

## ORIGINAL RESEARCH ARTICLE

# Investigating the association of pregnancy count, oral contraceptive use, and lifestyle with gallstone disease in Chlef, Algeria: A retrospective descriptive study

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## Abstract

This study seeks to explore the potential impact and the association between the number of pregnancies, oral contraceptive use, and lifestyle factors including physical activity and stress on the occurrence of gallstone disease (GSD) among 46 women diagnosed with this pathology. Data were collected using a structured questionnaire and analyzed with IBM SPSS Statistics. Cholesterol gallstones were predominant (76.1%), especially among women aged  $\geq 61$  years. A significant association was observed between the number of pregnancies and gallstone type ( $\chi^2(3) = 8.887$ ,  $p = 0.031$ ), with higher parity linked to cholesterol stones. Oral contraceptive use was reported by 60.9% of participants. Psychological stress was frequently reported, with 80.4% of patients experiencing frequent to very frequent stress. Physical activity levels showed a strong association with gallstone type ( $\chi^2(2) = 19.967$ ,  $p < 0.001$ ), with sedentary or occasional activity linked to cholesterol stones. The findings underscore the multifactorial etiology of GSD, indicating that reproductive factors, hormonal contraceptive use, and lifestyle-related behaviors may collectively contribute to its development. Public health strategies focusing on these modifiable risk contributors may help reduce the incidence of GSD in this population. (*Afr J Reprod Health* 2026; 30 [6]: 105-114).

**Keywords:** Gallstone disease; Pregnancy; Oral contraceptives; Physical inactivity

## Résumé

Cette étude cherche à explorer l'impact potentiel et l'association entre le nombre de grossesses, l'utilisation de contraceptifs oraux et les facteurs du mode de vie, y compris l'activité physique et le stress, sur la survenue de lithiase biliaire chez 46 femmes diagnostiquées avec cette pathologie. Les données ont été collectées à l'aide d'un questionnaire structuré et analysées avec IBM SPSS Statistics. Les calculs biliaires de cholestérol étaient prédominants (76,1 %), en particulier chez les femmes âgées de 61 ans. Une association significative a été observée entre le nombre de grossesses et le type de calculs biliaires ( $\chi^2(3) = 8,887$ ,  $p = 0,031$ ), avec une parité plus élevée liée aux calculs de cholestérol. L'utilisation de contraceptifs oraux a été signalée par 60,9 % des participants. Le stress psychologique a été fréquemment signalé, avec 80,4 % des patients souffrant de stress fréquent à très fréquent. Les niveaux d'activité physique ont montré une forte association avec le type de calculs biliaires ( $\chi^2(2) = 19,967$ ,  $p < 0,001$ ), avec une activité sédentaire ou occasionnelle liée aux calculs de cholestérol. Les résultats soulignent l'étiologie multifactorielle de la lithiase biliaire, suggérant que les facteurs reproductifs, l'usage de contraceptifs hormonaux et les comportements liés au mode de vie peuvent ensemble contribuer à son développement. Les stratégies de santé publique axées sur ces facteurs modifiables de risque peuvent aider à réduire l'incidence de la lithiase biliaire dans cette population. (*Afr J Reprod Health* 2026; 30 [6]: 105-114).

**Mots-clés:** Lithiase biliaire, Grossesse, Contraceptifs oraux, Sédentarité

## Introduction

Biliary lithiasis, also known as cholelithiasis, is a widespread condition, affecting almost 20% of the

global population. It has been found that common bile duct stones occur in about 10 to 33% of patients with symptomatic gallstones, depending on age.<sup>1</sup> While many cases remain asymptomatic and

medical intervention is not required, symptomatic cases often manifest through biliary colic, choledocholithiasis, cholecystitis, or acute cholangitis. In such instances, patients typically experience abdominal pain, particularly in the right upper quadrant.<sup>2</sup>

The gallbladder is a pear-shaped organ located beneath the liver, typically measuring up to 10 cm in length and 3 to 4 cm in width, with a bile capacity ranging from 40 to 70 ml.<sup>3</sup> Its structure includes mucosa, smooth muscle, subserosal connective tissue, and a serosal layer. This organ is often associated with various pathological issues such as congenital abnormalities, inflammation, and tumors, which often necessitating surgical removal. The most prevalent condition affecting the gallbladder is cholelithiasis, with women being 2 to 4 times more prone to developing gallstones compared to men. These gallstones can cause irritation that may lead to precancerous changes and potentially gallbladder cancer.<sup>4</sup> Cholelithiasis, or the formation of cholesterol-based gallstones, often remains asymptomatic during its early stages. However, when bile flow is obstructed, symptoms such as abdominal pain, nausea, vomiting, fever, and jaundice may appear. Diagnosis relies on imaging techniques such as ultrasound, CT scans, and MRIs. The standard treatment once symptoms become apparent is typically surgical removal of the gallbladder (cholecystectomy).<sup>5</sup> Gallstone disease (GSD) is characterized by the presence of gallstones in the gallbladder and, less frequently, in the bile ducts. Several factors contribute to its onset, including pregnancy, obesity, type 2 diabetes, metabolic syndrome, ethnic background, and hereditary predisposition.<sup>6</sup>

Gallstones (GS) are generally classified by composition as cholesterol, pigment, or mixed types. Their formation involves intricate interactions between genetic predisposition and environmental influences, such as hepatic overproduction of cholesterol, bile supersaturation, intestinal absorption disorders, and disturbances in the gut microbiota.<sup>7</sup> Nutrition plays a crucial role not only in the formation of gallstones but also in their prevention and management. Diets high in omega-3 fatty acids, proteins, and dietary fiber have demonstrated positive impacts on the biliary system. To support gallbladder health, it is important to follow a balanced diet that provides sufficient

vitamins and proteins while limiting fat and cholesterol intake.<sup>8</sup>

Through a retrospective descriptive approach, this study aims to investigate the association between the number of pregnancies, oral contraceptive use, and lifestyle factors (physical activity and stress) with the occurrence of gallstone disease (biliary lithiasis) among women in Chlef, Algeria. By analyzing patient data, the study intends to contribute to a better understanding of the epidemiological patterns of biliary lithiasis and to support targeted prevention and intervention strategies within the region.

## Methods

### Study design

This retrospective descriptive study was conducted from 12 February to 13 April 2025 in the General Surgery Department of Ouled Mohamed Public Hospital in Chlef (Algeria), a regional referral center serving a large and diverse population. The study focused on female patients diagnosed with gallstone disease (GSD) admitted for surgical management during the study period.

### Data collection

The study population consisted of 46 female patients from various municipalities within the Wilaya of Chlef. Eligible participants were those diagnosed with biliary lithiasis through clinical assessment and abdominal ultrasound, including uncomplicated cases (gallbladder stones) and complicated forms (acute cholecystitis, pancreatitis, cholangitis, and hydrocholecystitis). Data were collected using a structured, interviewer-administered questionnaire completed by two trained investigators to ensure consistency. The questionnaire consisted of three main sections:

Reproductive history: parity and number of pregnancies.

Hormonal factors: use of oral contraceptives and menopausal hormone therapy.

Lifestyle factors: physical activity and stress levels.

Physical activity was classified into three groups: regular (at least 30 minutes per day on five or more days per week), occasional (less than 30 minutes per day or fewer than five days per week), and sedentary (no physical activity). While stress levels were

recorded as rarely, frequently, or very frequently experienced. The type of gallstones (cholesterol or pigment) was confirmed intraoperatively. Participants were clearly informed that their participation was voluntary and that all collected data would remain confidential and used solely for research purposes. Interviews generally lasted 10–15 minutes, with elderly patients sometimes needing more time to provide detailed responses.

### ***Inclusion and exclusion criteria of participants***

All female patients with biliary lithiasis were included, covering both uncomplicated forms (such as gallbladder stones) and complications such as pancreatitis, cholangitis, cholecystitis, and hydrocholecystitis. This comprehensive approach aimed to capture the full clinical spectrum of the disease and its possible outcomes. Exclusion criteria included patients who refused to participate, as well as those who were unconscious or unable to communicate.

### ***Statistical analysis***

All data were entered and analyzed using IBM SPSS Statistics version 22. Descriptive statistics, including frequencies, percentages, and graphical representations, were used to summarize patient characteristics. Chi-square tests were performed to examine associations between categorical variables, and linear-by-linear association tests were applied for ordinal variables. Symmetric measures, including Phi and Cramer's V, were computed to assess the strength of associations. Statistical significance was set at  $p < 0.05$ . Although some chi-square tests included expected counts below five, they were retained for exploratory purposes and interpreted cautiously.

### ***Ethical consideration***

This study was reviewed and approved by the Ethics Committee of Ouled Mohamed Public Hospital in

Chlef, Algeria (approval date: February 12, 2025).

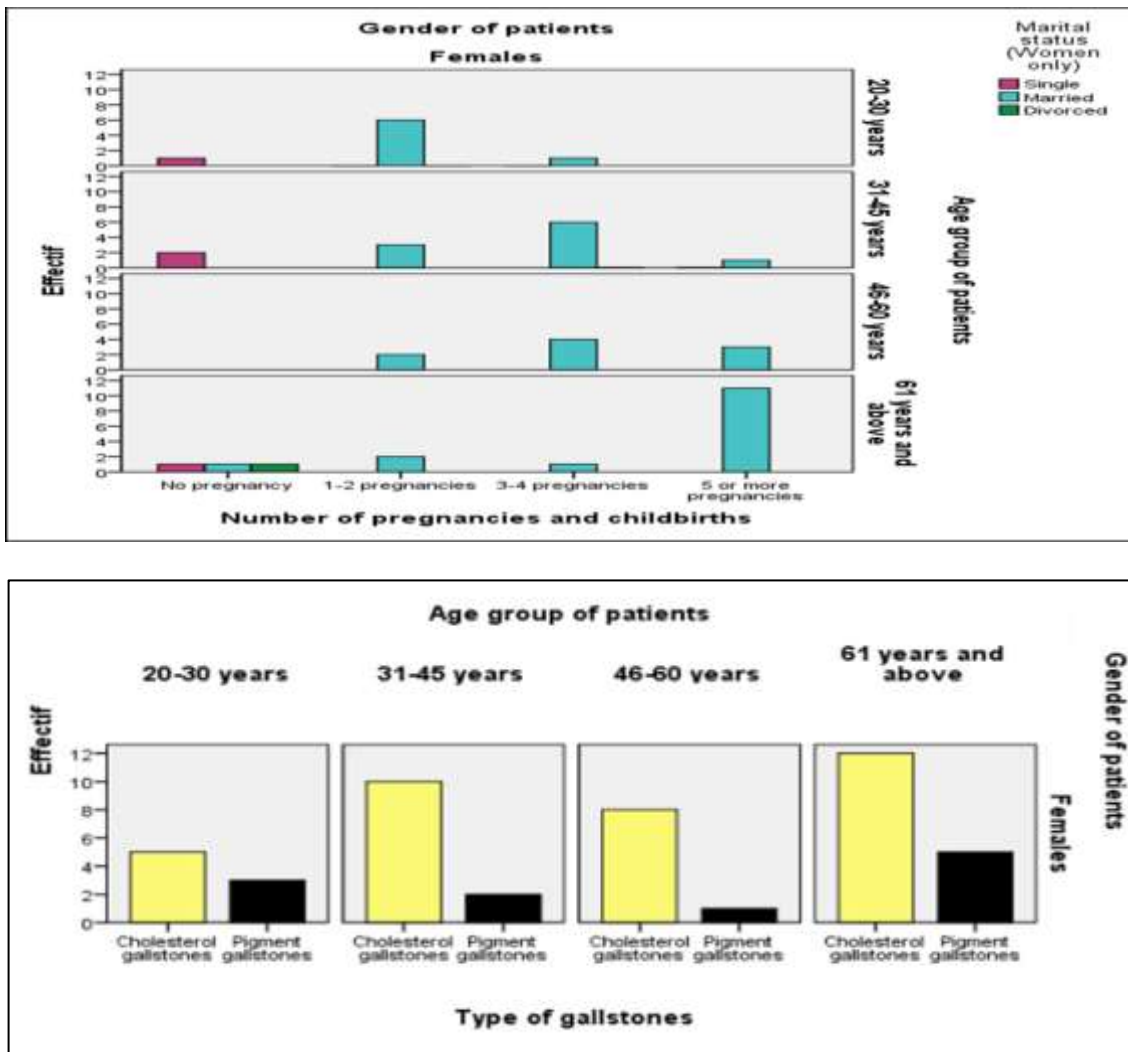
## **Results**

### ***Number of pregnancies and type of gallstones***

The study involved forty-six women diagnosed with gallstones. The predominant age group was women aged 61 years and above (37%), followed by those between 31–45 years (26.1%), 46–60 years (19.6%), and 20–30 years (17.4%). As for reproductive history, 15 women (32.6%) had five or more pregnancies, 13 women (28.3%) had one to two pregnancies, 12 women (26.1%) had three to four pregnancies, and 6 women (13.0%) had none. Overall, the results show that gallstone patients were most prevalent among older, married women with multiple pregnancies (Figure 1.a).

A total of 35 female patients (76.1%) had cholesterol stones, while 11 patients (24.0%) had pigment stones indicating a marked predominance of cholesterol calculi. A deeper examination of gallstone types across various age groups showed distinct trends. Among patients aged 61 years and above, cholesterol gallstones were more frequent, with 12 cases (70.6%) compared to 5 cases (29.4%) of pigment stones. In the 46-60 years group, cholesterol stones were highly prevalent with 8 cases (88.9%) compared to pigment stones with 1 case (11.1%). Similarly, in the 31-45 age group, cholesterol gallstones remained dominant, with 10 cases (83.3%) (Figure 1.b).

To examine the potential association between gallstone type and reproductive history (the number of pregnancies and childbirths), a cross-tabulation followed by a chi-square test of independence was conducted. The analysis showed that cholesterol gallstones were more frequent among women with higher pregnancy counts, with 37.1% having 5 or more pregnancies and 31.4% having 3 to 4 pregnancies, whereas pigment gallstones prevailed among those with fewer pregnancies, including 36.4% with no pregnancies and 36.4% with 1 to 2 pregnancies.



**Figure 1:** Age distribution, reproductive history (a), and gallstone types (b) among female patients

Cholesterol gallstones were most frequently observed in patients with 5 or more pregnancies (13 cases), followed by those with 3 to 4 pregnancies (11 cases). In contrast, pigment gallstones were more commonly observed in women with no pregnancies (4 cases) and those with 1 to 2 pregnancies (4 cases) (Table 1).

**Chi-square tests and symmetric measures**

Chi-square analyses revealed a significant association between the number of pregnancies and gallstone type ( $\chi^2(3)=8.887$ ,  $p = 0.031$ ), with a significant linear trend ( $\chi^2 = 6.247$ ,  $p = 0.012$ ),

suggesting a systematic relationship between increasing pregnancy count and gallstone type. The likelihood ratio test ( $\chi^2(3) = 8.256$ ,  $p=0.041$ ) corroborated this finding, further indicating that the number of pregnancies is associated with the type of gallstones (Table 2).

Moreover, the symmetric measures (Phi = 0.440, Cramer’s V = 0.440,  $p = 0.031$ ) indicate a moderate association between number of pregnancies and type of gallstone. These results further support the idea that the number of pregnancies may have an influence on the likelihood of developing either cholesterol or pigment gallstones (Table 3).

**Table 1:** Cross-tabulation of gallstone type by number of pregnancies

Number of pregnancies and childbirths		No pregnancy	1 to pregnancies	2 to pregnancies	3 to pregnancies	4 to pregnancies	≥5 pregnancies	Total
Type of gallstones	Cholesterol gallstones	2	9		11		13	35
	Pigment gallstones	4	4		1		2	11
Total		6	13		12		15	46

**Table 2:** Chi-square test

Test	Value	Df	Approx. Sig. (2-sided)
Pearson chi-square	8.887 <sup>a</sup>	3	.031
Likelihood ratio	8.256	3	.041
Linear by linear association	6.247	1	.012
Number of valid cases	46		

a.5 cells (62.5%) have an expected frequency less than 5.

**Table 3:** Symmetric measures

Measure	Value	Approx.sig.
Nominal by nominal	Phi	.440 .031
	Cramer’s V	.440 .031
Number of valid cases	46	

**Use of oral contraceptives**

Among the 46 female participants, 28 (60.9%) reported using oral contraceptives, whereas 18 (39.1%) did not, indicating a notable prevalence of contraceptive use within the study group. In contrast, none of the participants reported using hormonal medications related for menopause or fertility treatments, with all 46 women (100%) responding negatively to this question (Figure 2).

**Lifestyle factors: Stress in patients**

Stress is a known contributing factor to various health conditions. Among the 46 patients, 19 patients (41.3%) reported very frequent stress and (39.1%) stated frequent stress, while (19.6%) reported experiencing stress rarely in their daily lives prior to hospitalization and disease onset(Figure 3).

**Lifestyle factors: Physical activity**

To examine the potential association between gallstone type and pre-diagnosis physical activity levels, a cross-tabulation followed by a chi-square test of independence was performed. Most patients with cholesterol gallstones reported occasional

(50.0%) or sedentary (30.4%) physical activity levels, with only 19.6 % engaging in regular activity (Figure 4).

**Chi-square test and symmetric measures**

The chi-square test revealed a significant association between the level of physical activity and gallstone type ( $\chi^2(2) = 19.967, p < 0.001$ ). Additionally, the linear-by-linear association was also significant ( $\chi^2 = 19.231, p < 0.001$ ) (Table 4).Furthermore, the symmetric measures (Phi = 0.585 and Cramer’s V = 0.597,  $p < 0.001$ ) These results indicate a significant relationship between pre-diagnosis physical activity level and gallstone type (since the value is close to 1, which reflects a strong association) (Table 5).

**Discussion**

GS formation is attributed to multiple factors that disrupt the balance of bile composition and gallbladder (GB) function. An excessive dietary intake of cholesterol, along with an increased secretion of GB mucin, contributes to bile supersaturation. A reduction in bile salt concentration and impaired gallbladder contractility further promote nucleation and crystal aggregation.

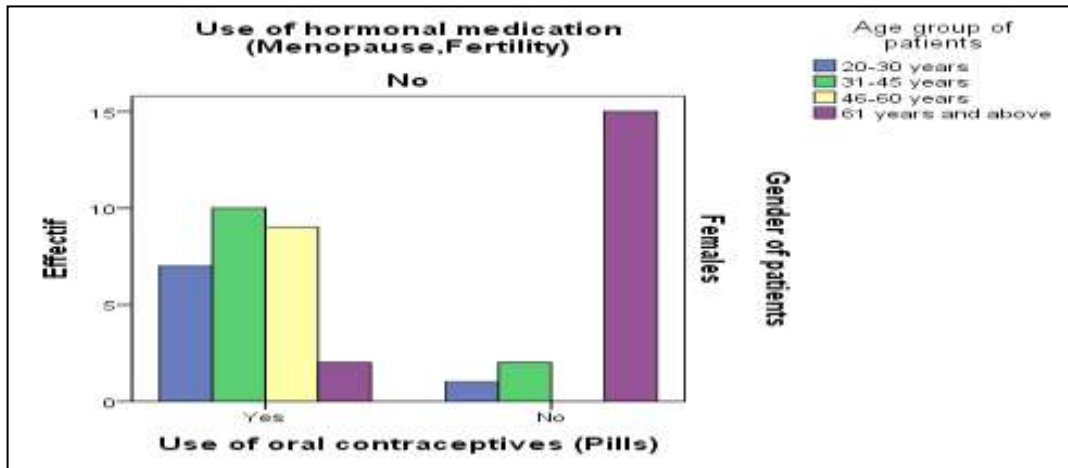


Figure 2: Patterns of oral contraceptive and hormone therapy use among patients by age group

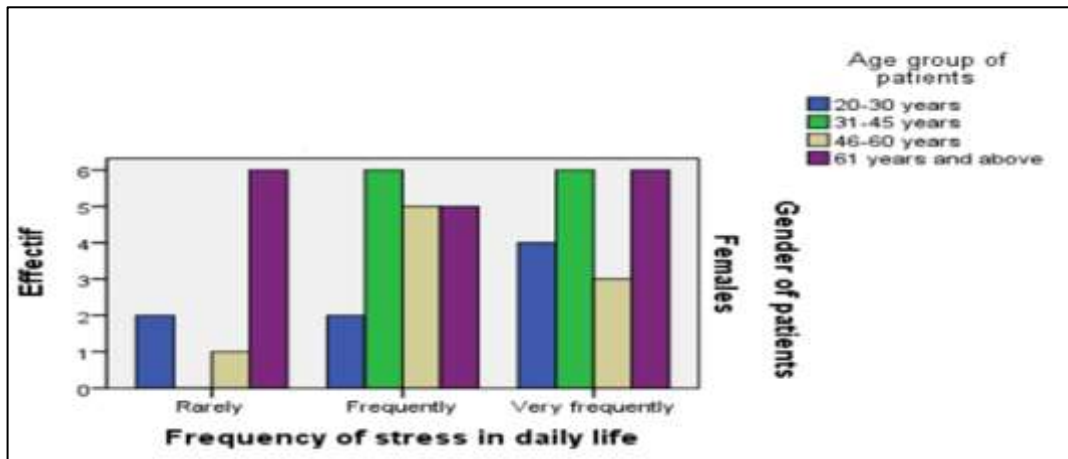


Figure 3: Frequency of daily life stress among patients by age group.

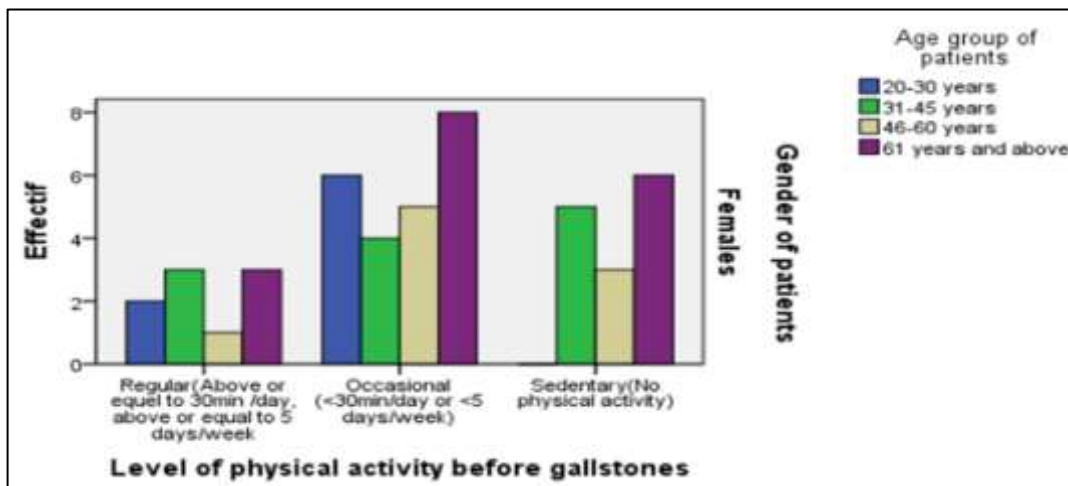


Figure 4: Distribution of physical activity among patients by age group

**Table 4:** Chi-square tests

Test	Value	Df	Approx. Sig. (2-sided)
Pearson chi-square	19.967 <sup>a</sup>	2	.000
Likelihood ratio	23.023	2	.000
Linear-by-linear association	19.231	1	.000
Number of valid cases	46		

a : 2 cells (33.3%) have expected count less than 5.

**Table 5:** Symmetric measures

Measure		Value	Approx.sig.
Nominal by nominal	Phi	.585	.000
	Cramer's v	.597	.000
Number of valid cases		46	

Additionally, prolonged intestinal transit time and an enhanced breakdown of bilirubin glucuronides lead to elevated bilirubin excretion into bile, fostering conditions favorable for GS development.<sup>9</sup>

GS are solid particles that develop in the GB and biliary system, varying in size and number among individuals.

They are classified into three main types: cholesterol, pigmented, and mixed GS. Cholesterol GS contain at least 50% cholesterol and form due to bile supersaturation, often linked to high-fat diets and elevated serum lipids. Pigmented GS, darker in color and composed mainly of bilirubin with less than 20% cholesterol, result from unconjugated bilirubin supersaturation.<sup>10</sup> The formation of cholesterol GS is influenced by multiple factors, primarily the oversaturation of bile with cholesterol. Normally, cholesterol is made soluble in bile by bile salts and lecithin. Reduced secretion of bile salts (e.g., in cystic fibrosis) or lecithin (due to genetic issues) also disrupts balance. This leads to cholesterol crystallizing, especially when aided by mucin and other bile proteins. These crystals then clump together and grow, a process further promoted by poor GB movement and high cholesterol levels in bile.<sup>11</sup>

Pigment GS are divided into black and brown types, each with different causes. Black pigment stones develop in sterile conditions and are mainly associated with chronic hemolysis, which raises levels of unconjugated bilirubin. When this exceeds bile's ability to dissolve it, calcium bilirubinate crystals form. Mucin overproduction and bile oversaturation worsen the process. Conditions like alcoholic cirrhosis, aging, and ileal

dysfunction increase the risk. Brown pigment stones, on the other hand, are linked to chronic infections and bile flow blockage. Bacterial enzymes break down bile components, contributing to pigment stone formation. The presence of mucin and bacterial waste then fuels ongoing stone development and infection.<sup>12</sup>

Research has confirmed that women face higher risks from gallstone disease (GSD) than men because of hormonal factors, particularly estrogen. Multiple scientific studies confirm the clear relationship in which advancing age raises the chances of developing GSD. A Taiwanese cross-sectional study demonstrated GSD develops more frequently as people get older reaching 25.4% in residents over 85 years old. The research study highlighted that advanced age functions as a major risk factor for GSD particularly in female patients.<sup>13</sup>

Gallbladder surgeries also rose over this period. Key risk factors identified for gallstone disease included older age, female sex, diabetes, liver disease, obesity (high BMI), physical inactivity, and the use of proton pump inhibitors.<sup>14</sup>

Pak and Lindseth<sup>15</sup> found that cholesterol GSD is particularly prevalent in individuals over 50, affecting about 50% of women aged 70-75. The study concluded that aging elevates the risk of GS formation by increasing biliary cholesterol secretion and intestinal absorption while reducing hepatic bile salt synthesis. Moreover, impaired GB motility in aging individuals is linked to decreased CCK-A receptor expression and reduced sensitivity to CCK, leading to GB stasis. These physiological changes contribute to a higher prevalence of GS in older adults. Furthermore, after age of 40, GS formation

becomes significantly more frequent due to the decline in cholesterol 7 $\alpha$ -hydroxylase activity, the key enzyme in bile acid synthesis. This reduction leads to increased biliary cholesterol saturation and impaired GB motility, creating favorable conditions for GS development.<sup>16</sup>

The chi-square test highlights the potential influence of reproductive history on the development of gallstone types. Women with multiple pregnancies appear more prone to developing cholesterol gallstones, while pigment stones are more commonly observed in those with fewer or no pregnancies. These findings suggest that hormonal and physiological changes associated with pregnancy may influence gallstone composition. Pregnancy increases the risk of cholesterol gallstones due to elevated estrogen and progesterone levels, which promote cholesterol supersaturation and reduce gallbladder motility.<sup>17</sup>

Postmenopausal hormone replacement therapy (HRT) is commonly utilized to alleviate menopausal symptoms and provide protection for bone and cardiovascular health. However, HRT presents both benefits and risks, as it has been associated with an increased incidence of breast, thyroid, and endometrial cancers. The relationship between HRT and GS formation remains debated, though the majority of studies suggest that HRT may contribute to a higher risk of GS.<sup>18</sup>

A study revealed that women using menopausal hormone therapy (MHT) have a higher likelihood of developing asymptomatic GS compared to those who have never used MHT. The risk was found to increase with prolonged use and decrease over time after discontinuation. Furthermore, the study suggested that women using non-oral MHT formulations may have a lower risk of developing asymptomatic GS.<sup>19</sup>

Pregnant individuals face a heightened risk of GS formation due to hormonal changes associated with pregnancy. Women, in general, are more susceptible to GS, and this risk further increases during gestation. Elevated hormone levels, particularly estrogen and progesterone, contribute to increased cholesterol concentration in bile and impaired GB motility, leading to bile stasis and GS development. Studies indicate that approximately 8% of pregnant women develop new GS by the third trimester, although only around 1% experience symptoms.

Among symptomatic cases, complications arise in less than 10% of individuals.<sup>20,21</sup>

Genetic investigations have successfully discovered particular gene mutations which enhance the risk of gallstone development. Weber et al.<sup>22</sup> researched a three-generation family with continuous gallstone cases and found that the p.D19H variant in ABCG5/ABCG8 genes demonstrated an effect on cholesterol transport and bile composition. The HNF4A rs1800961 polymorphism exhibited a significant connection to gallstone risk factors mainly in young and obese male patients.<sup>23</sup>

Research using GS-prone (C57L/J) and GS-resistant (AKR/J) mice has identified key genes involved in GS formation. Two major genes, Lith1 and Lith2, influence liver cholesterol secretion and bile flow. Their human equivalents, ABCG5 and ABCG8, produce transporter proteins that control cholesterol movement into bile or its elimination through the intestine. When these proteins do not function properly, cholesterol accumulates, increasing the risk of GS and heart disease. On the other hand, overactivity of these genes raises bile cholesterol levels, also promoting GS development. Specific genetic variants, like ABCG5-R50C and ABCG8-D19H, have been linked to GSD in various populations.<sup>24,25</sup>

The significant numbers of women who use oral contraceptives matches published findings which demonstrate hormonal contraceptives possibly raise the risk for developing gallstones. Medroxyprogesterone acetate and levonorgestrel intrauterine devices have been shown to elevate the need for cholecystectomy, thus strengthening the evidence for hormonal contraceptive-gallstone formation associations. A large population study which demonstrated that drospirenone-based oral contraceptive pills carry higher risks for gallbladder disease than levonorgestrel-based pills.<sup>26</sup> Psychological stress has been increasingly recognized as a potential contributor to gallstone disease. The high prevalence of stress among patients suggests a possible link between chronic stress and the development of gallstones. Supporting this observation, a study found that, while gallstone disease (GSD) is often studied medically, psychological factors like stress, anxiety, emotional instability, and poor coping skills may also play a

role in its development and symptom severity. Stress may indirectly raise cholesterol levels or cause bile retention, both contributing to gallstone formation.<sup>27</sup>

Supporting this observation, a cohort study which involved over 147,000 Korean adults, found that both prolonged sitting time and low levels of physical activity were independently associated with an increased risk of developing GSD. Specifically, individuals who sat for 10 or more hours per day had a 15% higher risk of GSD compared to those who sat for less than 5 hours daily. Similarly, those who were physically inactive or only minimally active also showed a significantly higher risk of developing GSD. These findings suggest that reducing sedentary behaviour and increasing physical activity are both crucial for lowering the risk of gallstones.<sup>28</sup>

The chi-square test results suggest a significant association between the level of physical activity and the type of gallstones (cholesterol vs. pigment), suggesting that physical activity influences gallstone composition. Specifically, sedentary and occasionally active individuals are more likely to develop cholesterol gallstones, whereas pigment gallstones are more common among those who engage in regular physical activity. The results are consistent with a study cited by Shephard<sup>29</sup>, which examined 200 consecutive cases to assess the link between levels of physical activity and the types of gallstones developed. The study revealed that cholesterol stones were the most common, making up 94% of all cases, and were more frequently seen in people with sedentary lifestyles. In contrast, pigment stones were more often found in physically active individuals.

In addition, a cross-sectional study conducted by Ahmad et al.<sup>30</sup> examined the influence of physical exercise and other lifestyle habits on gallstone disease among 100 adults aged over 30 years. The study found that 72% of the participants lived mostly sedentary lives. More than half of participants (59%) did not participate in indoor exercises, 63% rarely walked for 30 minutes per day or less and 55% avoided using the stairs. Physical activity is recommended because it is theorized to potentiate gallbladder emptying via release of cholecystokinin (the enzyme that stimulates release of bile acids into the intestine) and increase gallbladder motility.

## Conclusion

This study revealed a significant association between the type of gallstones, various reproductive, and lifestyle factors. Cholesterol gallstones were more frequent among those with a history of multiple pregnancies (especially three or more), sedentary lifestyles, and frequent psychological stress. On the other hand, pigment gallstones were more common among women with few or no pregnancies and those who engaged in regular physical activity. The oral contraceptive use was also prevalent among participants and contributed to the increased risk of cholesterol gallstones. Overall, these results highlight the multifactorial nature of gallstone disease and suggest that hormonal changes and low physical activity may all contribute to the development and type of gallstones. Preventive strategies focused on lifestyle modifications and awareness of hormonal influences could help reduce the incidence of GSD among women.

## Contribution of authors

RM and IH conceived and carried out statistical analysis as well as manuscript editing. SA, RM, FA MM and NK made data collection and manuscript writing. Finally, SA, RM, FA MM, NK and IH reviewed and approved the manuscript.

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