650,000 to 700,000 (17). In the USA and typically in Western nations, the rate of cholecystectomy increased after laparoscopic cholecystectomy was introduced in 1989 (20).

Cholelithiasis is somehow linked to more than 98% of all gallbladder and biliary tract conditions. As a result, with an estimated \$6.5 billion in costs, gallstone symptoms & complications rank among the most expensive digestive tract diseases in the USA, surpassing the sums for chronic liver disease and cirrhosis (\$1.6 billion), chronic hepatitis C (\$0.8 billion), and even pancreatic disease (\$2.2 billion) (17).

There has been a few research published in Africa. The range of prevalence was 4% to 10% (18). Gallstones were reported to be prevalent in 5.9% in Ghana (21), 4.4% in Nigeria (22), 19.2% in Morocco (23), and 10% of South African women (24).

In the past, cholelithiasis was thought to be uncommon in sub-Saharan Africa. Cholelithiasis will become more significant in these populations as many African nations experience fast urbanization and a continuous transition to a westernized diet. The frequency of cholecystectomy appears to be increasing over time (25). GI operations made up 33.8% of all non-emergency surgeries performed at the Khartoum Teaching Hospital. GSD treatment accounted for 17.6% of GI surgeries, making it the second most common surgery (26).

Recent years have seen an increase in the number of gallstone disease cases in Ethiopia. The statistics speak for themselves: 56 GSD cases are reported annually at Ayder Referral Hospital in Mekelle (27), while Ras Desta Damtew Memorial hospital conduct a total of 71 cholecystectomies each year (28). Moreover, the five-year GSD research conducted at Tikur anbesa specialized hospital (TASH) reveals 78 GSD cases annually (29), which is indicative of a changing pattern in GSD. According to the available data, the surgical ward of Zewditu Memorial Hospital appears to be performing a significant number of gallbladder surgeries. In fact, these surgeries account for 22% of all non-emergency surgeries, making it the second most commonly performed surgical service at the hospital (30).

It appears that almost 40% of the admissions to TASH's surgical ward were due to gastrointestinal issues. Out of all the GI illnesses requiring inpatient care, cholelithiasis/cholecystitis accounted for 25.9%, making it the most common reason for admission. Additionally, cholelithiasis or cholecystitis were among the top ten disorders of surgical inpatient care, comprising 10.3% (31). The total prevalence of GSD is 10.2% among patients who were admitted to the St. Paulos hospital Millennium Medical College (SPHMC), Addis Abeba (32) and 5.2% in Gondar University Hospital (33).

The frequency of gallstone disease in Ethiopia has been the subject of few investigations, and to the best of my knowledge, no published research has examined the risk factors linked with GSD. It is unfortunate that most studies only discuss the prevalence of GSD and do not provide sufficient information. Moreover, there has been no research conducted on the prevalence and associated risk factors of GSD at Debre birhan comprehensive specialized hospital (DBCSH). Therefore, the importance of the present study is further underscored by the prevalence and potential significance of risk factors for GSD.

### 1.3 Significance of the study

Ethiopia, like many other African nations, is rapidly urbanizing, and there has been a gradual move towards a westernized diet, which has led to an increase in the prevalence of gallstone disease in recent years. There were limited studies on the prevalence of gallstone disease and associated risk factors in Ethiopian populations. Most of the studies provide insufficient information as they focus only on the prevalence of GSD; as a result, it is important to recognize the prevalence and associated risk factors. Due to the lack of community-based research and the fact that the majority of patients are asymptomatic at the time of diagnosis, it is still challenging to diagnose GSD early, which raises the likelihood of missed diagnoses and leaves the true prevalence of the condition unknown.

The findings of the study provide valuable information to create effective screening systems for early disease diagnosis and community education. Additionally, governmental and non-governmental organizations (NGO) that focus on non-communicable illnesses can benefit from the results of this study. Overall, this research serves as a foundation for further investigations by other researchers in the field.

## 2. Literature review

### 2.1 Prevalence of GSD

According to a study of global sonographic, epidemiologic, and population-based studies on the incidence of gallstones, the mean prevalence rate of the GSD is 10-12% in European people and 3-4% in Asians (18). According to a survey of published articles, the prevalence of gallstone disease is often reported to range from 2% to 5% in Africa and Asia, 10% to 12% in the USA, and 9.7% to 19.5% in European nations (10,16,34).

Gallstone disease was present in 9.7% of Guadalajara, Spain's adult population (35), 8.03% in Linköping, Sweden (36), 0.67% per year in Italy (37), 20.5% in Rosario, Argentina (38), 5.0% in central Taiwan (39), 6.83% in Shanghai China (40), 8.6% in other study at southwest, China (41), 2.4% in southeast Iran (42), 5.53% in Sana, Yemen (43), 11.7% in Saudi high altitude population (44), 6.2% in northern India (45), 4.4% in sonographic study in Adult individuals of Igbo in Southeast Nigeria (22), 5.9% in Kumasi, Ghana (21), 19.2% in rural Morocco (23), 10% in South African (18), 10.2% in SPHMC, Addis Abeba, there was an upward trend in stone disorders, which grew by 10.8% (32), another study done at Saint Paul's Hospital shows 7% of cases had stones in the bile duct (46), 5.2% among patients visited radiology department of Gondar University Hospital (33).

GSD was found to be prevalent in 24.8% of diabetic (DM) individuals in northern Italy, 17.7% of type 2 DM patients in North India, and 17.5% of DM individuals in Ibadan, Nigeria, had GS. The prevalence of GS in Nigeria identified by ultrasound screening in type 1 DM and type 2 DM was 10% and 18.11%, respectively (47–49). According to a Taiwanese study, there was a greater overall incidence of GSD in the type 2 DM cohort compared to the non-diabetes group but a lower total incidence of GSD in the type 1 DM cohort (50). The overall prevalence of GSD was 31% among spinal cord injury (SCI) patients in an American study: with 19.6% of patients having gallstones whereas 11.1% undergoing cholecystectomy for gallstones as a result of their SCI, and 25% among Chilean male patients with SCI (51,52). According to a study done in Japanese, the prevalence of GSD among individuals who underwent esophagectomy was found to be 23%. The incidence of cholelithiasis after five years of esophagectomy increased significantly to 16%, which was substantially higher compared to the 5.9% incidence before the surgery. The incidence of gallstones continued to rise over time and stabilized at 34% ten years after the surgery (53).

## 2.2 Risk factors of GSD

### 2.2.1 Socio-demographics characteristics

The main socio-demographic risk factors identified were advanced age, female gender, and ethnicity (11,17,34). GSD was more common as people aged. That was evidenced by a study done in Guadalajara, Spain (35), Rosario, Argentina (38), southwest China revealed that the frequency of GSD reached its maximum between the ages of 80 and 90, and then started to decrease (41), rural Morocco shows the condition is more prevalent (71.2%) in those over 40 (23), SPHMC, Addis Ababa shows in males, the incidence of gallstones increased with age, but decreased in females (32), and Gonder University Hospital (33).

The survey conducted in northern India revealed that the age groups of 20-30 and 40-60 had a higher incidence of GSD patients (45). According to a study conducted in Igbo, southeast Nigeria, people over 80 and under 20 are less likely to have GS, but those between the ages of 31 and 40 are more likely to have them (22).

Research from Guadalajara, Spain (35); Rosario, Argentina (38); central Taiwan and Shanghai, China, (39,40); southeast Iran (42); and an Igbo, southeast Nigeria, sonographic study (22) has shown that age has a substantial correlation with the development of GSD.

The average age of the research participants varied across different locations. 43.9 years old on average, with a standard deviation (SD) of 13.1 years in southwest China (41), 44.3 years old on average, with a SD of 10.2 years, and a median age of 43 years in Saudi high-altitude population (44), 37 years old on average, with a SD of 17.2 years in Sana, Yemen (43), 33.88 years on average with a SD of 12.60 years in Igbo, southeast Nigeria (22), 47.7 years on average in rural Morocco (23), 47.3 years old on average with a SD of fifteen years in South Africa (20), 49 years on average in Saint Paul's Hospital on the surgical therapy of choledocholithiasis (46), 40.3 years on average with an SD of 11.2 years in TASH on the pathogenesis and clinical presentation of biliary tree blockage outside the liver (55), and 42 years on average in a five-year study of GSD at TASH (29).

The participants' ages ranged from 25 to 85 years old in Saudi high-altitude population (44), 18–92 years in Igbo, southeast Nigeria (22), 8 to 96 years in rural Morocco (23), 16 to 87 years in Saint Paul's Hospital on the surgical therapy of choledocholithiasis, patients' (46), and 21 to 80 years in TASH on the pathogenesis and clinical presentation of biliary tree blockage outside the liver (55).

In the final five years of the South African trial, more younger patients than in the previous five underwent surgery for GSD, indicating that age is not the only significant risk. This demonstrates how the GSD pattern is shifting (20).

GSD was significantly correlated with female sex, as evidenced by a study conducted in Rosario, Argentina (38), northern India (45), Saudi high-altitude population (44), Sana, Yemen (43), southeast Iran (42), Igbo, southeast Nigeria (22), Kumasi, Ghana (21), rural Morocco (23), and Gonder University Hospital (33). However, according to screening studies conducted in central Taiwan and Shanghai, China, sex does not show statistical significance (39,40).

The research participants were 50.9% women in the Saudi high-altitude population (44), 51.5% men in Sana, Yemen (43), 50.6% women in Igbo, southeast Nigeria (22), 23.4% men with the female to male ratio was 3.27:1 in rural Morocco (23), female to male ratio was 5.7:1 in South Africa (20), 71.6% women in Mekelle Ayder Referral Hospital (27), 84% female with female-to-male ratio was 5:1.5 in Zewditu Memorial and TASH study on the surgical results of biliary stone illness (54), 53.3% women with females to males was 1:1.14 in TASH on the pathogenesis and clinical presentation of biliary tree blockage outside the liver (55), and the ratio of female to male was 5:1 in a five-year study of GSD at TASH (29).

### **2.2.2 Gallstone-related characteristics**

The majority of patients with gallstones have no symptoms (34). That was supported by a study conducted in Rosario, Argentina, which revealed 72.2% of cases were symptoms-free (38); the SPHMC study on the trends in stone disease revealed 65.2% of the patients reported no clinical symptoms at the time of diagnosis (32); and 88.2% of the study participants were asymptomatic in a study from Gonder University Hospital (33). However, a study conducted in the high-altitude population of Saudi Arabia reveals that 86.7% of the stones were newly diagnosed, and of those, 61.5% had at least one GS suggestive symptom, whereas 38.5% had no symptoms at all. The discrepancy might be due to genetic and environmental factors as well as unknown causes (44).

The primary symptoms of GSD were abdominal pain, primarily in the right upper quadrant (RUQ) region, followed by the epigastric and left upper quadrant (LUQ) areas. Fatty meals exacerbate the pain, which radiates to the right shoulder and back. Which was described by a study conducted in Ayder Referral Hospital in Mekelle (27), Zewditu Memorial and TASH on the surgical results of biliary stone illness (54), Saint Paul's Hospital on the surgical treatment of common bile duct stones (46), TASH on a 5-year evaluation of the GSD (29), and TASH on the pathogenesis and clinical presentation of biliary tree blockage outside the liver (55). Fever, nausea, vomiting, fatty meal indigestion, jaundice and anorexia are among the other complaints (27, 46, 55, 56). Furthermore explained by the patients were RUQ pain (57.8%) and Murphy's sign (18.7%) (27). Tenderness at the RUQ was the most frequently seen physical indication (29, 57).

### **2.2.3 Pathologic and metabolic conditions**

Pathologic and metabolic risk factors for GSD were obesity, DM, high cholesterol, low-fiber diets, Crohn's disease, rapid weight loss, liver cirrhosis, hepatitis B/C infection, SCI, prolonged fasting, mutation, and hemolytic diseases (10,17,34). There was a substantial correlation between DM and GSD that was evidenced by a study conducted in central Taiwan and Shanghai (39,40), a Japanese population-based cohort (57), another Taiwanese study (58), a North Indian (45), Mexico (59), Addis Ababa, Ethiopia on the relationships of GSD and DM (60), and SPHMC on patterns in stone disease (32).

High blood pressure has been linked to an increased risk of gallstone disease, according to a Japanese population-based cohort study. Additionally linked to a higher risk of cholelithiasis was treatment for hypertension (57), and in southwest China, a study revealed a strong correlation between GSD and hypertension (41).

Body mass index (BMI)  $\geq 25$  and fatty liver have significant associations with the development of GSD, according to studies conducted in central Taiwan, Shanghai, China (39,40), and southeast Iran (42). According to a Chilean study, a strong correlation between cholelithiasis and chronic SCI was found using statistical analysis (52).

The study conducted at Zewditu Memorial and TASH on the surgical outcomes of choledocholithiasis with symptoms (54), and TASH on the clinical presentation and pathogenesis of biliary tree blockage outside the liver (55), found that DM and high blood pressure were the most commonly associated comorbidities with GSD cases. In southwest China, a study reveals that hypertension (21.8%) is the most frequently found comorbidity (41). According to a screening survey conducted in rural Morocco, 89% of respondents consumed a western-style diet. DM affects 7.2% of individuals (23). According to a study at SPHMC on patterns in stone disease, the most common comorbidities were DM, an enlarged gallbladder filled with mucus (hydrops), an umbilical hernia, and empyema (acute cholecystitis) (23).

#### **2.2.4 Genetic and behavioral factors**

Genetic and behavioral risk factors identified were octreotide medication, family history (10,17,34,39,40), Smoking, use of hypolipidemic medications, use of oral contraceptives, and physical activity (35, 39,40, 42). According to a study in Guadalajara, Spain, drinking alcohol for fewer than five years had a negative correlation with GSD (35). Weekly alcohol use is linked to the growth and formation of GS, according to Swedish forward cohort research (36). According to a study conducted in Mexico, a history of alcohol abuse is preventative of gallstone disease. Subjects who moderately consume alcohol have a lower incidence of gallstones (59).

Italian researchers have found that individuals with gallstones are more likely to have first-degree relatives with gallbladder disease (GD). The prevalence of GD was much higher in the first-degree relatives of individuals with gallstones (28.6%) compared to those without (12.4%), indicating a potential genetic link. The study also found that mothers and sisters had the highest relative risks for GD, suggesting that the disease is passed down through dominant sex-linked features (61). According to screening studies conducted in central Taiwan and Shanghai, China, first-degree relative history of GSD and use of oral contraceptives have significant associations with the development of GSD (39,40). The study conducted in the high-altitude population of Saudi Arabia reveals that the first-degree relatives' history of GSD was substantially associated with GSD based on regression analysis (44). A study carried out in northern India found a substantial association between first-degree relatives' family history of GSD and GSD (45). According to a screening study conducted in a rural area of Morocco, smoking and certain genetic and family factors were positively correlated with gallstones. Physical exercise and alcohol consumption had the opposite impact (23).

### 2.2.5 Others factors

Based on different researchs, certain risk factors are associated with the development of GSD. These factors include the use of exogenous estrogens, long-term total parenteral nutrition (10,16,34), GI surgery history (39,40), and parity (23,39,40,42). According to a Rosario, Argentina, study, the prevalence of GSD rose with parity. In age- adjusted regression, having four or more pregnancies was substantially linked to GSD (38). A sonographic study carried out in Nigeria revealed a strong association between parity and GSD. Hormone therapy during menopause has been linked to a higher incidence of GSD (22). According to a study conducted in northern India, there was a higher chance of GS in those with parity and those who had undergone prior GI surgery (45). According to a study conducted on Japanese males, individuals who had had a gastrectomy in the past had a 3.7-fold higher prevalence of GSD than men who had not (63). A study conducted in Hungary demonstrates that vagotomy and GS have a positive association (64).

### 2.3. Conceptual framework

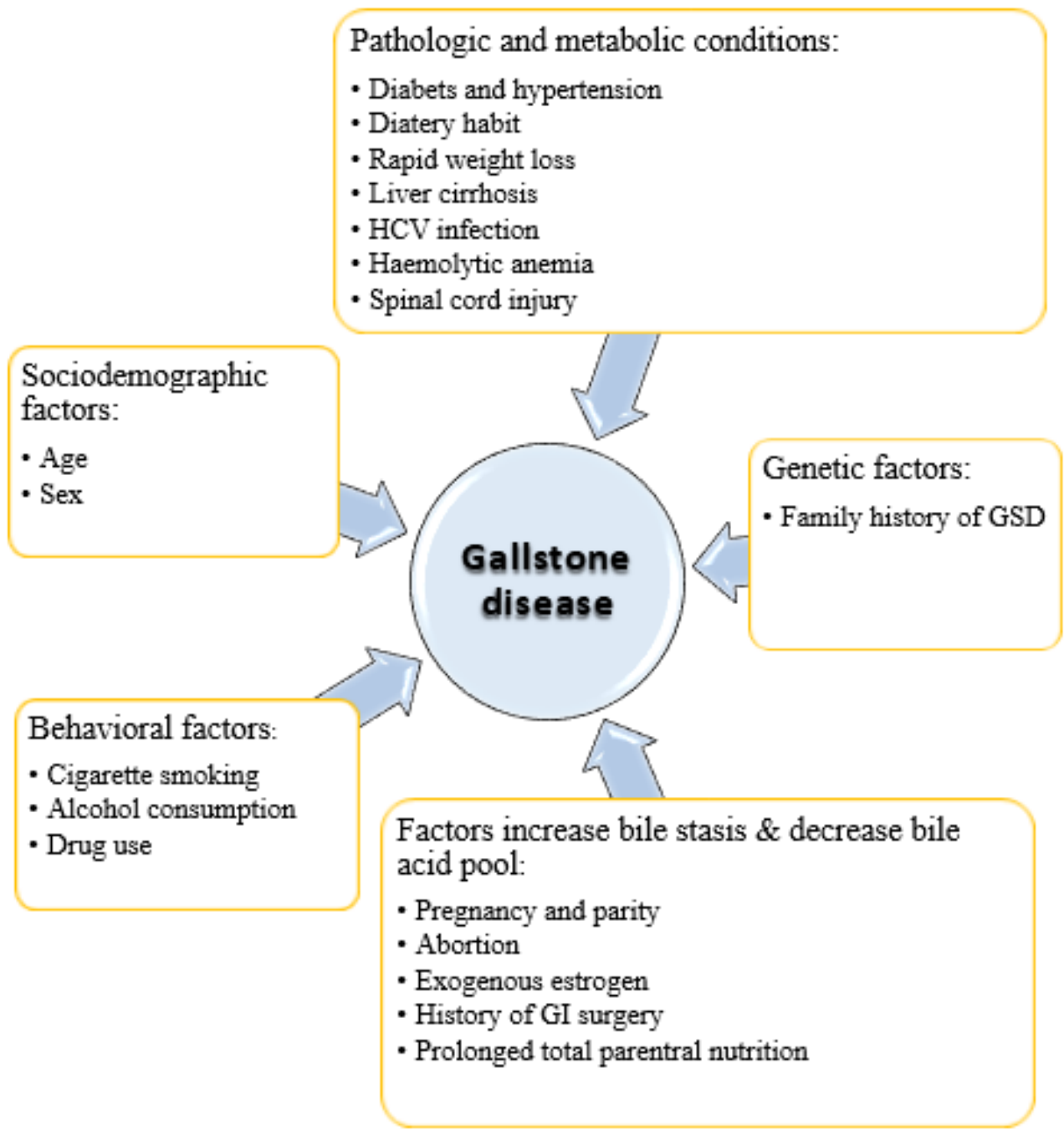


Figure 1: Conceptual framework for the determinants of gallstone disease developed from literature review.

### **3. Objectives of the study**

#### **3.1. General objective:**

- ❖ To assess the prevalence of gallstone disease and associated risk factors among patients who visited the surgical department of DebreBirhan comprehensive specialized hospital.

#### **3.2. Specific objectives:**

- ✚ To determine the prevalence of gallstone disease among patients who visited the surgical department of DebreBirhan comprehensive specialized hospital.
- ✚ To identify the determinants of gall stone disease among patients who visited the surgical department of DebreBirhan comprehensive specialized hospital.

## 4. Methods and Materials

### 4.1. Study area and period

The study was conducted at the Debre Birhan Comprehensive Specialized Hospital located 130 kilometers north of Addis Ababa in the Amhara region, in the north shewa zone of Debre Birhan district. It is the largest public referral hospital in the North Shewa zone. It offers services in pediatrics, emergency care, surgery, medical, gynecology, psychiatry, ophthalmology, anti-retroviral therapy (ART), neonatal intensive care unit, microbiological laboratories, viral load, and other medical specialties for more than 3 million individuals within its catchment region. The surgical department performs orthopedic, elective, and emergency surgeries. The surgical department includes inpatient (surgical ward) and outpatient (surgical outpatient (OPD) and surgical referral clinic). According to the report from DebreBirhan, a comprehensive specialized hospital the number of patients diagnosed with GSD shows an increasing trend in recent years; however, the true prevalence of GSD in the region is unknown. The study was conducted from January 2020 to December 2022.

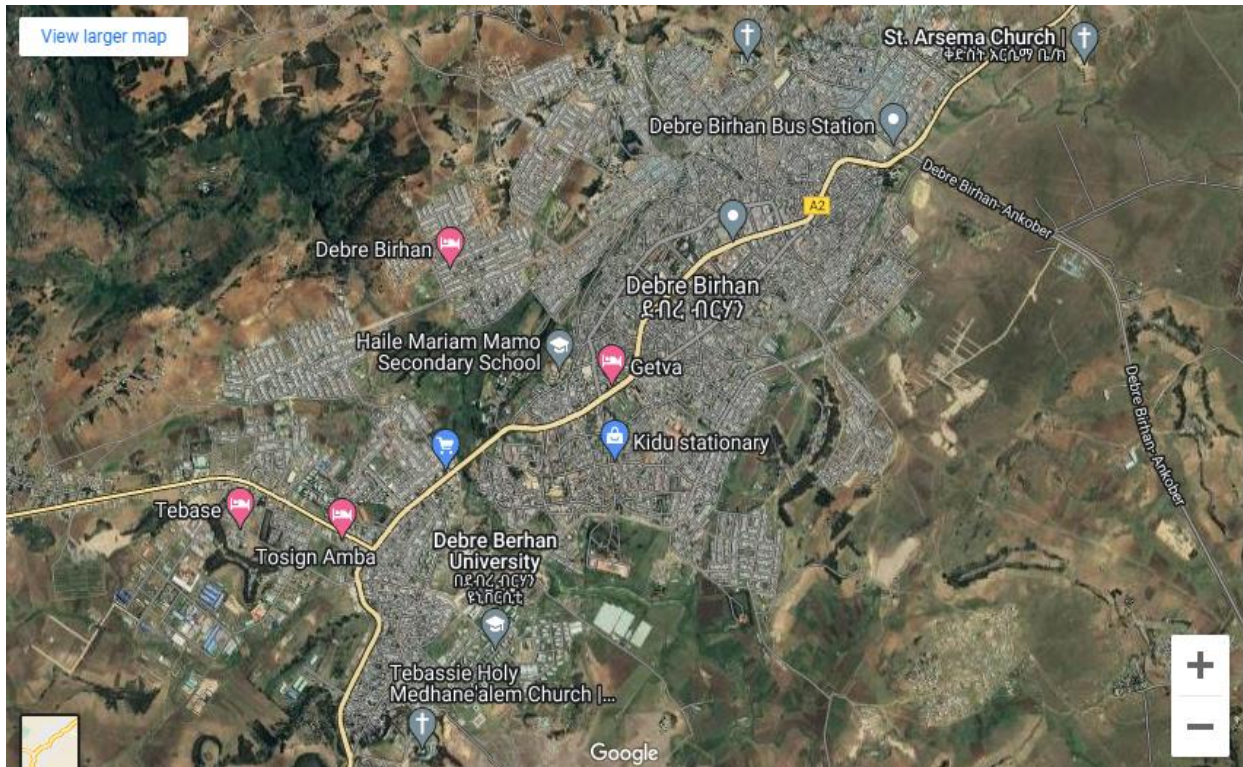


Figure 2: Map of DebreBerhan city in which the current study takes place.

## 4.2. Study design

A retrospective institution-based cross-sectional study design was used.

## 4.3. Population

### 4.3.1. Source population

All patients who visited the surgical department of DebreBirhan comprehensive specialized hospital.

### 4.3.2 Study population

All patients who visited the surgical department of DebreBirhan comprehensive specialized hospital from January 2020 to December 2022.

### 4.3.3 Study participants

All randomly selected patients who visited the surgical department of DebreBirhan comprehensive specialized hospital from January 2020 to December 2022.

## 4.4. Sample size calculation

The required sample size was determined using a single population proportion formula that had a 95% confidence interval, a 5% margin of error, and a population proportion of 10.2% that was taken from a retrospective study on patients admitted to St. Paul's Hospital, Millennium Medical College, Addis Abeba (32) because the study shows a thirteen-year trend of gallstones as well as an institutionally based study setting.

$$n = \frac{(Z \alpha/2)^2 \cdot P(1-Q)}{D^2} \quad \text{Where,} \quad n = \text{the required sample size}$$

$\alpha$  = 95% confidence interval

D = margin of error

P = population proportion

$$n = \frac{(1.96)^2 (0.102)(0.898)}{(0.05)^2} = 140.75 = 141 \text{ by considering the 20\% of non-response}$$

rate, and incomplete patient cards, the total sample size was 169.

#### 4.5. Sampling techniques and procedure

Between January 2020 and December 2022, 25,004 patients visited the DBCSH surgical department. Of them, the surgical ward, surgical OPD, and surgical referral clinic served 5,229, 8,173, and 11,602 patients, respectively. Every patient who visited the DBCSH surgical department had their medical record number recorded. During the study period, data was gathered from the hospital's health management information system (HMIS) registration book. The sampling frame was the hospital's HMIS records, from which 55 patients from the surgical OPD, 78 patients from the surgical referral clinic, and 36 patients from the surgical ward were chosen proportionally using a computer-generated simple random sampling (SRS) method, resulting in a total of 169 patients.

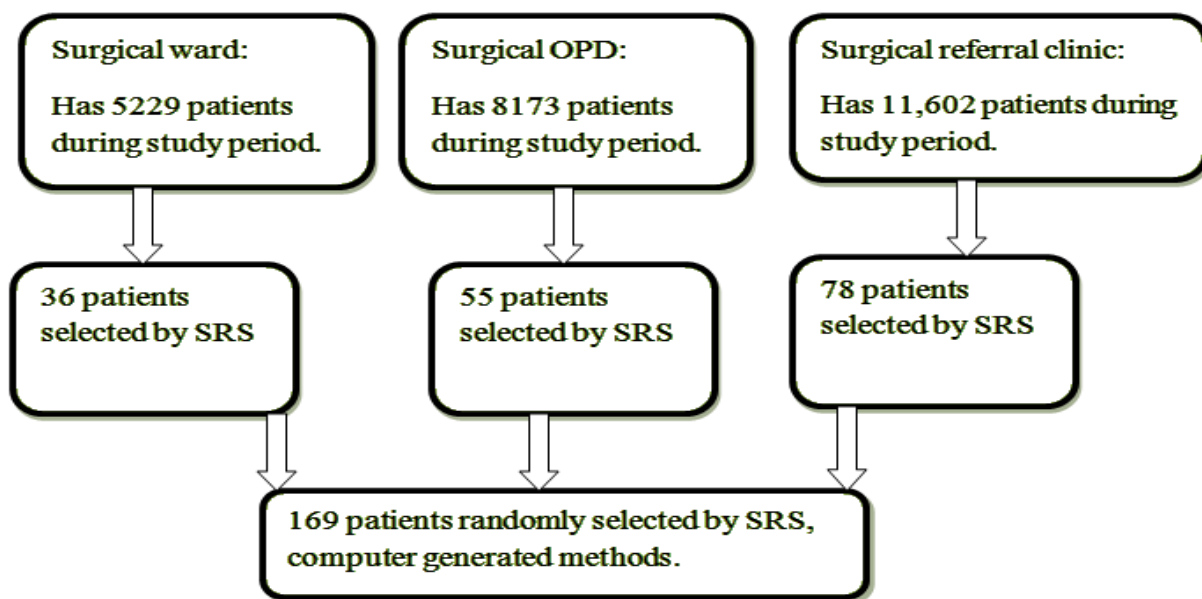


Figure 3: Sampling procedure in the surgical department of DBSCH.

#### 4.6. Eligibility criteria

##### 4.6.1. Inclusion criteria:

All patients who visited the surgical department of DBSCH and recorded on HMIS from January 2020 to December 2022.

##### 4.6.2 Exclusion criteria:

Incomplete patient records

A missing card among patients

A subsequent visit to the surgical department for the same diagnosis

Patients under 18 years of age (22,41) since GSD is uncommon at a younger age.

## **4.7. Study variables**

### **4.7.1. Dependent variable**

Gallstone disease

### **4.7.2. Independent variable**

Sociodemographic factors like age, sex, educational level, occupation and residence

Genetic and behavioral characteristics include the history of GSD in the first-degree relatives.

Cigarette smoking, alcohol intake, physical activity and drug use for more than 6 month

Pathologic conditions like hypertension, diabetes, liver cirrhosis, hemolytic anemia, chron's disease, HCV/HBV infection, ascarislumbicoides, and SCI

Metabolic conditions like obesity, and rapid weight loss

Factors related to bile stasis include pregnancy, exogenous estrogen, prolonged parenteral nutrition, history of GI surgery, parity, and previous history of abortion

## **4.8. Data collection tool and techniques**

For the data collection, three BSc nurses and one medical doctor were recruited. The data was collected using a standardized checklist derived from previous research that covered sociodemographics, behavioral traits, genetics, family history, metabolic and pathological disorders, comorbidities, and other risk factors, along with phone calls. The Kobo Toolbox server and open data kit (ODK) version 1.25.2 software were used to collect and store the data.

## **4.9. Data quality control and management**

To guarantee the quality of the data, data collectors and the supervisor attended a two-day training session covering the ODK program and basic data collection procedures. 5% of the patients who were not selected underwent a pre-test at the DBCSH surgical OPD to assess the structured checklists. Each question was correctly coded. The supervisor and every data collector participated in pre-testing and checklist standardization. Before the start of data collection, problems that arose during the pre-test were resolved, including coding and decoding variables, extracting patient information, and exporting data from the ODK application into SPSS. Throughout the pre-test and the data-collecting phase, continuous supervision was given by the principal investigator and supervisor. The data were checked for consistency and completeness on each day of data collection.

#### **4.10. Data processing and analysis**

Each filled-out form was reviewed for completeness following data collection by ODK version 1.25.2 before being exported to SPSS version 25 for analysis. The results of the descriptive statistics were presented using the following metrics: frequency and percentage for categorical data, and mean, median, mode, and standard deviation for continuous data. To identify determinants of gallstone disease, binary logistic regression analyses with two or more variables were performed. Based on the value of  $p < 0.2$  on bivariate logistic regression, independent variables were selected as candidates for multivariate analysis. Forward stepwise multivariate regression analysis were performed. The adjusted odds ratio (AOR) with a 95% confidence interval (CI) was used to show the estimates of the strength of the association. A 5% level of significance was considered statistical significance. In the end, text, tables, and charts were used to present the results.

#### **4.11. Operational definition**

Symptomatic stones, defined as gallstones that have positive ultrasonography, produce biliary pain expressed as abdominal pain in the hypochondrium and/or epigastrium lasting longer than a half-hour and makes them to lie down or take painkillers, and/or consequences in the last 5 years (4).

The ultra-sonographic findings that were used to indicate the presence of stones in the gallbladder are one or more echogenic, distantly shadowing, potentially movable structures within the gallbladder; one or more echogenic, movable, but not shadowing, structures within the gallbladder; and Echogenic structures with persistent shadowing in the area of the gallbladder fossa, with little to no visualization of the gallbladder. The following final gallbladder status was noted to determine the prevalence of gallstone disease: Ultrasonography results could be: normal, gallstone-positive, biliary sludge-positive, previous cholecystectomy, or Inconclusive or uncertain. Gallstone positive and a history of cholecystectomy was used to define gallstone disease. Those with no gallbladder lumen on ultrasonography, a confirmed history of cholecystectomy, and a pertinent abdominal scar on physical examination were considered cases of cholecystectomy (4). History of GI surgery includes upper GI surgeries with or without vagotomy which were done for trauma and chronic tumor. Like esophagectomy, gastrectomy, and hiatal hernia repair.

The diagnosis of metabolic disorders, such as obesity, hypertension, and diabetes, was made under the accepted guidelines. For people who smoked for five years or longer, smoking was defined as the number of cigarettes smoked per day. Drinkers are persons who have been drinking over 10 grams of alcohol daily for at least five years. Those who didn't use tobacco or alcohol for at least the last three years were categorized as non-users. A quantitative score was used to evaluate alcohol and cigarette usage, with four categories: no use, light use, moderate use, and excessive use (4). A high-calorie diet low in dietary fiber and high in carbohydrates can be characterized as the Western diet (15).

#### **4.12. Ethical consideration**

Before the study began, ethical approval was obtained from the Research Ethics Review Committee of the Anatomy Department. The chief officer of the hospital approved the ethical approval obtained from the Anatomy department. The hospital's research ethics review board reviewed the proposal. The hospital's surgical department and Cardroom received a formal letter of support and ethical clearance from the hospital's research ethics review board. After obtaining hospital consent, the study ensured confidentiality at all stages only the medical record number of study participants was utilized without stating their names. The information gathered was also kept in a secure location. There was no direct benefit or harm from participation in the study.

#### **4.13. Dissemination of the result**

The results of our research will be shared with the Addis Ababa University Department of Anatomy, School of Medicine, College of Health Sciences, to partially fulfill the prerequisites for the Master degree in Medical Anatomy. The study's findings will be shared with the surgical department of the Debre Birhan Comprehensive Specialized Hospital, the Debre Birhan City Health Office, the North Shewa Health Office, and other pertinent institutions. For the benefit of the scientific community, the study's findings were submitted for publication and discussed at conferences and meetings.

## 5. Results

### 5.1. Socio-demographic characteristics

Between January 2020 and December 2022, 25,004 patients visited the DBCSH surgical department. Of them, the surgical ward, surgical outpatient department, and surgical referral clinic served 5,229, 8,173, and 11,602 patients, respectively. 165 (97.6%) of the 169 patients whose medical records were obtained had complete cards for analysis. 86 (52.1%) of the 165 patients were men, and 79 (47.9%) were women; the male-to-female ratio was 1.17 to 1. The participants' average age was  $41.58 \pm 16.185$  years. The upper age limit was 84 years old, and the minimum age was 18. The age range of 41 (24.8%) patients was 26–35 years old. In contrast, 35 (21.2%) were between the ages of 36 and 45, 30 (18.2%) were between the ages of 18 and 25, 27 (16.4%) were between the ages of 56 and 65, 19 (11.5%) were between the ages of 46 and 55, and 13(7.9%) were over the age of 65. 106 (64.2%) individuals were between the ages of 18 and 45, and 46 (27.9%) were between 46 and 65. Rural dwellers made up 92 patients (55.8%), while urban dwellers made up 73(44.2%). as shown in Table 1.

Table 1: Socio-demographic characteristics of patients who visited the surgical department of DBSCH.

Variables				Total Frequency	Percentage %
Age		No of males	No of females		
	18-25	19	11	30	18.2
	26-35	15	26	41	24.8
	36-45	14	21	35	21.2
	46-55	7	12	19	11.5
	56-65	18	9	27	16.4
	>65	13	0	13	7.9
	Total	86	79	165	100
Sex	Female			79	47.9
	Male			86	52.1
Educational level	Illiterate			63	38.2
	Primary education			28	17
	Secondary education			39	23.6
	College diploma & above			35	21.2
	Total			165	100
Occupation	Farmer			53	32.1
	Governmental			28	17.0
	Private work			36	21.8
	House wife			39	23.6
	Others (students...)			9	5.5
	Total			165	100
Residency	Rural			92	55.8
	Urban			73	44.2
	Total			165	100

In the current study, 38.2% of participants had no literacy, followed by 23.6% with a secondary education, 21.2% with a college diploma or above, and 17% with a primary education, as indicated in Figure 4.

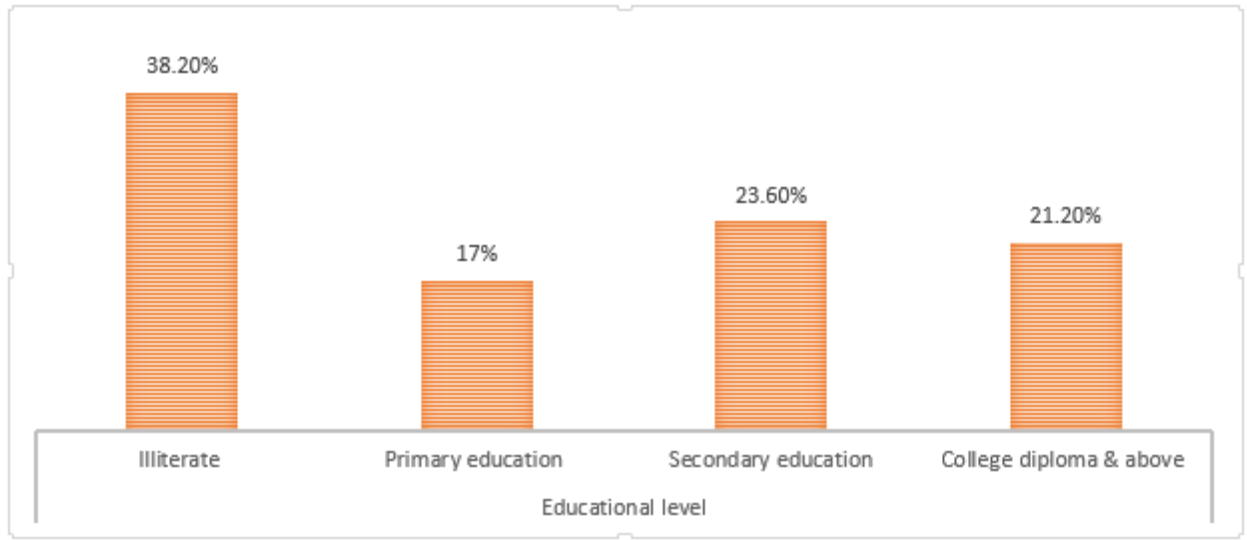


Figure 4: Educational status of study participants who visited the surgical department of DBSCH.

32.10% of the study participants were farmers, compared to 23.6% housewives, 17% government employees, 21.82% private workers, and 5.5% others, as shown in Figure 5.

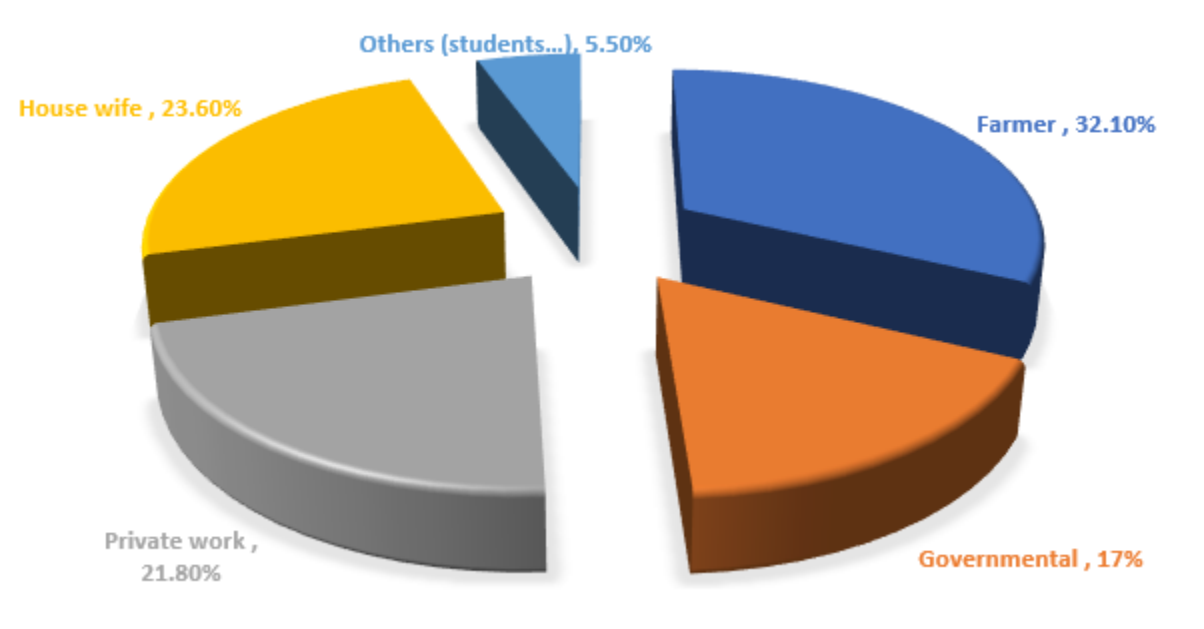


Figure 5: Occupational status of study participants who visited the surgical department of DBSCH.

The age and sex distribution of respondents among different age categories are shown in Figure 6.

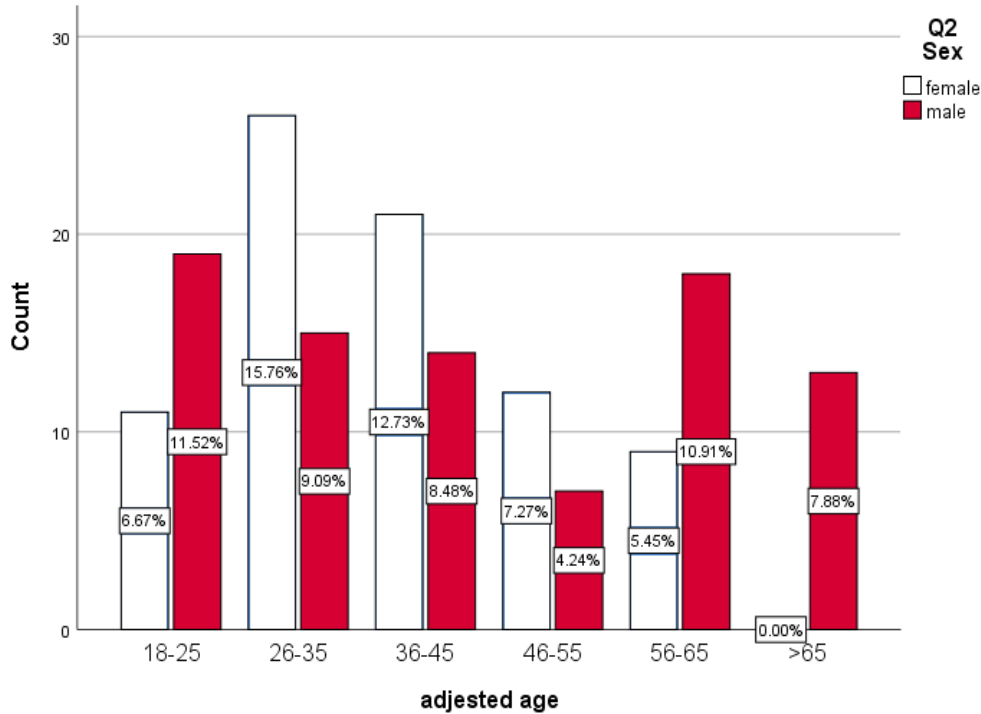


Figure 6: The relationship between age and sex of respondents who visited the surgical department of DBSCH.

## 5.2. Gallstone related characteristics

In the current study, the overall prevalence of GSD among individuals who visited the DBCSH surgical department was 7.9% (12 patients had GSD & 1 patient had a history of cholecystectomy). Gallstone disease was more prevalent in women (15.2%) than men (1.2%). According to the statistics, 30.6% of the individuals with GSD were between 26 and 35 years old. Additionally, 30.6%, 7.72%, and 23.1% of the population were between 36 and 45, 46 and 55, and 56 and 65 years old, respectively. The prevalence of GSD reaches its peak (61.3%) between the ages of 26 and 45. After the age of 65, the prevalence tends to decrease. The distribution of GSD among different ages categories is shown in Figure 7.

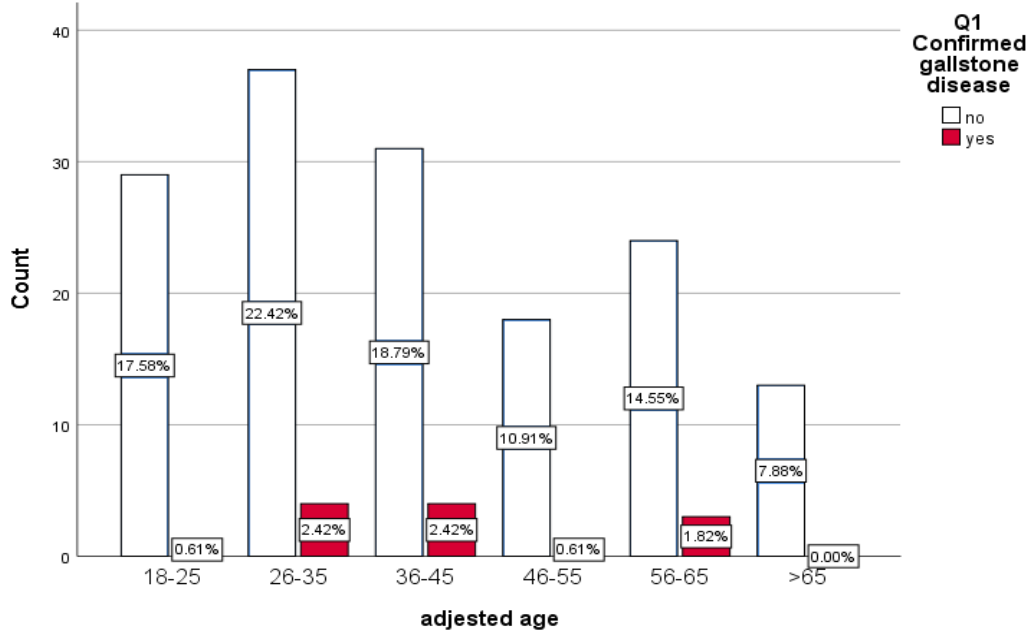


Figure 7: The relationship between age and GSD of respondents who visited the surgical department of DBSCH.

It was found that out of all the patients diagnosed with GSD, 92.3% were female, while only 7.7% were male. 66.7% of females with GSD had more than four pregnancies, compared to 25% who had two to four pregnancies and 8.3% who were nulliparous. Of the patients diagnosed with GSD, 30.7% and 69.3% were rural and urban dwellers, respectively.

Concerning GSD symptoms, When the condition was first diagnosed, 30.8% of the patients had symptoms, while 69.2% of the patients had none at all. In all patients with symptomatic GSD, vomiting and abdominal pain were the most common symptoms. Additional symptoms that may manifest include nausea, jaundice, fever, and black urine or stools. The abdominal pain experienced by symptomatic GSD patients was characterized by biliary colic, primarily in the RUQ, epigastric area, and LUQ. The pain was intensified mainly by fatty meals followed by physical activity. The pain radiates to the shoulder and back. RUQ tenderness, Murphy's sign positive, and jaundice were observed in patients with symptomatic GSD by physical examination.

36 patients (21.8%) who visited the DBCSH surgical department had previously undergone an ultrasound scan for RUQ, compared to 129 patients (78.2%) who had not. Of the patients who had previously undergone an ultrasound scan for RUQ, 58.3% had normal results, 33.3% had gallstone-positive results, 5.6% had unclear or inconclusive results, and 2.8% had a prior cholecystectomy. All verified GSD patients have had RUQ ultrasound scanning, which showed positive results for gallstones and previous cholecystectomy.

In the present study, GSD is higher in individuals aged 26–45, females, urban dwellers, and women having more than four pregnancies, as shown in Table 2.

**Table 2: The relationship between GSD and some variables in patients who visited the surgical department of DBSCH.**

		Confirmed gallstone disease		Total frequency
		Yes	No	
Age	18-25	1 (7.7%)	29	30
	26-35	4 (30.8%)	37	41
	36-45	4 (30.8%)	31	35
	46-55	1 (7.7%)	18	19
	56-65	3 (23.1%)	24	27
	>65	0	13	13
	Total	13	152	165
Sex	Female	12 (92.3%)	67	79
	Male	1 (7.7%)	85	86
	Total	13	152	165
Residency	Rural	4 (30.8%)	88	92
	Urban	9 (69.2%)	64	73
	Total	13	152	165
Have you ever had an ultrasound scan for RUQ?	Yes	13 (100%)	23	36
	No	0	129	129
	Total	13	152	165
Parity	Nulliparous	1 (8.3%)	12	13
	Two- four pregnancies	3 (25%)	25	28
	>4 pregnancies	8 (66.7%)	30	38
	Total	12	67	79

### 5.3. Pathologic and metabolic conditions

In the present investigation, diabetes and hypertension were the most common co-morbidities found. In this case, 155 individuals (93.9%) did not have diabetes, while 6.1% patients did. Figure 8 illustrates that of the total patients, 4.24% had blood pressure above 140/90 mm Hg, 1.82% had blood pressure below 90/60 mm Hg, and 155 (93.94%) had normal blood pressure.

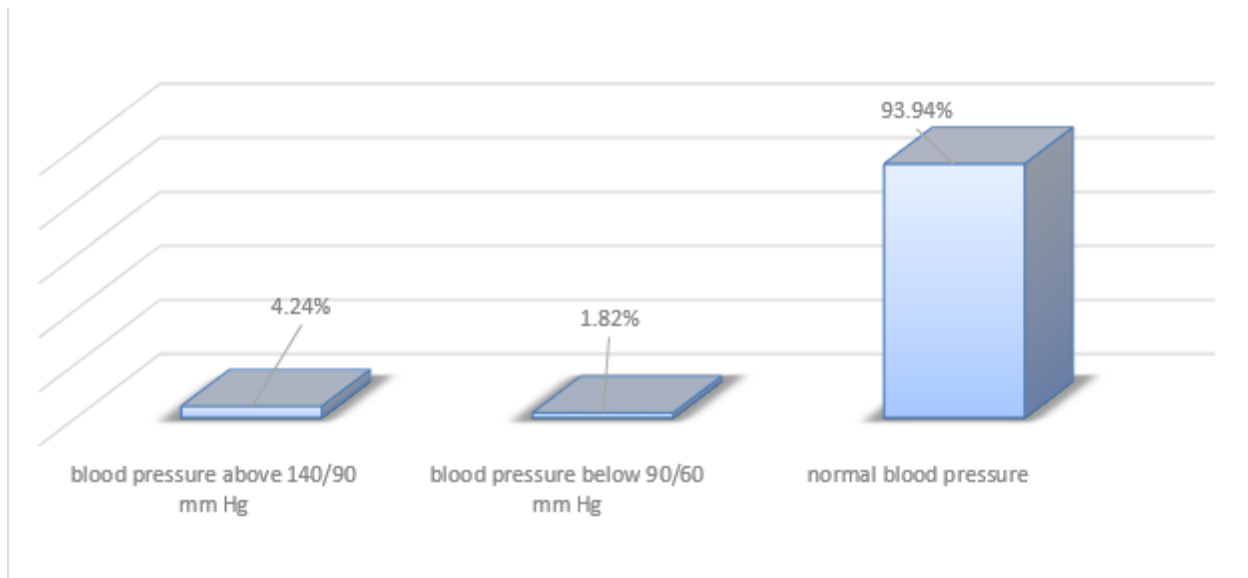


Figure 8: The frequency of the study participants' blood pressure measurement at the time of visit to the surgical department of DBSCH.

According to the current investigation, out of the total individuals, 97.6% did not have any prior history of spinal cord injuries while only 2.4% of patients had such a history. The investigation also showed that none of the patients had hemolytic anemia, HCV/HBV infection, or liver cirrhosis. Interestingly, although no patient tried diet therapy to lose weight, a significant majority of 95.8% of patients had a mixed dietary habit, while only a small number of 4.2% of patients were vegetarians.

#### **5.4. Genetic and behavioral factors**

Of all the GSD cases, 23.1% of the patients had first-degree relatives with a proven gallstone or a history of cholecystectomy. There were no reported cases of smokers. Of the total patients, 135 (81.8%) did not drink alcohol, while 30 (18.2%) did. Of the patients who consumed alcohol, 40% and 60% had done so for longer or shorter than five years, respectively. It was challenging to evaluate the types and quantities of alcohol consumed each day, as well as the short and long term effects on GSD; a more prospective study on the relationships between alcohol and GSD is necessary.

#### **5.5. Other factors**

Of the female participants, 6.3% reported being pregnant, while 5.1% had a history of abortion. Additionally, 13.9% of females had been taking oral contraceptive pills (OCP) for over a year, while 48.1% had more than four pregnancies. On the other hand, 16.5% of the women had never been pregnant, while 35.4% had two or more pregnancies. It is worth noting that only one participant in the study received exogenous estrogen medication for longer than six months. Furthermore, 12.12% of the participants had undergone gastrointestinal surgery in the past, while the remaining 87.88% had not.

#### **5.6. Factors associated with GSD**

In this study, independent variables like socio-demographic characteristics such as age, sex, educational status, occupation, and residency; pathologic and metabolic conditions such as hypertension, DM, dietary habit, SCI, and history of rapid weight loss; genetic and behavioral factors such as a history of GSD/cholecystectomy in first-degree relatives; and alcohol intake; and other variables like pregnancy, exogenous estrogen, history of GI surgery, parity, abortion history, and OCP uses for more than six months were first analyzed with confirmed GSD by bivariate logistic regression. Based on the value of  $p < 0.2$  on bivariate logistic regression, independent variables like sex, DM, hypertension, alcohol intake for more than five years, family history of GSD in first-degree relatives, history of GI surgery, parity, history of abortion, residency, history of SCI and use of oral contraceptives were selected as candidates for multivariate analysis with confirmed GSD as shown by Table 3.

Table 3: The results of bivariant logistic regression for patients who visited the surgical department of DBCSH.

Independent variables	COR	P	CI	Remark
Age	3.18	0.085	1.33- 21.58	
Gender	15.2	0.01	1.93- 120.2	
Educational status	0.733	0.075	0.207- 2.59	
Occupation	2.50	0.219	0.58- 10.78	
Residency	3.41	0.047	1.02-11.7	
Diabetes	6.21	0.017	1.39- 27.7	
Hypertension	10.8	0.004	2.13- 55.4	
Spinal cord injury	6.7	0.038	1.1-40.9	
Dietary habit		1.00		
history of rapid weight loss		1.00		
Family history of GSD	13.6	0.013	1.75-106	
Alcohol intake for more than 5 years	4.3	0.014	1.35- 14.1	
History of GI surgery	5.7	0.006	1.66-19.7	
Parity	2 – 4 pregnancies	10.2	0.048	1.02 – 102.4
	More than 4 pregnancies	22.6	0.004	2.72 – 188.86
Abortion history	10.8	0.015	1.56-73.9	
Exogenous estrogen		1.00		
total parentran nutrition		1.00		
OCP uses	8.8	0.007	1.84-42.3	
pregnancy	21.25	0.052	1.12-40.03	

The result of multivariate logistic regression shows female gender ( $P = 0.014$ ,  $OR = 6.88$ ,  $CI = 2.348-20.2$ ), alcohol intake for more than five years ( $P = 0.007$ ,  $OR = 4.27$ ,  $CI = 2.761-66.83$ ), and gastrointestinal surgery ( $P = 0.049$ ,  $OR = 6.5$ ,  $CI = 1.011-42.77$ ) were significantly associated with GSD. In females, parity ( $>4$  pregnancies) ( $P = 0.011$ ,  $OR = 8.5$ ,  $CI = 2.745-26.35$ ), and when the effect of alcohol intake was adjusted, diabetes ( $P = 0.047$ ,  $OR = 4.6$ ,  $CI = 1.03-13.7$ ) and hypertension ( $P = 0.035$ ,  $OR = 1.37$ ,  $CI = 1.21-15.1$ ) were significantly associated with GSD. Table 4 describes the results of multivariate logistic regression.

Table 4: The results of multivariate logistic regression for patients who visited the surgical department of DBCSH.

Independent variables		COR	AOR	P	CI	Remark
Gender	Female	15.2	6.88	0.014*	2.34- 20.2	
	Male			1.00		
Residency		3.41				
Diabetes	Yes	6.21	4.6	0.047*	1.03- 13.7	When alcohol intake was adjusted
	No			1.00		
Spinal cord injury		6.7				
Family history of GSD		13.6				
Alcohol intake for > 4 years	Yes	4.3	4.27	0.007*	2.76- 66.8	
	No			1.00		
History of GI surgery	Yes	5.7	6.5	0.049*	1.01-42.7	
	No			1.00		
Parity	>4 pregnancies	22.6	8.5	0.011*	2.74 – 26.35	When sex is adjusted.
	Nulliparous			1.00		
Abortion history		10.8				
OCP uses		8.8				
Hypertention	Yes	10.8	1.37	0.035*	1.21- 15.1	When alcohol intake was adjusted
	No			1.00		

## 5. Discussion

In the present study, 86 (52.1%) were males and 79 (47.9%) were females, yielding a male to female ratio of 1.17:1. This is in agreement with a study conducted at TASH on the pathogenesis and clinical presentation of biliary tree blockage outside the liver; where the proportion of the females was 53.3%, and the ratio of females to males was 1:1.14 (55). The gender distribution varied across different populations. In Igbo, southeast Nigeria, 50.6% of the participants were women, while in southwest China, 53.8% were male. In Saudi Arabia, 50.9% of respondents from a high-altitude population were women, and in Sana, Yemen, men made up 51.5% of the study participants, which is also consistent with the findings of this study (22,41,43,44).

In contrast, according to a study conducted on the surgical results of biliary stone illness at Zewditu memorial and TASH, 84% of patients were female, and the female-to-male ratio was 5:1.5. According to a five-year study of GSD at TASH, the ratio of females to males was 5:1. There were 71.6% more women than men in research conducted at the Mekelle Ayder Referral Hospital. The South African survey found that women outnumbered men by 5.7:1. Based on a screening study conducted in rural Morocco, the female-to-male ratio was 3.27:1, with 23.4% of men (20,23,27,29,54,62). The discrepancy with the present study was explained by those studies, that used confirmed cases of GSD patients as study participants, whereas, the present study used patients who visited the surgical department of DCSH.

### 5.1. Prevalence of GSD

In the current study, the total prevalence of GSD among patients who visited the surgical department of DBCSH was 7.9%. This is nearly in agreement with 10.2% of what is indicated in the study done in St. Paulos Hospital Millennium Medical College (SPHMC), Addis Abeba. There was an upward trend in stone disorders, which grew by 10.8%. Another study done at Saint Paul's Hospital shows 7% of cases had stones in the bile duct, 10% in South Africa, 6.83% in Shanghai, China, 8.6% in another study in the southwest, China, 6.2% in northern India, 9.7% in Guadalajara, Spain's adult population, and 8.03% in Linkoping, Sweden (18,32,35,36,40,41,45,46).

In the current study, the total prevalence of GSD was slightly higher than 5.0% in central Taiwan, while dietary practices and environmental factors can alter the pigment types and composition of stones, and a population-based study describes the slightly lower prevalence of GSD, 5.53% in Sana, Yemen; 5.9% in Kumasi, Ghana; and 5.2% in the radiology department of Gondar University Hospital. The differences in methodology may have contributed to the variation in prevalence rates. (21,33,39,43). However, it is slightly lower than 11.7% of the Saudi high-altitude population. The cluster sampling method, combined with the use of couples as a study unit who share similar environmental risk factors, can contribute to a slightly higher prevalence of GSD (44).

In contrast to the following studies, the total prevalence of GSD in the current study was much lower; GSD was found to be prevalent in 24.8% of diabetic individuals in northern Italy, 17.7% of Type2 DM patients in North India, and 17.5% of diabetic individuals in Ibadan, Nigeria, had GS. The prevalence of GS in Nigeria identified by ultrasound in type 1 diabetes and types 2 diabetes was 10% and 18.11%, respectively. It has been suggested that having impaired glucose metabolism raises the chance of getting GS, which could explain the higher prevalence of GSD among diabetes (47–49).

It was found that the prevalence of GSD in the current study was much lower compared to an American study where 31% of SCI patients had gallstones. Similarly, among Chilean male patients with SCI, the prevalence was 25%. The study also revealed that a higher incidence of GSD in patients with SCI is linked to impaired gallbladder relaxation, which was usually limited to patients with SCI at or above T10 (51,52).

A Japanese study found the prevalence of GSD among individuals who underwent esophagectomy was 23%, which is not consistent with the present study. The Japanese study concluded that gallbladder hypomotility and biliary stasis due to truncal vagotomy could increase the risk of gallstone development in all forms after esophagectomy. (53,63).

The prevalence of GSD found in the current study was significantly lower than what Italian researchers have reported. According to their study, the prevalence of GD was much higher in first-degree relatives of individuals with gallstones (28.6%) compared to those without (12.4%), indicating a possible genetic connection (61).

Similarly, a higher prevalence of GSD was reported in Rosario, Argentina (20.5%), where a larger percentage of the population were immigrants from Europe, and 19.2% in rural Morocco due to higher consumption of western-style diet (89%) (23,38).

The total prevalence of GSD in the current study was higher than 2.4% in southeast Iran due to the small sample size, 4.4% in the sonographic study on adult Igbo individuals in southeast Nigeria. The lower prevalence of GSD in Nnewi, Nigeria, was explained by the protective effects of the hereditary, environmental, and dietary habits of the Igbo population (22,42).

## 5.2. Determinants of GSD

**Age:** In the present study, it was found that the ages of the participants did not have a significant association with GSD. This could be due to the changing age pattern of the disease. Additionally, the short period of the study, along with the small sample size and other unknown factors, may have also played a role.

In contrast to the present study, age has significant associations with the development of GSD according to a sonographic study carried out in Nigeria, screening studies conducted in central Taiwan and Shanghai, China, a study done in southeast Iran, and a screening survey conducted in Guadalajara, Spain (22,35,39,40,42).

According to the current study, the highest prevalence of GSD is observed in individuals aged between 26 and 45 years (61.3%). However, after the age of 65, it tends to decrease. This could be attributed to changing disease age patterns, indicating the presence of additional significant risk factors besides age, and majority of female participants in the current study were at reproductive age group in which the highest prevalence of GSD were attributed to the effects of sex hormones.

The finding of the current study was in agreement with a study conducted in Igbo, southeast Nigeria, which found that ages between of 31 and 40 are more susceptible to it. Interestingly, a survey conducted in South Africa revealed that in the final five years of the trial, more younger patients underwent surgery for GSD than in the previous five years, suggesting that age is not the only significant risk factor. This indicates a shift in the pattern of GSD and is consistent with a survey conducted in northern India, which found that age groups of 20–30 and 40–60 had a higher incidence of GSD patients (20,22,45).

In contrast to the present study, a study on patients who were admitted to the St. Paulos hospital Millennium Medical College (SPHMC), Addis Ababa, shows in males, the incidence of gallstones increased with age, but it decreased in females this may be because estrogen increases biliary cholesterol secretions (particularly during pregnancy) and causes cholesterol supersaturation of bile, a study done in Gonder university hospital displays GSD prevalence rises with patient age, based on a screening study conducted in rural Morocco, The condition is more prevalent (71.2%) in those over 40, the research in southwest China revealed that the frequency of GSD increased with age, reached its maximum between the ages of 80 and 90, and then started to decrease and according to a Rosario, Argentina study, GSD was more common as people aged (23,32,33,38,41).

**Female gender:** It was found in the study that the vast majority of patients diagnosed with GSD were female 92.3%, while only 7.7% were male. The study also revealed that women were more likely than men to have GS, which is consistent with findings from other studies conducted in various regions such as Igbo in southeast Nigeria, rural Morocco, Saudi's high-altitude population, Sana in Yemen, Rosario in Argentina, and Italy where researchers have found that mothers and sisters had the highest relative risks for GD (22,23,38,43,44,61). A considerably higher rate of GSD in women is due to conception, the impact of sex hormones and the disease is passed down through dominant sex-linked features.

According to the present research, female gender was significantly associated with GSD. The study found that women have a 6.88 times higher risk of developing GSD than men. This finding is consistent with several other studies, including Gonder University Hospital study, a sonographic study carried out in Nigeria, a survey conducted in northern India , and a high-altitude population study in Saudi Arabia (22,33,44,45). The reason behind this gender difference could be due to early marriages, longer reproductive periods, and the effect of sex hormones, which make females more prone to GS.

However; the present study finding was in contrast to the screening studies conducted in central Taiwan and Shanghai, China, sex does not show statistical significance, which was explained by the pigment types of stones common in Asian populations (39,40).

**Parity:** In the present study, it was found that 66.7% of females with GSD had more than four pregnancies, while 25% had two to four pregnancies and 8.3% were nulliparous. The present study shows that parity was significantly associated with GSD, with women who had four or more pregnancies having an 8.5 times higher risk of GSD than nulliparous women. These findings are consistent with a study in Rosario, Argentina, northern India, as well as a sonographic study in the Igbo region of Nigeria. (22,38,45).

**Alcohol intake:** The present study has shown that individuals who consumed alcohol for more than five years were at a significantly higher risk of developing GSD, with a 4.27 times higher risk than non-drinkers but majority of patients with GSD were women who consumes alcohol less than men. However, the available literature on the effect of alcohol intake for more than 5 years is inconsistent and conflicting. The present study was consistent with a study conducted in a rural area of Morocco, and Mexico showed that a history of alcohol abuse is preventative of gallstone disease. Possibly explained by alcohol decreases the saturation of bile cholesterol, which reduces cholesterol calculi and the fact that females consume small amount of alcohol inconsistently (23,59). The present study was inconsistent with a study conducted in Guadalajara, Spain, and Swedish forward cohort researches revealed that weekly alcohol use was linked to the growth and formation of GS. (35,36,).

**History of gastrointestinal surgery:** It has been found in the present study that individuals with a previous history of gastrointestinal surgery were significantly at a higher risk of developing GSD. The study reports that such individuals had a 6.5-fold greater risk of developing GSD. Similarly, studies conducted in Hungary after vagotomy, Japanese men after gastrectomy, central Taiwan, Shanghai, China and northern India have also found a correlation between a history of gastrointestinal surgery and the prevalence of GSD. (39,40,45,62,63). The possible scientific justification might be, even in cases where a vagotomy is not done, the surgical process of a gastrectomy may cause damage to the vagal nerves, which might lead to biliary stasis as a result of gallbladder dilatation and incomplete emptying (64). The cholecystograms following surgery showed gross dilatation. There were very few and compromised contractual responses. Following a total vagotomy, gallbladder hypotonia, and increased gallstone production (63).

**Diabetes:** The present study found a strong link between diabetes and GSD. The research shows that individuals with diabetes have a 4.6 times greater risk of developing GSD compared to those without diabetes. The findings of this study are consistent with previous research conducted in various regions, including Addis Ababa, Ethiopia, on the association between DM and GSD, SPHMC on the patterns of stone disease, central Taiwan, Shanghai, China, Mexico, and other parts of the world. These studies have also found a significant association between GSD and DM, highlighting the importance of diabetes management in preventing the development of GSD (32,39,40,47,55,59,60). There are probably several contributing factors to the higher frequency of GS in DM. Patients with diabetes have larger fasting gallbladder volumes than controls, which may indicate hypotonicity of the gallbladder results in bile stasis. In diabetics, cholecystokinin's impact on bile ejection also decreased. By lowering gallbladder motility, diabetic neuropathy also contributes. Changes in the metabolism of glucose also impact (47).

**Hypertension:** According to the present study, when the effect of alcohol intake was adjusted hypertension was found to be significantly associated with GSD. The risk of GSD was also observed to increase by 1.37 times among hypertensive individuals compared to non-hypertensive ones. There is evidence linking hypertension to an increased risk of gallstone disease, which is supported by a Japanese population-based cohort study where high blood pressure and treatment for hypertension were associated with a higher risk of cholelithiasis. Similarly, in southwest China (41,57). A study conducted at Zewditu memorial and TASH on the surgical outcomes of choledocholithiasis with symptoms, TASH on the clinical presentation and pathogenesis of biliary tree blockage outside the liver (54,55), and southwest China reveals that hypertension is the most frequently found co-morbidity (41).

## **6. Strength and limitations**

The strength of the present study includes sampling methods in which participants were selected proportionally on the base of yearly patient flow from the three units in the surgical department of DBCSH and study design.

The current study had the following limitations to be considered: first lack of laboratory investigations and sonographic study to all study participants; secondly, in relation to the use of secondary data variables like obesity (body-mass-index) and level of physical activity were not included which may affect GSD; Thirdly, institutional based study along with short study period; and finally the retrospective nature of the study.

## **7. Conclusion**

In the present study, the prevalence of GSD was found to be 7.9%. GSD was higher in females than males. GSD was more common between 26 – 45 years of age. The majority of patients with gallstones were asymptomatic. Abdominal pain and vomiting were leading symptoms present in all patients with symptomatic GSD. The most comorbidity identified was diabetes and hypertension. Female gender, alcohol intake for more than five years, and history of gastrointestinal surgery were significantly associated with GSD. For females parity and when alcohol intake was adjusted diabetes and hypertension were significantly associated with GSD. It was found that neither age nor family history of GSD were associated with GSD.

## **8. Recommendation**

Based on the findings of the current study, it was strongly recommended that: health institutions should focus on public education on GSD; early diagnosis and treatment of GSD to minimize missed diagnosis and detect silent stones; proper management of chronic comorbidities. finally, they should provide quality surgical services. Finally researchers should consider population-based studies to show the true prevalence of GSD and further prospective cohort studies should be conducted.

## References

1. Murphy MC, Gibney B, Gillespie C, Hynes J, Bolster F. Gallstones top to toe: what the radiologist needs to know. *Insights Imaging*. 2020 Feb;11(1):13.
2. Abou-Khalil JE, Bertens KA. Embryology, Anatomy, and Imaging of the Biliary Tree. *Surgical Clinics of North America*. 2019;99(2):163–74. Available from: <https://doi.org/10.1016/j.suc.2018.12.005>
3. Beckingham JJ. ABC of diseases of liver, pancreas, and biliary system: Gallstone disease. *British Medical Journal*. 2001;322(7278):9:1–4.
4. Feinstein AR, Wells CK. Re: “epidemiology of gallstone disease in Italy: Prevalence data of the multicenter Italian study on cholelithiasis (M.I.COL).” *American Journal of Epidemiology*. 1995;142(6):666.
5. Friedman GD, Raviola CA, Fireman B. Prognosis of gallstones with mild or no symptoms: 25 years of follow-up in a health maintenance organization. *Journal of Clinical Epidemiology*. 1989;42(2):127–36.
6. Gracie WA, Ransohoff DF. The Natural History of Silent Gallstones. *New England Journal of Medicine*. 1982;307(13):798–800. Available from: <https://doi.org/10.1056/NEJM198209233071305>
7. Festi D, Letizia M, Reggiani B, Attili AF, Loria P, Pazzi P, et al. Natural history of gallstone disease : Expectant management or active treatment ? Results from a population-based cohort study. *Journal of Gastroenterology and Hepatology*. 2010;25:719–24. Available from: [doi:10.1111/j.1440-1746.2009.06146.x](https://doi.org/10.1111/j.1440-1746.2009.06146.x) jgh\_6146
8. Kim IS, Myung SJ, Lee SS, Lee SK, Kim MH. Classification and nomenclature of Gallstones revisited. Vol. 44, *Yonsei Medical Journal*. 2003. p. 561–70.
9. Nd WHA, Small DM. The Physicochemical Basis of Cholesterol Gallstone Formation in Man. *Journal of Clinical Investigation*. 1968;47(1043):1043–52.
10. Kose SH, Grice K, Orsi WD, Ballal M, Coolen MJL. Metagenomics of pigmented and cholesterol gallstones: the putative role of bacteria. *Scientific Reports*. 2018;8(1):1–13. Available from: <http://dx.doi.org/10.1038/s41598-018-29571-8>
11. Diehl AK. Epidemiology and natural history of gallstone disease. *Gastroenterology Clinics of North America*. 1991;20(1):1–19.
12. Wang DQ h. Aging: is an independent risk factor for cholesterol gallstone formation in

- gallstone susceptible mice. *Journal of Lipid Research* . 2002;43(11):1950–9. Available from: <http://dx.doi.org/10.1194/jlr.M200078-JLR200>
13. Kern F, Everson GT, Demark B, Mckinley C, Showalter R, Erfling W, et al. Biliary Lipids , Bile Acids , and Gallbladder Function in the Human Female. *Journal of Clinical Investigation*. 1981;68(November):1229–42.
  14. Eliakim R, Abulafia O, Sherer DM. Estrogen, progesterone and the gastrointestinal tract. *Journal of Reproductive Medicine*. 2000 Oct;45(10):781–8.
  15. Shaffer EA. Epidemiology of gallbladder stone disease. *Best Practice and Research: Clinical Gastroenterology*. 2006;20(6):981–96.
  16. Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: Cholelithiasis and cancer. *Journal of Gut and Liver*. 2012;6(2):172–87.
  17. Shaffer EA. Epidemiology and risk factors for gallstone disease: Has the paradigm changed in the 21st century? *Current Gastroenterology Reports*. 2005;7(2):132–40.
  18. Kratzer W, Mason RA, Kächele V. Prevalence of gallstones in sonographic surveys worldwide. *Journal of Clinical Ultrasound*. 1999;27(1):1–7.
  19. Russo MW, Wei JT, Thiny MT, Gangarosa LM, Brown A, Ringel Y, et al. Digestive and Liver Diseases Statistics, 2004. *Gastroenterology*. 2004;126(5):1448–53.
  20. Khan ZA, Khan MU, Brand M. Increases in cholecystectomy for gallstone related disease in South Africa. *Scientific Reports*. 2020;10(13516):1–5. Available from: <https://doi.org/10.1038/s41598-020-69812-3>
  21. Gyedu A, Aday-Aboagye K, Badu-Peprah A. Prevalence of cholelithiasis among persons undergoing abdominal ultrasound at the Komfo Anokye Teaching Hospital, Kumasi, Ghana. *African Health Sciences*. 2015;15(1):246–52.
  22. Eze CU, Ezugwu EE, Ohagwu CC. Prevalence of cholelithiasis among igbo adult subjects in Nnewi, Southeast Nigeria: A community-based sonographic study. *Journal of Diagnostic Medical Sonography*. 2017;33(2):83–90.
  23. Bahja S, Hammoumi W, Figuigui M, Abid H, Yousfi M El, Benajah DA, et al. Epidemiology of Biliary Lithiasis in a Moroccan Rural Population: Results of a Screening Survey Including 1358 Citizens. *Saudi Journal of Medicine*. 2022;7(5):272–7.
  24. Walker AR, Segal I, Posner R, Shein H, Tsotetsi NG, Walker AJ. Prevalence of gallstones in elderly black women in Soweto, Johannesburg, as assessed by ultrasound. *American*

- Journal of Gastroenterology. 1989 Nov;84(11):1383–5.
25. Rahman GA. Cholelithiasis and cholecystitis: Changing prevalence in an African community. *Journal of the National Medical Association*. 2005;97(11):1534–8.
  26. Mahadi SI, Nasr AO, Fahad K, Hospital U. Pattern of Surgical Operations in One Unit at Khartoum Teaching Hospital. *Sudan Medical Journal*. 2022;(February): 50(1): 1-8.
  27. Kidanu M, Amdeslasie F. The magnitude and clinical profile of gallstone disease in ayder referral hospital , mekelle , ethiopia : a cross-sectional descriptive study. *Ethiopian Medical Journal*. 2017;55(3).
  28. Bekele Z, Tegegn K. Cholecystitis: the Ethiopian experience, a report of 712 operated cases from one of the referral hospitals. *Ethiopian Medical Journal*. 2002 Jul;40(3):209–16.
  29. Ersumo T. Gallstone disease in a teaching hospital Addis Ababa a 5 year review. *Ethiopian medical journal*. 2006; 44(1): 49-59
  30. Gebresellassie HW, Tamerat G. Audit of surgical services in a teaching hospital in Addis Ababa , Ethiopia. *BMC Research Notes*. 2019;12(678):1–5. Available from: <https://doi.org/10.1186/s13104-019-4709-y>
  31. Adem A, Abebe A, Abdurahman M. Pattern of surgical admissions to Tikur Anbessa. *Ethiopian Medical Journal*. 1997;353:74–7.
  32. Alealign T, Debella A, Tessema TS, Petros B. Thirteen Years Trend in the Magnitude of Urolithiasis and Cholelithiasis in Ethiopia: Evidence from Hospital-Based Retrospective Study. *Research Square*. 2019;13:1–25. Available from: <https://orcid.org/0000-0001-8384-2593>
  33. Getachew A. Epidemiology of gallstone disease in Gondar University Hospital, as seen in the department of radiology. *Ethiopian Journal of Health Development*. 2009;22(2): 206-211.
  34. Yoo EH, Lee SY. The prevalence and risk factors for gallstone disease. *Clinical Chemistry and Laboratory Medicine*. 2009;47(7):795–807.
  35. De Pancorbo CM, Carballo F, Horcajo P, Aldeguer M, De La Villa I, Nieto E, et al. Prevalence and associated factors for gallstone disease: Results of a population survey in Spain. *Journal of Clinical Epidemiology*. 1997;50(12):1347–55.
  36. Halldestam I, Kullman E, Borch K. Incidence of and potential risk factors for gallstone

- disease in a general population sample. *British journal of surgery*. 2009;96:1315–22.  
Available from: doi: 10.1002/bjs.6687
37. Festi D, Dormi A, Capodicasa S, Staniscia T, Attili AF, Loria P, et al. Incidence of gallstone disease in Italy : Results from a multicenter , population-based Italian study ( the MICOL project ). *World Journal of Gastroenterology*. 2008;14(34):5282–9.
  38. Brasca AP, Pezzotto SM, Stat M, Berli D, Villavicencio R, Fay O, et al. Epidemiology of Gallstone Disease in Argentina : Prevalences in the General Population and European Descendants. *Digestive Diseases and Sciences*. 2000;45(12):2392–8.
  39. Chen CH, Huang MH, Yang JC, Nien CK, Etheredge GD, Yang CC, et al. Prevalence and risk factors of gallstone disease in an adult population of Taiwan: An epidemiological survey. *Journal of Gastroenterology and Hepatology (Australia)*. 2006;21(11):1737–43.
  40. Song ST, Shi J, Wang XH, Guo Y Bin, Hu PF, Zhu F, et al. Prevalence and risk factors for gallstone disease: A population-based cross-sectional study. *Journal of Digestive Diseases*. 2020;21(4):237–45.
  41. Zhang Y, Sun L, Wang X, Chen Z. The association between hypertension and the risk of gallstone disease : a cross - sectional study. *BMC Gastroenterology*. 2022;22(138):1–10.  
Available from: <https://doi.org/10.1186/s12876-022-02149-5>
  42. Ansari-Moghaddam A, Khorram A, Miri-Bonjar M, Mohammadi M, Ansari H. The Prevalence and Risk Factors of Gallstone Among Adults in South-East of Iran: A Population-Based Study. *Global Journal of Health Science*. 2015;8(4):60–7.
  43. Aklan HM, Al-mikhlaify A, Al-goshae HA. Frequency of Gallbladder Stones Among Patients Underwent Abdominal Ultrasound in a Tertiary Hospital in Sana ' a City , Yemen . *Malaysian Journal of Medicine and Health Sciences*. 2020;16(August):5–9.
  44. S.A. Abu-Eshy, A.A. Mahfouz, A. Badr, M.N. El Gamal, M.Y. Al-Shehri, M.I. Salati MER et al. prevalence and risk factors of gallstone disease in a high altitude Saudi population. *Eastern Mediterranean Health Journal*. 2007;13(4):794–802.
  45. Unisa S, Jagannath P, Dhir V, Khandelwal C, Sarangi L, Roy TK. Population-based study to estimate prevalence and determine risk factors of gallbladder diseases in the rural Gangetic basin of north India. *Hepato-pancreatico-biliary Journal*. 2011;13(2):117–25.  
Available from: <http://dx.doi.org/10.1111/j.1477-2574.2010.00255.x>
  46. Kassa S, Kotisso B, Deneke A. Surgical Management of Common Bile Duct Stones at

- Saint Paul's Hospital, Addis Ababa, Ethiopia. *Ethiopian Medical Journal*. 2009;14(1):18–23.
47. Pagliarulo M, Fornari F, Fraquelli M, Zoli M, Giangregorio F. Gallstone disease and related risk factors in a large cohort of diabetic patients. *Digestive and Liver Disease*. 2004;36:130–4. Available from: doi:10.1016/j.dld.2003.10.007
  48. Sodhi JS, Zargar SA, Khateeb S. Prevalence of gallstone disease in patients with type 2 diabetes and the risk factors in North Indian population : A case control study. *Indian Journal of Gastroenterology*. 2014;33(December):507–11.
  49. Agunloye AM, Adebakin AM, Adeleye JO, Ogunseyinde AO. Ultrasound prevalence of gallstone disease in diabetic patients at Ibadan , Nigeria. *Nigerian Journal of Clinical Practice*. 2013;16(1):71–5.
  50. Chen C hua, Lin C li, Hsu C y, Kao C hung. Association Between Type I and II Diabetes With Gallbladder Stone Disease. *Journal of Endocrinology*. 2018;9(November):1–8.
  51. Moonka R, Stiens SA, Resnick WJ, Mcdonald JM, Eubank WB, Dominitz JA, et al. The Prevalence and Natural History of Gallstones in Spinal Cord Injured Patients. *Journal of American College of Surgery*. 1997;189(3):274–81.
  52. Rotter KP, Larraõâ CG. Gallstones in spinal cord injury ( SCI ): a late medical complication ? *International Spinal Cord Society*. 2003;41:105–8.
  53. Tsunoda K, , Yoshio Shirai , Toshifumi Wakai1 , Naoyuki Yokoyama1 KA, Hatakeyama and K. Increased risk of cholelithiasis after esophagectomy. *Journal of Hepatobiliary Pancreatic Surgery*. 2004;8(11):319–23. Available from: DOI 10.1007/s00534-004-0914-7
  54. Prakash A, Gonemo A, Halabo TT. A retrospective analysis of operative outcomes of symptomatic biliary stone disease at 2 referral hospitals in Addis Ababa, Ethiopia. *East and Central African Journal of Surgery*. 2021;25(March 2022):1–17.
  55. Abebe E, Tsehay A, Muleta MB. Analysis of the etiological spectrum and clinical profile of extra-hepatic biliary tree obstruction at a tertiary hospital in original article analysis of the etiological spectrum and clinical profile of extra- hepatic biliary tree obstruction at a tertia. *Ethiopian Medical Journal*. 2019;57(January 2021):125–32.
  56. Bekele Z, Yifru A. Obstructive jaundice in adult Ethiopians in a referral hospital. *Ethiopian Medical Journal*. 2000 Oct;38(4):267–75.

57. Id KH, Id EN, Hawke P, Fujimoto S. Risk factors for gallstone disease onset in Japan : Findings from the Shizuoka Study , a population-based cohort study. *PLoS One*. 2022;17(12):1–13. Available from: <http://dx.doi.org/10.1371>.
58. Chen C yen, Lu C liang, Huang Y shin, Tam T nip, Chao YEE, Chang F young, et al. Age is one of the risk factors in developing gallstone disease in Taiwan. *British Genatncs Society*. 1998;27:437–41.
59. Buchner AM, Ph D, Sonnenberg A, Sc M. Factors Influencing the Prevalence of Gallstones in Liver Disease : The Beneficial and Harmful Influences of Alcohol. *American Journal of Gastroenterology*. 2002;97(4):0–4.
60. Iasu YT, Kebede T. The Association of Diabetes Mellitus with Cholelithiasis and Liver Diseases in Addis Ababa - Ethiopia. *East and Central African Journal of Surgery*. 2012;17(1):70–6.
61. Attili AF, Santis A De, Attili F, Roda E, Festi D, Carulli N, et al. Prevalence of gallstone disease in first-degree relatives of patients with cholelithiasis. *World Journal of Gastroenterology*. 2005;11(41):6508–11.
62. Ikeda Y, Shinchu K, Kono S, Tsuboi K, Sugimachi K. Risk of Gallstones Following Gastrectomy in Japanese Men. *Surgery Today*. 1995;25:515–8.
63. Ihasz M, Griffith CA. Gallstones After Vagotomy. *American Journal of Surgery*. 1981;1:48–50.
64. Roden ADN De, Pourbaix A, Aupaix F, Coumans P, Therasse G. Cholelithiasis : a serious complication after total gastrectomy. *British Journal of Surgery*. 1988;7:899–900.

Annex: I – checklists

MRN: \_\_\_\_\_

Part I: Socio-demographic					
s.no	Questions	Answers	Code		
101	Age	_____years (in completed years)			
102	Sex	A. Male			
		B. Female			
103	Education level	I. Illiterate			
		II. Primary education			
		III. Secondary			
		IV. College diploma & above			
104	Occupation	a) Governmental			
		b) Private work			
		c) Housewife			
		d) Farmer			
		e) Others(like student)			
105	Residency	1. Urban			
		2. Rural			
Part II: Gallstone related characteristics					
201	Confirmed gallstone disease	1) Yes			
		2) no			
202	If yes to Q 201, symptoms at the diagnosis?	a) Yes			
		b) No			
202	If yes to Q 202, identified symptoms	Abdominal pain	Type	A. Biliary colic	
				B. Sharp	
				C. Others	
		Exacerbation	I. Fatty meal		
			II. Exercise		
		Site/ location	1. RUQ		
			2. Epigastric		
			3. LUQ		
		Radiation	A. Back		
			B. Shoulder		
			C. None		
		Vomiting	A. Yes		
			B. No		
		Nausea	1. Yes		
2. No					
Dark urine and stool	I. yes				
	II. no				
Jaundice	1. yes				
	2. no				
203	Have you ever had an ultrasound scan	A. yes			

	for RUQ?	B. no	
204	if yes, ultrasound finding	I. normal,	
		II. gallstone-positive,	
		III. biliary sludge-positive,	
		IV. previous cholecystectomy, or	
		V. Inconclusive or uncertain	
205	History of cholecystectomy	a) Yes	
		b) No	
Part III: Pathologic and metabolic conditions:			
301	Diabetes	I. yes	
		II. no	
302	Liver cirrhosis	I. yes	
		II. no	
303	HCV infection/HBV	I. yes	
		II. no	
304	Haemolytic anemia	I. yes	
		II. no	
305	Spinal cord injury	I. yes	
		II. no	
306	Dietary habit	a) vegetarian	
		b) fatty meal	
		c) mixed	
307	Have you ever attempted a diet to lose weight?	I. yes	
		II. no	
308	If yes to Q309, the weight lost in kg?		
Part IV: Genetic and behavioral factors:			
401	History of GSD (gallstones &/or cholecystectomy) in 1 <sup>st</sup> degree relatives	1) yes	
		2) no	
402	Cigarette smoking	a) yes	
		b) no	
403	If yes to Q402, for how long do you smoke?	I. More than 5 years	
		II. Less than 5 years	
404	Alcohol consumption	C. yes	
		D. no	
405	If yes to Q404, for how long do you drink?	I. More than 5 years	
		II. Less than 5 years	
406	History of drug use for more than 6 months	A. yes	
		B. no	
408	If yes to Q407, types of drug used	_____	
Part V: Others factors			
501	Pregnancy	a) yes	
		b) no	

502	Administration of exogenous estrogen	I. yes	
		II. no	
503	History of GI surgery	1. yes	
		2. no	
504	prolonged total parenteral nutrition	a) yes	
		b) no	
505	Parity	i. less than two pregnancies	
		ii. two-four pregnancies	
		iii. more than four pregnancies	
506	History of Abortion	1) yes	
		2) no	
507	Use of oral contraceptives for more than 6 months?	A. Yes	
		B. No	
Part VI : physical examination at the admission			
601	Vital sign	Tempreture	
		Blood pressure	a) Below 90/60 mmhg
			b) Between 90/60 mmhg- 140/90 mmhg
			c) Above 140/90 mmhg
		Heart rate	
Respiratory rate			
602	RUQ tender ness	i. Yes	
		ii. No	
603	Murpghy's sign	A. Yes	
		B. No	

Thank you !