ORIGINAL ARTICLE

Impact Of Gender, Age And Body Mass Index On The Presence Of Gallstone (Cholelithiasis) As Diagnosed Through Ultrasound: Retrospective Study

Siti Nur Wahida Ithnan [1], Leong Sook Sam [1], and Khairunnisa Abd Manan [1]*

[1] Centre of Medical Imaging, Faculty of Health Sciences, Universiti Teknologi MARA Cawangan Selangor Kampus Puncak Alam, 42300 Bandar Puncak Alam, Selangor, Malaysia

ABSTRACT

Introduction: Cholelithiasis is a prevalent condition characterised by the development of gallstones, which cause severe abdominal pain with significant medical and economic impacts. This study aims to determine the effect of gender, age, body mass index (BMI), and the presence of gallstones diagnosed through ultrasound. **Material and Methods:** The retrospective review of gallstones, which occurred between January 2023 and December 2023, included 156 patients from the Department of Radiology, Hospital Sungai Buloh, between 18 and 80 years old, who had undergone abdominal ultrasound tests. **Results:** The study found that 55% were female, and the mean age was 53.19 years in middle-aged patients at 45%. The prevalence of gallstones demonstrates an apparent increase in individuals with a BMI of more than 23 kg/m, further categorised according to the WHO obesity classification. This includes the categories of pre-obese (18.8%), Obese I (22.5%), Obese II (23.8%), and Obese III (20%). The study used Pearson's Chi-square tests to examine the relationship between demographic factors and the presence of gallstones diagnosed by ultrasound. The variables included gender, age, and Body Mass Index (BMI). The results showed no significant association between gender, age, and gallstone presence. There was a significant association between BMI category and gallstones in the 80 participants diagnosed with gallstones. **Conclusion:** In conclusion, higher BMI and middle age specific in the Obese II group are major risk factors, but gender does not appear to play a significant role in this study.
Malaysian Journal of Medicine and Health Sciences (2025) 21(SUPP5): 277–283. doi:10.47836/mjmhs.21.s5.35

Keywords: Cholelithiasis, Gallstone, Body Mass Index (BMI), Age, Obese

Corresponding Author:
Khairunnisa Abd Manan
Email: khairunnisa@uitm.edu.my or
khairunnisaabdmanan08@gmail.com
Tel: +6019-3154640 or +03-32584412

INTRODUCTION

The gallbladder is a little pear-shaped organ located below the liver. It serves as the main storage site for bile, a digestive fluid synthesised by the liver. The liver is in the right upper quadrant above the transverse colon. In adults, it usually has a length of 7 to 10 cm and a width of 3 to 4 cm (1). The gallbladder wall thickness exhibited variation based on distension while consistently maintaining an average measurement of 2 mm (2).

Gallstone disease was a frequent condition, and previously published work had found that numerous risk factors, including gender, age, and BMI, were consistently associated with the outcome across different populations. The study by Shahzad et al. (3) showed the increased prevalence of cholelithiasis even in normal-weight adults. Although a great number of research have been conducted on these risk factors independently, to our knowledge, there is no such work regarding the sex, age and BMI interaction in GSD occurring simultaneously throughout Malaysia. This also allows the study to investigate the differences between different subgroups of obesity and why they may have had a significantly higher risk than those within normal weight categories. It is hoped that this would provide a more nuanced view of the contribution to gallstone formation from different factors in separate subsets within the obese group and allow for directable prevention or treatment strategies.

Gallstone disease, or cholelithiasis, is a prevalent entity worldwide that contributes to greater abdominal morbidity. One principal reason for a substantial health care dependence of those subjects

is the fact that cholelithiasis per se represents just an epiphenomenon, directly connecting (as biliary colic to choledocholithiasis) in life-threatening conditions demanding medical or surgical therapy [4]. The majority of Western gallstones, which account for about 80–90% in societies such as the United States and Europe, are composed predominantly or almost exclusively of pure cholesterol.

Cholelithiasis, commonly called gallstone disease, is a persistent entity amongst the global population and carries increased abdominal morbidity. Moreover, the illness itself exerted a heavy burden on healthcare systems because of some of its complications-abutting biliary colic to choledocholithiasis, which can be fatal (4). About 80-90% of gallstones in Western societies, like the United States and Europe, are made from cholesterol. However, in other communities like Asians, the predominant type of gallstone is pigment stones generated mainly from bilirubin salts or polymers and black due to calcium carbonate (4). A study by Tanaja et al. (5) mentioned that the development of cholelithiasis is due to polyetiological occurrences involving genetic and environmental factors in addition to lifestyle.

Cholelithiasis is characterised by the precipitation of cholesterol or bile pigments, resulting in solid crystal deposits within the gallbladder. The liver stores bile acids and bile salts, waiting until they are needed to aid in the digestion of fatty foods (6). These deposits can block bile outflow, causing biliary colic, eructation, and food intolerance. Hence, severe right upper abdominal pain radiates to the right shoulder (7).

The worldwide prevalence of gallstone disease, severe health consequences, and associated economic costs (3). The frequency of gallstone disease varied markedly across groups and was determined by demographic characteristics (age) or physiologic traits (gender; BMI). This knowledge was critical for the rational management and prevention of these relationships, decreasing the risk factors for incidence consequences and reducing the burden on healthcare systems.
A previous study by Mehmood et al. (7) showed that obesity is more common in females, making them prone to gallstone formation. Overweight individuals are also at higher risk of having stones inside the gallbladder. The study failed to specify the characteristics of obesity. It did not stratify the obese group into different grades (according to the WHO classification for obesity) when analysing its association with gallstone prevalence. Therefore, it was essential to study this relationship and bridge the existing information gap.

This research aims to assess the prevalence of gallstones among gender, age group, and BMI categories when diagnosed through ultrasound. The second objective is to determine the association between BMI, gender, and age and the presence of gallstones diagnosed through ultrasound. The significance of the study was to establish a relationship among BMI, age, and gallstones diagnosed by ultrasound. On assessment from a clinical viewpoint, the study found probable associated risk factors, i.e. age, gender, and BMI, for which this investigation might be important in diagnosing, managing, and preventing gallstones by healthcare professionals. Emphasising these risk factors presented weight management even in metabolically healthy patients. The study's results, such as disease prevalence and possible complications from cholelithiasis, were significant for strategies to minimise its public health impact. The study's results, such as disease prevalence and possible complications from cholelithiasis, were substantial for strategies to minimise its public health impact. Findings could help with the design of lifestyle changes and prevention strategies to educate such high-risk populations through health education programs on overweight factors leading to gallstones.

MATERIALS AND METHODS

The retrospective review of gallstones, which took place between January 2023 and December 2023, included 156 patients between the ages of 18 and 80 who had undergone abdominal ultrasound tests. All patient data were analysed at the Department of Radiology, Hospital Sungai Buloh via Picture Archiving Communication System (PACS). The study retrieved demographic, clinical, and pathology data from an electronic database.

Population and Sample

The sample size for population calculation in the research was calculated by using Raosoft Sample Size Calculator software. Sample size estimation of 260 patient records with a margin of error set at +5% and confidence interval (CI) -95%. The recommended minimum sample size for the current study was 156, which satisfied the criteria. Patients 18 through 80 years of age who had abdominal ultrasound testing with imaging reports stating the presence or absence of gallstones were recruited (inclusion criteria). Eligible patients had retrievable charts with demographic information, clinical history, laboratory results and relevant imaging findings during the specified time intervals. All patients who did not have an active treatment or scheduled surgery due to cholelithiasis during the data collection period. In contrast, it was observed that secondary gallstones, age younger than 18 years old, incomplete medical records, and not confirmed diagnoses were important exclusion criteria.

Ethical Consideration

This study followed the standard guidelines for research conducted by undergraduate students in Malaysia. The study was approved by the local institutional ethical committee of the National Medical Research in Malaysia (NMRR) reference ID-24-00641-K0S (IIR) and the secretariat Faculty of Health Sciences, UITM with

reference number FERC/FSK/MR/2024/0018. Before collecting the data, an ethics committee was established.

Data Collection

This study was conducted over 3 months (from March 2024 to May 2024), for collecting the retrospective data from the hospital database were collected systematically. Data abstraction from electronic health records centred around key patient demographics (age, gender and Body Mass Index [BMI]) and detailed clinical history of cholelithiasis. The diagnosis of gallstones was confirmed by abdominal ultrasonography reports obtained from a qualified physician. According to the criteria outlined by Su et al. (8), the presence of gallstones was confirmed by identifying a stable hyperechoic mass within the gallbladder cavity, accompanied by a distinct acoustic shadow, and demonstrating gravitational movement upon positional changes. The age range spanning from 18 to 80 years old can be classified into three distinct categories: early adulthood (18-29 years old), middle adulthood (30- 59 years old), and senior adulthood (60-80 years old). Each stage encompasses distinct health objectives and problems, necessitating a comprehensive understanding to tailor healthcare initiatives and effectively address the significant issues individual age groups face (9).

Additionally, BMI was classified based on the Clinical Practice Guidelines (CPG) for the Management of Obesity with definitions from underweight to Obese I, II and III situations (10). This process guaranteed a methodical and comprehensive gathering of information, which would be useful for an in-depth analysis involving determinants of gallstone occurrence.

Statistical Analysis

The data collected were processed, calculated and analysed using the Statistical Package for Social Sciences (SPSS) version 28.0. Descriptive data were calculated on the prevalence of gallstones by gender, age group and BMI category. The number of patients with gallstones was described using frequencies and percentages according to gender, age group and BMI category. The basic tendency and variability of age and BMI in patients with and without gallstones were described using metrics, including means, medians, and standard deviations, to describe the overall tendency and distribution of age metrics by way of measuring category gallstones and without gallstones. Cross tabulation demonstrated the changes in gallstone prevalence according to demographic and BMI status, which enabled us to explore whether there was a distribution pattern of stones.

The Chi-square test of independence was used in this study to determine any significant relationships between categorical factors, such as gender, BMI categories, and age groups, and the occurrence of gallstones. Chi-square statistics and corresponding p-values were used to evaluate whether differences in gallstone presence by gender, BMI or age group arose due to chance. The research provides novel insights into the relationship between gender, BMI and age with gallstone risk by highlighting significant associations and notable trends in the data.

RESULTS

Demographic characteristics and prevalence of gallstones among gender, BMI categories, and age groups

Table I shows a summary of the demographic characteristics and prevalence of gallstones among gender, BMI categories, and age groups. It included 157 participants, which are broken down as follows: 53.2% female and 46.8 % male. Participants' average age is 48.51, among which their age spans so widely, with the largest standard deviation being approximately 19.18 years. From the age distribution data, 24.4 percent of the population belongs to the early adult (18-29 years), 43.6% to the middle adult group (30–59 years) and 32.1 percents belongs older adult group ages between(60 -80 years). Participants had a mean BMI of 28.82 with a standard deviation of 6.88 kg/m2, showing a wide range of body weights among the participants. The Body Mass Index (BMI) classifications, as per the recommendations of the World Health Organisation (WHO), exhibited notable differences. The percentages were as follows: 8.3% (underweight), 10.9% average weight, and the highest in pre-obese group I with 25%, followed by Obese II with 18.4%, and Obese III (14.1%) categories. With relation to gallstones, 51.3% of the cohort (80 participants) had gallstone disease diagnosed with gallstones, whereas 48.7% (76 participants) did not show any signs of gallstones.

Table I: Demographic characteristics and prevalence of gallstone among gender, BMI categories, and age groups

Variable	N (%)	Mean (SD)
Gender		
Male	73 (46.8)	
Female	83 (53.2)	
Age Group (years old)		48.51 (19.18)
Early Adults (18-29)	38 (16.3)	
Middle Adults (30-59)	68 (45.0)	
Older Adults (60-80)	50 (38.8)	
BMI Category (kg/m2)		28.82 (6.88)
Underweight (<18.4)	13 (8.3)	
Normal Weight (18.5 – 22.9)	17 (10.9)	
Pre-Obese (23.0 – 27.4)	39 (25.0)	
Obese I (27.5 – 32.4)	38 (24.4)	
Obese II (32.5 – 37.4)	27 (17.3)	
Obese III (>37.5)	22 (14.1)	
Presence of Gallstone		
No	76 (48.7)	
Yes	80 (51.3)	

The association between BMI, Gender, Age, and the presence of gallstones diagnosed through Ultrasound

Based on Table II, Pearson's Chi-square tests were used to examine the associations between demographic factors and the presence of gallstones diagnosed by ultrasound. The variables included gender, age, and Body Mass Index (BMI). The significance level for all tests was established at $\alpha < 0.05$. A chi-square independent test showed no significant association between gender and the presence of gallstones, X2 (1, N = 80) =.080, p=.778. There is no significant relationship between the two variables within our sample of 80 participants diagnosed with gallstones X2(2, N = 80) =4.987, p=.083. However, a significant association exists between BMI category and gallstone within our sample of 80 participants diagnosed with gallstones X2(5, N = 80) =12.596, p=.027.

Table II: The Chi-Square test result of BMI, gender, age, with gallstone diagnosed through Ultrasound

Variable	X^2 Statistic (df)	*P*-value
Gender		
Male	080 (1)	.778
Female		
Age Group (years old)		
Early Adults (18-29)		
Middle Adults (30-59)	4.987(2)	.083
Older Adults (60-80)		
BMI Category (kg/m2)		
Underweight (<18.4)		
Normal Weight (18.5 – 22.9)		
Pre-Obese (23.0 – 27.4)		
Obese I (27.5 – 32.4)	12.596(5)	**.027***
Obese II (32.5 – 37.4)		
Obese III (>37.5)		

DISCUSSION

Prevalence of gallstones among gender, BMI categories, and age groups

The descriptive study on the prevalence of gallstones across different genders reveals a slightly higher susceptibility. This result aligns with previous research by Shahzad et al. (3), who observed that the incidence of cholelithiasis is high in females and is commonly attributed to sex hormones. They further explain that estrogen plays a significant role in increasing the production of cholesterol in bile. This hormonal effect leads to bile cholesterol oversaturation, contributing to the formation of gallstones. Additionally, Baddam et al. (11) corroborate these findings by highlighting the higher incidence of cholelithiasis in females, though noting a female-to-male ratio of 3:1 in their study. The effect of estrogen on bile composition and gallstones should also be further investigated, given that it could explain why women are more likely to suffer from this problem (5).

There was a gradual increase in the prevalence of gallstones with age, which shows that most cases occurred between 30 to 59 years among all ages. Physiological changes brought on by ageing may make gallstones more likely to occur, among other health issues. Bile normally consists of a mixture of cholesterol, bile salts and phospholipids to facilitate the solubilization and dissolution of cholesterol (6). But, this equilibrium can be disturbed with growing old and in a few circumstances creates cholesterol supersaturation. This condition occurs when there is more cholesterol than can remain in the solution, causing cholesterol crystals to form. Eventually, these crystals can come together and form bigger crystalline clumps that become gallstones.

Furthermore, changes induced by ageing on liver function may impair bile composition as well. The study by Matsui et al. (12) and Hu et al (13) highlighted that the liver produces and secretes bile, and any alteration in its function can impact bile composition and the risk of gallstone formation. Conditions like diabetes can alter the composition of bile, making it more prone to gallstone formation.

The incidence of gallstones according to the different and lower BMI groups demonstrates that those with a BMI higher than 23 kg/m2 are excessive. This includes the categories of Pre-obese, Obese I, Obese II and Obesity III in addition to the obese classification by the WHO. Additionally, Liu et al. (14 stated that in eight studies, cholelithiasis was more common among overweight or obese patients. Their findings were consistent with a study by Shahzad et al. (3) indicated that most patients with gallbladder stones had BMIs in the overweight and obese categories, where more than half of them had a BMI>25 as either being overweight or obese.

The association between BMI, gender and age with gallstone diagnosis through ultrasound

The findings of this study indicate no statistically significant association between gender and the presence of gallstones. Similar research by Al Atsariyah et al. (15) carried out at Dr Kariadi's hospital showed no relationship between cholelithiasis and gender. They pointed out that Asian women are likely to have more significant effects on the dynamics of the disease due to the earlier onset of menopause and a twofold risk linked to estrogen's role in cholesterol levels (15). Similarly, with specific reference to gender and whether it is the primary driver for gallstone disease susceptibility, this was attributed by Shahzad et al (3) stated that as is due to any of many factors involved in a gender- dependent manner via common routes related to metabolic syndrome, hypertension and obesity.

Nevertheless, contrary to research by Bansal et al. (16), this result stated that estrogen's role in promoting cholesterol gallstone formation is well-established, with elevated hormone levels leading to increased cholesterol secretion into bile and altered bile composition.

These changes assist in cholesterol crystallisation, leading to gallstones. Pregnancy, oral contraceptives and hormone replacement therapy are the principal promoters of elevated estrogen levels, with each representing a unique risk factor for gallstone formation (16). In certain scenarios, alternative remedies and lifestyle changes might be suggested to alleviate the burden of gallstones, especially in patients with other susceptibilities (16).

The output showed no relationship between these two variables within the sample of gallstone patients included in our study. The reason this happens is that our sample is too small, and we do not dig deeper to look if there is another variable like food consumption. The evidence study by Rahman et al. (17) and Su et al. (8) showed a significant increase in patients with gallstones from 31–40 and 41-50 years were observed, reflecting the role of ageing within their development. They highlight that the multiple ageing-related processes, including bile composition alteration, reduction in gall bladder motility, as well as comorbidities, lead to the formation of gallstones (8) (17). The gall bladder's primary function is to store and concentrate bile, then release it into the gut lumen (bile serves as an important digestive fluid). Gallbladder contractions expel bile, but age can reduce the strength of these contractions. But if the contraction strength decreases there is a insufficient squeezing effort and therefore bile does not empty, creating what is known as biliary stasis which consists in that these sludges of remaining gall are left for long periods within the vesicle (18) This stagnation allows bile components, particularly cholesterol, to concentrate, increasing the risk of crystallisation and stone formation. Additionally, slower gallbladder emptying means bile spends more time in the gallbladder, further promoting cholesterol crystallisation.

This finding contrasted with research by Al Atsariyah et al. (15), who reported a strong association between cholelithiasis and age. In their opinion, gallstone disease is particularly prevalent among those aged 65 or older, and susceptibility increases markedly from age 40. This was due to enhanced cholesterol release profile and elongated fat digestion duration in older individuals (15). Usually, bile contains a balance of cholesterol, bile salts, and phospholipids that help keep cholesterol dissolved. However, Afdhal Nezam H et al. (4) stated that this balance can be disrupted with age, leading to cholesterol supersaturation. This condition occurs when there is more cholesterol than can remain in the solution, causing cholesterol crystals to form. Over time, these crystals can aggregate and grow into gallstones.

The analysis indicates that BMI increases significantly with cholelithiasis, establishing a clear association between BMI and gallstones. Obesity, in turn, affects the factors involved in lipid metabolism, and this leads to a higher concentration of cholesterol levels in bile, which is directly related to gallstone formation (19). This process is dependent on the alteration of concentration and composition in biliary lipids, cholesterol esterification enzymes dysregulation, regulatory signalling pathways failure and gallbladder motility (19). In addition, Song et al. (2) study reported that as the levels of obesity, determined by BMI (body mass index), increase, so does the risk of gallstones, with an even greater effect for a BMI of 24kg/m and above. This connection could be because obesity increases the secretion of cholesterol in bile, which can add to a person's likelihood of developing gallstones. Bile is normally a bile acid, phospholipid and cholesterol-containing fluid that maintains the balance of its constituents, which help to dissolve cholesterol (17). A disruption of this balance in obese individuals could occur due to the excessive secretion of cholesterol into bile (5). As a result, the bile becomes supersaturated with cholesterol and forms precipitates of choleric crystals. With obesity-related elevated cholesterol levels already, obese individuals were more likely to develop gallstones (5).

CONCLUSION

The study aimed to evaluate the effect of age, sex and body mass index (BMI) on the ratio of gallstones. The study found that gender was not a significant risk factor for gallstone presence, confirming findings from previous research but differing with other studies stressing the influence of estrogen. This is in contrast to an established literature indicating a need for one of the largest age-related effects, and can likely be attributed either to limited sample sizes or omitted variables. There is also an age-related increase in the burden of gallstones, most pronounced for subjects between 30 and 59 years. There are also physiological changes that occur more frequently in the elderly, such as variations in bile composition or altered gallbladder motility. These alterations result in cholesterol supersaturation within bile, which allows for the precipitation of cholesterol crystals that coalesce into gallstones. Nevertheless, the marked relationship between BMI and gallstones highlights perhaps more than anything else that obesity must be managed to reduce this serious complication. The population that displays a high prevalence of gallstones is those with higher BMIs (greater than 23 kg/m2), such as WHO categories Pre-obese, Obese I, II and III. Overall, our findings illustrate the consideration of gender in assessing gallstone risk and highlight other demographic factors epidemiologists should be adjusting for more carefully, such as age or BMI.

Furthermore, any individual between the ages of 18 to 80 was also excluded from this study. As this exclusion would likely be removing many positive gallstone/cellulose association cases, i.e. false negatives, important data on prevalence and features of stones in the young or old could potentially escape inclusion altogether,leading to selective bias and under-

representation such that vanishingly few details are included upon which one might accurately assess the study's conclusions as applying across all age categories. Neither study recorded detailed clinical information about important factors as imaging findings, histology or gallstone composition, nor postoperative complications. These findings are crucial for a complete comprehension of the scenario of gallstone disease and its clinical relevance. Since the study itself lacks an in-depth analysis of disease pathology and outcomes, their absence precludes further exploration on this front.

Despite offering an important contribution to our knowledge on the relation between demographic factors and BMI with gallstone prevalence, some limitations have been identified for this study. Although some limitations of the protocol, including its retrospective design and single-centre nature with a limited number of patients can be counted against it due to increased risk for patient selection bias in addition to reduced generalizability using non-specified datasets, age range constraints as well as gender highlight the main problem areas that could have impacted our findings. Standardised diagnostic criteria and methodologies with reduced variability can enhance the reliability of results. The implementation of these, along with further study in this area, is likely to help achieve a more complete understanding of gallstone disease and its risk factors, ultimately improving patient outcomes and guiding suitable clinical practice.

ACKNOWLEDGMENT

Special thanks to all the members and radiographers who contributed to this research and their collaboration, especially during data collection and analysis. The authors would also like to thank their families and loved ones for their unwavering encouragement and understanding during the writing of this manuscript.

COMPETING INTEREST

The authors declare that they have no competing interests.

ETHICAL CLEARANCE

We obtained approval from the Secretariat of Health Science Faculty at UITM under reference number FERC/FSK/MR/2023/00075 and the National Medical Research Register in Malaysia (NMRR) with reference ID-23-01861.

FINANCIAL SUPPORT

No funding was received for this work.

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