

# Prevalence of cholelithiasis among persons undergoing abdominal ultrasound at the Komfo Anokye Teaching Hospital, Kumasi, Ghana.

Adam Gyedu<sup>1,2</sup>, Kwadwo Adaye-Aboagye<sup>2</sup>, Augustina Badu-Peprah<sup>3</sup>

1. Department of Surgery, School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
2. Directorate of Surgery, Komfo Anokye Teaching Hospital, Kumasi, Ghana
3. Directorate of Diagnostics, Komfo Anokye Teaching Hospital, Kumasi, Ghana

## Abstract

**Background:** The prevalence of gallstones among Ghanaians is unknown. We aimed to determine the prevalence of gallstones among persons undergoing abdominal ultrasound at the Komfo Anokye Teaching Hospital (KATH).

**Methods:** We performed a cross-sectional study of patients aged  $\geq 14$  years presenting to KATH for abdominal ultrasound between 2009 and 2012. Patient demographics were recorded. The gallbladder was assessed by ultrasonography. Cholelithiasis was defined as presence of gallstones or absence of gallbladder. Data was expressed as descriptive and inferential statistics.

**Results:** There were 2824 participants. 55% were females. Mean age was  $47 \pm 18$  years. Mean body mass index (BMI) was  $24.0 \pm 5.5$ . Mean parity among females was  $3 \pm 3$ . Prevalence of cholelithiasis was 5.9 (95%CI:5.0,6.8). Females had a high prevalence compared to males (6.8 vs 4.7). Prevalence increased steadily by age. Prevalence was 6.6, 5.1 and 8.8 for patients with BMI  $< 18.5$ , 18.5-24.9 and  $\geq 30$  respectively. Prevalence among women with parity of 0, 1-5 and  $> 5$  was 3.1, 6.7 and 6.4 respectively. On multivariate regression analysis, female sex (AOR=1.55;  $p < 0.05$ ), age  $\geq 40$  years (AOR=2.05;  $p < 0.01$ ), BMI  $< 18.5$  (AOR=1.25;  $p > 0.05$ ) or BMI  $\geq 30$  (AOR=1.39;  $p > 0.05$ ) and family history of gallstones (AOR=11.9;  $p < 0.01$ ) increased the odds of cholelithiasis.

**Conclusions:** Prevalence of cholelithiasis among patients undergoing ultrasonography at KATH was 5.9. Patient age, sex and family history significantly influenced the prevalence.

**Key words:** Cholelithiasis, Prevalence, Kumasi, Ghana

**DOI:** <http://dx.doi.org/10.4314/ahs.v15i1.32>

## Introduction

Cholelithiasis is a worldwide problem and it remains a common cause of surgical intervention, contributing substantially to health care costs. Its prevalence however, varies widely among different populations. Among American adults the prevalence of cholelithiasis is about 10% while in Western Europe the prevalence ranges from 5.9% to 21.9%<sup>1</sup>. Prevalence rates of 3.2% to 15.6% have been reported from Asia<sup>2</sup>.

Cholelithiasis has historically been considered rare in sub-Saharan Africa<sup>3,4</sup>. As many African countries undergo rapid urbanization with a steady shift towards a westernized diet cholelithiasis will assume importance in these populations<sup>4</sup>.

There appears to be a rise in the incidence of cholecystectomy in Ghana over the years. Korle-Bu Teaching Hospital in Accra recorded an increase from 2-11 cholecystectomies per year in the 1980s to 38 in 1990 and 60 in 1991<sup>5</sup>. A similar trend has been noticed in our institution, Komfo Anokye Teaching Hospital, where from unpublished data there has been an increase in the number of cholecystectomies performed from 2006 to 2013. Estimating prevalence or incidence of cholelithiasis from patients with clinical gallstone disease, however, has a major limitation in that most gallstones remain asymptomatic during a lifetime. The prevalence of cholelithiasis among Ghanaians remains unknown. This study aimed to determine the prevalence of cholelithiasis among persons undergoing an abdomi-

nal ultrasound at the Komfo Anokye Teaching Hospital (KATH). KATH is located in Kumasi, Ghana and it is the second-largest referral hospital in Ghana.

## Methods

We designed a cross-sectional descriptive study of all patients aged 14 years and above presenting to the Radiology department of KATH for abdominal ultrasonography (USG) between May 2009 and May 2012. Only patients who gave informed consent were recruited. After obtaining consent demographic data was recorded from each patient. We measured patient's weight using a BR9012-model Camry® mechanical scale (Guandong, China) after having them take off shoes and heavy outer clothing. Height was measured with a graduated paper strip attached to the wall.

The gallbladder was assessed with two ultrasound machines: Siemens Sonoline Sienna (Siemens Healthcare, Erlangen, Germany) and Siemens Sonoline G50 (Siemens Healthcare, Erlangen, Germany), employing probes of 3.5-5 MHz depending on the size of the patient. A consultant radiologist supervised all the sonographic investigations. The data was entered into a Microsoft Access (Redmond, WA) database and after data cleaning it was exported to Stata v11 (College Station,

TX) for analysis. Continuous variables were reported as mean and standard deviation. Categorical variables were reported as proportions.

Cholelithiasis was defined as presence of gallstones on ultrasound or absence of gallbladder on ultrasound with a history of cholecystectomy<sup>2</sup>. Prevalence of the various gallbladder findings was reported as percentages with 95% confidence intervals (CI). Association between the various demographic variables and cholelithiasis was expressed as odds ratio (OR) with 95% CI. Adjusted ORs (AOR) were estimated by multiple logistic regression to determine the effect of different variables on cholelithiasis. Parity of the participants was excluded in the multiple logistic regression since it did not exist for males (45% of the sample).

The study was approved by the institutional review board of Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

## Results

Patient demographics are summarized in Table 1. There were 2824 participants in the study. Fifty-five percent were females. Mean age was  $47.0 \pm 18.0$  years. Sixty-one percent were 40 years or above. Mean body mass index (BMI) was  $24.0 \pm 5.5$ . Mean parity among females was  $3 \pm 3$ .

Table 1: Patient demographics (N=2824)

Variable	Female	Male	Total
<b>Age, mean (SD), years</b>	44.9±16.6	50.7±19.0	47.0±18.0
<b>Age group (n, %)</b>			
<40	677 (43.8)	391 (30.6)	1068 (37.8)
$\geq 40$	861 (55.7)	876 (68.5)	1737 (61.5)
Missing	7 (0.5)	12 (0.9)	19 (0.7)
<b>BMI (n, %)</b>			
<18.5	196 (12.7)	167 (13.1)	363 (12.9)
18.5-24.9	638 (41.3)	691 (54.0)	1329 (47.1)
25.0-29.9	340 (22.0)	277 (21.6)	617 (21.8)
$\geq 30.0$	289 (18.7)	88 (6.9)	377 (13.3)
Missing	82 (5.3)	56 (4.4)	138 (4.9)
<b>Family history of gallstones (n, %)</b>			
Yes	23 (1.5)	16 (1.2)	39 (1.3)
No	1521 (98.4)	1262 (98.7)	2783 (98.6)
Missing	1 (~0.1)	1 (~0.1)	2 (~0.1)
<b>Diabetes Mellitus (n, %)</b>			
Yes	228 (14.8)	162 (12.7)	390 (13.8)
No	1316 (85.1)	1116 (87.2)	2432 (86.1)
Missing	1 (~0.1)	1 (~0.1)	2 (~0.1)
<b>Parity</b>			
0	285 (18.4)		
1-5	792 (51.3)		
>5	342 (22.1)		
Missing	126 (8.2)		
<b>Total</b>	<b>1545 (100.0)</b>	<b>1279 (100.0)</b>	<b>2824 (100.0)</b>

## Corresponding author:

Adam Gyedu  
 Department of Surgery, School of  
 Medical Sciences Kwame Nkrumah  
 University of Science and Technology,  
 Kumasi, Ghana  
 Email: drgyedu@gmail.com

On USG, 141 patients had gallstones present and 25 had undergone cholecystectomy (Table 2).

Table 2: USG finding of gallbladder N=2824

Finding	Frequency	Prevalence (95% CI)
Normal	2657	94.1 (93.2, 94.9)
Gallstones*	141	5.0 (4.2, 5.9)
Cholecystectomy	25	0.9 (0.6, 1.3)
Gallbladder sludge	25	0.9 (0.6, 1.3)
Cholecystitis	21	0.7 (0.5, 1.1)
Calculous cholecystitis	8	0.3 (0.1, 0.6)

\*Frequency and prevalence of cholelithiasis: 166 and 5.9 (95% C.I; 5.0, 6.8) respectively.

Per our working definition, the number of patients with cholelithiasis was thus 166. Among 141 patients with evidence of gallstones on USG, 8 had cholecystitis. Twenty-five patients had biliary sludge on USG, nine of whom also had gallstones present. Table 3 summarizes the prevalence of cholelithiasis for various demographic variables by gender.

Table 3: Prevalence of cholelithiasis

	Female prevalence (95% CI)	Male prevalence (95% CI)	Total prevalence (95% CI)
<b>Sex</b>	6.9 (5.7, 8.2)	4.7 (3.6, 6.0)	5.9 (5.0, 6.8)
<b>Age, years</b>			
<40	3.8 (2.5, 5.6)	3.3 (1.8, 5.6)	3.7 (2.6, 5.0)
≥40	9.3 (7.4, 11.4)	5.3 (3.9, 6.9)	7.3 (6.1, 8.6)
<b>BMI</b>			
<18.5	6.1 (3.2, 10.4)	7.2 (3.8, 12.2)	6.6 (4.3, 9.7)
18.5-24.9	5.5 (3.9, 7.5)	4.8 (3.3, 6.6)	5.1 (4.0, 6.4)
25.0-29.9	7.4 (4.8, 10.6)	2.9 (1.3, 5.6)	5.4 (3.7, 7.4)
≥30.0	9.7 (6.5, 13.7)	5.7 (1.9, 12.8)	8.8 (6.1, 12.1)
<b>Parity</b>			
0	3.9 (1.9, 6.8)		
1-5	6.7 (5.1, 8.7)		
>5	6.4 (4.1, 9.6)		
<b>Family history of gallstones</b>			
Yes	39 (20, 61)	44 (20, 70)	41 (25, 58)
No	6.4 (5.2, 7.7)	4.2 (3.2, 5.5)	5.4 (4.6, 6.3)
<b>Diabetes Mellitus</b>			
Yes	7.0 (4.1, 11.1)	6.2 (3.0, 11.1)	6.7 (4.4, 9.6)
No	6.8 (5.5, 8.3)	4.5 (3.3, 5.9)	5.8 (4.9, 6.8)

The overall prevalence of cholelithiasis among the population was 5.9 (95% CI: 5.0, 6.8). Prevalence among females [6.9 (95% CI: 5.7, 8.2)] was significantly higher than that among males [4.7 (95% CI: 3.6, 6.0)] ( $p < 0.01$ ). Likewise prevalence was significantly higher among patients 40 years or older than among those under 40 years ( $p < 0.001$ ). Prevalence among patients <20 years was 2.8 and this rose steadily to 9.4 among those 50-59

years. The prevalence then fell to 5.3 in the 70-79 year group, rising again after 80 years (fig 1). Prevalence was higher among females in all age groups except for ages less than 20 years.

Patients with a normal BMI had a prevalence of 5.1 (95% CI: 4.0, 6.4). Patients who were underweight (BMI

<18.5) or overweight (BMI 25.0-29.9) had a statistically non-significant higher prevalence of cholelithiasis, respectively, compared to those with normal BMI. Obese patients, on the hand, had a statistically significant higher prevalence of cholelithiasis compared to patients with normal BMI. The prevalence of cholelithiasis among nulliparous women was 3.9 (95% CI: 1.9, 6.8).

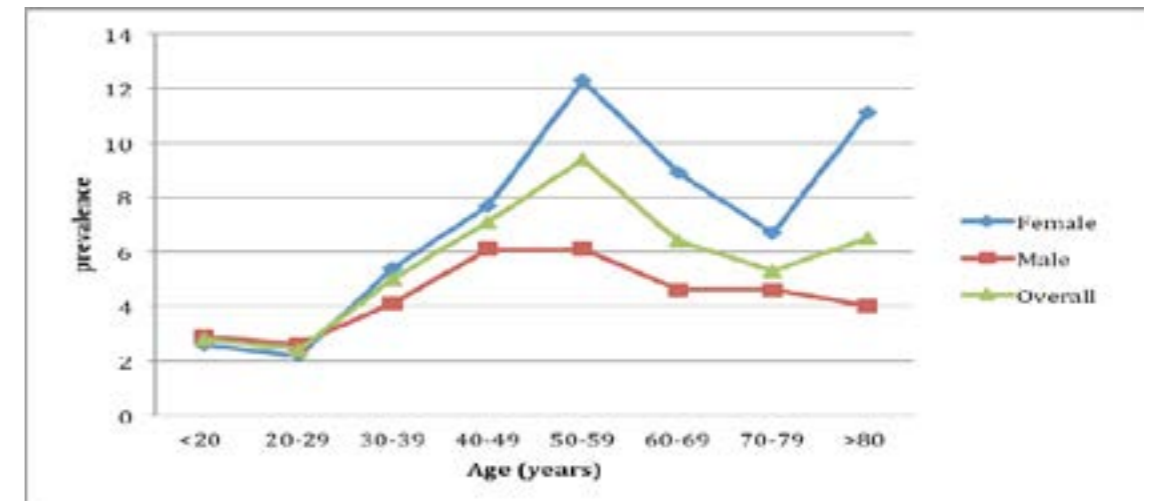


Fig 1: Prevalence of cholelithiasis among different age groups

The prevalence was higher among women with parity 1-5 ( $p < 0.05$ ) and also among women with parity greater than five ( $p > 0.05$ ). Among the 39 patients with a positive family history of cholelithiasis, 16 had cholelithiasis giving a prevalence of 41 (95% CI: 25, 58). The prevalence was 6.7 (95% CI: 4.4, 9.6) among patients with a history of diabetes mellitus.

Multivariate regression analysis (Table 4) showed that female sex (AOR=1.55;  $p < 0.05$ ), age 40 years and above (AOR=2.05;  $p < 0.001$ ), BMI less than 18.5 (AOR=1.25;  $p > 0.05$ ) or BMI of at least 30 (AOR=1.39;  $p > 0.05$ ) and family history of gallstones (AOR=11.9;  $p < 0.001$ ) were associated with increased odds of developing cholelithiasis. Diabetes mellitus however was associated with decreased odds of developing cholelithiasis (AOR=0.94;  $p > 0.05$ ).

Table 4: Odds of developing cholelithiasis

	Univariate		Multivariate	
	O.R (95% C.I)	P-value	AOR (95% C.I)	P-value
<b>Sex</b>				
Female vs Male	1.50 (1.08, 2.07)	<b>0.02</b>	1.55 (1.09, 2.20)	<b>0.02</b>
<b>Age (years)</b>				
≥40 vs <40	2.06 (1.42, 2.98)	<b>&lt;0.001</b>	2.05(1.39, 3.01)	<b>&lt;0.001</b>
<b>BMI*</b>				
<18.5	1.31 (0.81, 2.12)	0.27	1.25 (0.76, 2.04)	0.38
25.0-29.9	1.05 (0.68, 1.61)	0.83	0.96 (0.62, 1.48)	0.84
≥30.0	1.78 (1.15, 2.74)	0.01	1.39 (0.88, 2.20)	0.16
<b>Parity</b>				
1-5 vs 0	1.79 (0.92, 3.47)	0.09		
>5 vs 0	1.71 (0.82, 3.59)	0.16		
<b>Family history</b>				
Yes vs No	12.2 (6.3, 23.60)	<b>&lt;0.001</b>	11.9 (6.0, 23.6)	<b>&lt;0.001</b>
<b>DM</b>				
Yes vs No	1.16 (0.76, 1.80)	0.48	0.94 (0.59, 1.51)	0.81

\* Reference BMI: 18.5-24.9

## Discussion

This study attempts to estimate the prevalence of cholelithiasis among persons having an abdominal ultrasound at KATH. It also tries to determine the predictors of cholelithiasis among this population. The overall prevalence of cholelithiasis among the population was 5.9. Patient age, sex, and family history significantly increased the odds of developing cholelithiasis.

There have been studies from sub-saharan Africa reporting increasing rates of cholecystectomy for cholelithiasis over the years<sup>5-7</sup>. This has been attributed to either a true rise in the incidence of gallstones or better diagnosis due to increased physician awareness and increased use of ultrasonography. Surgeons' attitude towards indications for cholecystectomy may also influence cholecystectomy rates<sup>8</sup>, however the prevalence of gallstone disease in a population seems to have little influence on the incidence of cholecystectomy<sup>9</sup>. In addition, only 20% of patients with gallstones ever develop symptoms<sup>10</sup>. Thus estimating gallstone prevalence or incidence from symptomatic patients is likely to yield much higher estimates. Our estimated prevalence of cholelithiasis of 5.9% is comparable to the 5.2% reported from both Sudan and Ethiopia<sup>11</sup>. It is however slightly higher than that reported from most Asian countries but much lower than that reported for the Americas and most of Western Europe<sup>2</sup>. It must be noted though that most of the studies from the Americas and Western Europe were population-based. Population-based work on cholelithiasis prevalence in Ghana is needed to fully understand the burden of the disease. A higher cholelithiasis rate may not necessarily translate into more complications of cholelithiasis. However knowledge that the condition is not too uncommon in our population will increase the index of suspicion among clinicians when faced with the appropriate patient.

## Predictors of cholelithiasis

### Age

Increasing age has been universally regarded as a significant risk factor for cholelithiasis. Long-term exposure to chronic environmental factors may account for the increased relative risk<sup>8,11,12</sup>. Our data showed a steady rise in cholelithiasis prevalence with age with patients 40 years or older having significantly increased odds of cholelithiasis.

## Sex

With the exception of patients of age less than 20 years, prevalence was higher among females in all age groups. Females had significantly increased odds of cholelithiasis compared to males. The risk of gallstone disease is greater in women than in men at all ages in the majority of studies<sup>2</sup>. Exceptions are studies from Taiwan reporting no statistical significance in the prevalence of cholelithiasis among males and females<sup>12-14</sup>. The more commonly found pigment stones in that population have been offered as a possible reason for this exception. Cholesterol stones are presumed to be related to metabolic disorders, which are more commonly seen in women<sup>12</sup>.

## Parity

Increased parity was associated with increased odds of cholelithiasis in our population on univariate analysis although this increase was not statistically significant. Most studies document an increased odds of cholelithiasis associated with childbearing and parity<sup>15-17</sup>. There are other studies, however, that could not verify these findings<sup>18,19</sup>.

## Obesity

Obesity has been identified as a major risk factor for developing cholelithiasis irrespective of gender<sup>2, 15,20,21</sup>. Our findings are in agreement with this observation although the increased odds among patients with BMI less than 18.5 or BMI of at least 30.0 estimated from our population were not statistically significant. There are studies that have found no association between BMI and cholelithiasis<sup>8</sup>, or even reduced odds of cholelithiasis among individuals with higher BMI<sup>22</sup>.

## Diabetes Mellitus

Diabetes mellitus is associated with cholelithiasis and the association has been linked to increased cholesterol saturation in gallbladder bile<sup>20,23</sup>. In our population diabetes mellitus was associated with non-significant decreased odds of cholelithiasis on multivariate analysis. Not formally testing our patient population could have affected our results and may explain our observation.

## Family history

Some studies have shown a positive relationship between prevalence of cholelithiasis and family history of the disease<sup>24,25</sup>. Others have not been able to show such a positive relationship<sup>26</sup>. Our data suggests that pa-

tients with a positive family history have significantly increased odds of developing cholelithiasis. Since positive family history was not based on screening for cholelithiasis among patients' relatives, our ability to fully interpret this observation is limited. The study has some limitations. Firstly, diabetes mellitus status was ascertained from history taking, not from formal testing. This could affect the true prevalence of diabetes mellitus among our participants. Secondly, a positive family history of gallstones was not based on screening for gallstones among patients' relatives. This limits our ability to fully interpret our observation, as family members with gallstones could be asymptomatic and may not have undergone cholecystectomy. Thirdly, BMI could not be determined in 138 patients because they were bedridden or kyphotic. Fourthly, our working definition of cholelithiasis included patients who had undergone a cholecystectomy. Although cholecystectomy could be due to acalculous cholecystitis, the rare nature of this condition implies that the numbers it may contribute to cholecystectomized patients is expected to be very small indeed<sup>27</sup>. Finally, although participants of our study were persons coming for an abdominal ultrasound for any indication mostly on an outpatient basis, they may not fully represent the population of Kumasi.

## Conclusion

Cholelithiasis is not an uncommon condition among persons undergoing abdominal ultrasonography in KATH, Ghana. Patient age, sex and family history significantly increased the odds of developing cholelithiasis.

**Acknowledgement:** We wish to thank Dr. Samuel Nguah for his support.

**Conflict of interest:** The Authors declare no financial or personal conflict of interest.

## References

1. Barbara L, Sama C, Morselli Labate AM, Taroni F, Rusticali AG, Festi D, et al. A population study on the prevalence of gallstone disease: the Sirmione Study. *Hepatology* (Baltimore, Md). 1987 Sep-Oct;7(5):913-7.
2. Shaffer EA. Epidemiology and risk factors for gallstone disease: has the paradigm changed in the 21st century? *Current gastroenterology reports*. 2005 May;7(2):132-40.

3. Perissat J. Laparoscopic surgery: A pioneer's point of view. *World J Surg*. 1999 Aug;23(8):863-8.

4. Rahman GA. Cholelithiasis and cholecystitis: changing prevalence in an African community. *Journal of the National Medical Association*. 2005 Nov;97(11):1534-8.

5. Darko R, Archampong EQ. The changing pattern of cholelithiasis in Accra. *West Afr J Med*. 1994 Oct-Dec;13(4):204-8.

6. Ajao OG. Cholecystitis and cholelithiasis in a tropical African population. *Tropical doctor*. 1982 Oct;12(4 Pt 1):164-6.

7. Bremner CG. The changing pattern of disease seen at Baragwanath hospital. *S Afr J Surg*. 1971 Jul-Sep;9(3):127-31.

8. Halldestam I. Gallstone disease: Population based studies on risk factors, symptomatology and complications [Doctoral thesis]. Linköping: Linköping University; 2008.

9. Pedersen G, Hoem D, Andren-Sandberg A. Influence of laparoscopic cholecystectomy on the prevalence of operations for gallstones in Norway. *The European journal of surgery = Acta chirurgica*. 2002;168(8-9):464-9.

10. Gracie WA, Ransohoff DF. The natural history of silent gallstones: the innocent gallstone is not a myth. *The New England journal of medicine*. 1982 Sep 23;307(13):798-800.

11. Getachew A. Epidemiology of gallstone disease in Gondar University Hospital, as seen in the department of radiology. *Ethiop J Health Dev*. 2008;22(2):206-11.

12. 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*. 2006 Nov;21(11):1737-43.

13. Chen CY, Lu CL, Huang YS, Tam TN, Chao Y, Chang FY, et al. Age is one of the risk factors in developing gallstone disease in Taiwan. Age and ageing. 1998 Jul;27(4):437-41.

14. Lai SW, Ng KC. Risk factors for gallstone disease in a hospital-based study. *Southern medical journal*. 2002 Dec;95(12):1419-23.

15. Angelico F, Del Ben M, Barbato A, Conti R, Urbinati G. Ten-year incidence and natural history of gallstone disease in a rural population of women in central Italy. The Rome Group for the Epidemiology and Prevention of Cholelithiasis (GREPCO). *Italian journal of gastroenterology and hepatology*. 1997 Jun;29(3):249-54.

16. Diehl AK, Rosenthal M, Hazuda HP, Comeaux PJ,

- Stern MP. Socioeconomic status and the prevalence of clinical gallbladder disease. *Journal of chronic diseases*. 1985;38(12):1019-26.
17. Novacek G. Gender and gallstone disease. *Wiener medizinische Wochenschrift (1946)*. 2006 Oct;156(19-20):527-33.
  18. Caroli-Bosc FX, Deveau C, Harris A, Delabre B, Peten EP, Hastier P, et al. Prevalence of cholelithiasis: results of an epidemiologic investigation in Vidauban, southeast France. General Practitioner's Group of Vidauban. *Digestive diseases and sciences*. 1999 Jul;44(7):1322-9.
  19. Walcher T, Haenle MM, Kron M, Hay B, Mason RA, von Schmiesing AF, et al. Pregnancy is not a risk factor for gallstone disease: results of a randomly selected population sample. *World journal of gastroenterology : WJG*. 2005 Nov 21;11(43):6800-6.
  20. Attili AF, Capocaccia R, Carulli N, Festi D, Roda E, Barbara L, et al. Factors associated with gallstone disease in the MICOL experience. Multicenter Italian Study on Epidemiology of Cholelithiasis. *Hepatology (Baltimore, Md)*. 1997 Oct;26(4):809-18.
  21. Torgerson JS, Lindroos AK, Naslund I, Peltonen M. Gallstones, gallbladder disease, and pancreatitis: cross-sectional and 2-year data from the Swedish Obese Subjects (SOS) and SOS reference studies. *The American journal of gastroenterology*. 2003 May;98(5):1032-41.
  22. Salinas G, Velasquez C, Saavedra L, Ramirez E, Angulo H, Tamayo JC, et al. Prevalence and risk factors for gallstone disease. *Surgical laparoscopy, endoscopy & percutaneous techniques*. 2004 Oct;14(5):250-3.
  23. De Santis A, Attili AF, Ginanni Corradini S, Scafato E, Cantagalli A, De Luca C, et al. Gallstones and diabetes: a case-control study in a free-living population sample. *Hepatology (Baltimore, Md)*. 1997 Apr;25(4):787-90.
  24. Attili AF, De Santis A, Attili F, Roda E, Festi D, Carulli N. Prevalence of gallstone disease in first-degree relatives of patients with cholelithiasis. *World journal of gastroenterology: WJG*. 2005 Nov 7;11(41):6508-11.
  25. Chapman BA, Frampton CM, Wilson IR, Chisholm RJ, Allan RB, Burt MJ. Gallstone prevalence in Christchurch: risk factors and clinical significance. *The New Zealand medical journal*. 2000 Feb 25;113(1104):46-8.
  26. Rome Group for the Epidemiology and Prevention of Cholelithiasis (GREPCO). Prevalence of gallstone disease in an Italian adult female population. *American journal of epidemiology*. 1984 May;119(5):796-805.
  27. Huffman J, Schenker S. Acute Acalculous Cholecystitis: A Review. *Clin Gastroenterol Hepatol*. 2010;8(1):15-22.