



Association between Gallstone and Oral Contraceptive Pills

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ABSTRACT

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Background: Recently, oral contraceptives have been the subject of concerns over the risk of gallbladder disease associated with their use.

Objectives: The aim of this study was to determine the association between the use of oral contraceptive pills and gallstones.

Methodology: The design of the study was descriptive analytic, involving 51 females consecutively recruited from the Teaching Hospital for Gastroenterology and Hepatology in Sulaimani Province/Kurdistan Region/Iraq from 3/7/2024 to 31/8/2024. The study tools included two parts. The data were collected through direct interviews, and the association between the use of oral contraceptives and gallstones was determined by chi-square. Statistical analysis was performed using the SPSS 24.0 software (IBM SPSS Statistics). The level of significance was set at $p=0.01$. Inferential statistics were used to analyze the data.

Results: The results show that there was a statistically significant association only between the level of education and the use of oral contraceptive pills. However, there was no statistically significant association between BMI, gallstones, and the use of oral contraceptive pills.

Conclusion: There was no statistically significant association between the use of oral contraceptive pills and gallstones.

Keywords: Contraceptive pills and Gallstone.

INTRODUCTION

The most prevalent condition affecting the hepatobiliary system is cholelithiasis. Over 85% of participants exhibit no symptoms. Annually, gallstones affect 2% (1-3%) of the population, and among those who develop symptoms, 2% (1-3%) present with biliary colic rather than other conditions associated with gallstones. The incidence of gallstones increases with age, with 20% of women and 5% of men between the ages of 50 and 65 affected. (1, 2).

The etiology of cholelithiasis is multifactorial, involving the interplay between environmental and genetic variables. Factors such as heredity, obesity, hormone therapy, female gender, diabetes mellitus, rapid weight loss, lack of physical activity, and the use of oral contraceptives are among the most frequent risk factors associated with cholelithiasis. Notably, female gender exhibits the most compelling association with gallstone disease, particularly during the fertile years (3,4).

Approximately 100 million women globally utilize oral contraceptives as their primary method of

birth control. Significant side effects linked to the long-term use of these medications include deep vein thrombosis, stroke, and pulmonary embolism ⁽⁵⁾. Additionally, research has indicated that both progesterone and estrogen are crucial in the development of gallstones. The relative risk of gallbladder disease associated with various oral contraceptive formulations, particularly newer formulations, remains uncertain ⁽⁶⁾.

For young women, oral contraceptives have become the primary source of exogenous estrogen due to their widespread use in daily life. Numerous studies have explored the connection between oral contraceptives and the prevalence of gallstones; however, the findings have been conflicting. Some studies, for instance, have demonstrated a positive correlation between oral contraceptives and the incidence of gallstones, while others have indicated that oral contraceptives have no significant effect on gallstone prevalence ^(7, 8).

From 1990 to 2019, Iraq saw progress in the use of contemporary contraceptive techniques. The effectiveness and safety of a method with few side effects may influence a woman's choice of contraception. While some women rely on medical advice, others rely on their friends' and family's experiences. Occasionally, the decision may be made by the family. Selecting a method may depend on factors such as family members, financial status, and level of education ^(9, 10).

The primary significance of this study is to raise women's awareness of the potential risks associated with contraceptive pills and the importance of focusing on their health while using medication. Secondly, the development of preventative measures, such as routine health examinations and lifestyle changes to lower the incidence of gallstones, can result from the discovery of a connection between contraceptive pills and gallstone disease. Additionally, the results can be used to develop healthcare policies and recommendations, ensuring that women receive

proper guidance and assistance when selecting methods of contraception. Furthermore, research in this area may also aid in improved treatment by enabling medical professionals to assist women who develop gallstones while using contraceptive tablets with better treatment alternatives and management techniques. Finally, researchers may assist in improving women's health outcomes, making educated family planning decisions, and implementing focused healthcare treatments by investigating the connection between gallstones and contraceptive pills in Kurdistan.

In order to effectively educate patients with cholelithiasis, nurses must cover the following topics: Nurses provide comprehensive information on cholelithiasis, including the characteristics of gallstones, their development, and possible side effects or symptoms. This includes describing the gallbladder's general function and its role in digestion. Additionally, nurses inform patients about dietary choices, family history, obesity, and other risk factors linked to gallstone formation. They emphasize the importance of maintaining a healthy weight, eating a balanced diet, and getting regular exercise, highlighting the value of a diet high in fiber and low in fat, and avoiding significant weight reduction. They might also discuss the potential benefits of quitting smoking. Nurses offer practical guidance on how to incorporate healthy eating practices into the patient's lifestyle and explain how dietary decisions affect the development of gallstones ⁽¹¹⁾.

Additionally, nurses help patients identify the symptoms of gallstones, such as jaundice, nausea, vomiting, and abdominal discomfort. They provide recommendations on when to seek medical care for severe or worsening symptoms. Furthermore, if medication management is part of the treatment plan, nurses explain the intended use, dosage, and possible side effects of prescribed medications. They discuss ways to encourage compliance and ensure patients understand the importance of taking their medications as prescribed. Moreover, nurses help

patients manage their gallstone symptoms by providing self-care techniques. This could include suggesting dietary changes during pain episodes, emphasizing the importance of staying hydrated, and offering techniques for managing pain at home ^(11,12).

Finally, if surgery is required, nurses inform patients about the procedure's justification, potential risks, benefits, and aftercare. They address any questions or concerns the patient might have and provide details on the recovery phase. Nurses emphasize the need for scheduling follow-up visits and monitoring for any potential issues. They inform patients about symptoms that indicate problems, such as infection or bile duct blockage, and provide advice on when to seek immediate help ^(11,13).

AIMS OF THE STUDY

The aim of this study was to determine the association between the use of oral contraceptive pills and gallstones.

METHODOLOGY

Setting of the Study

The present study was conducted at the Teaching Hospital for Gastroenterology and Hepatology in Sulaimaniyah city, which provides inpatient and outpatient services for patients diagnosed with hepatobiliary diseases.

Study Population

This descriptive analytic study enrolled 51 patients with a history of gallstones or newly discovered gallstones from July 3rd, 2024, to August 31st, 2024. Inclusion criteria were being female, willingness to participate in the study, and confirmed diagnosis of gallstones. Exclusion criteria included female who were using other types of contraceptives other than pills, cancer, intestinal disorders, autoimmune diseases, or unwillingness to participate.

Ethical Approval

The research was approved by the Ethical Committee at the College of Medicine, University of Sulaimani. All study participants gave verbal consent.

Furthermore, the confidentiality of all personal information was ensured throughout the study to ensure the participants' anonymity.

Data Collection

Data were collected using a structured questionnaire through face-to-face interviews. The questionnaire consisted of two parts:

- **Part I:** Socio-demographic characteristics: Includes age, level of education, occupation, and residence.
- **Part II:** Clinical characteristics: Includes body mass index (BMI), family history of gallstones, parity, and duration of oral contraceptive pill use.

Participants' BMI was classified according to WHO guidelines as follows: underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{-}24.9 \text{ kg/m}^2$), overweight ($25\text{-}29.9 \text{ kg/m}^2$), and obese ($\geq 30 \text{ kg/m}^2$) ⁽⁸⁾.

Statistical Methods

All statistical computations were performed using SPSS 24. Data were coded, tabulated, and presented descriptively. The statistical procedures applied included: Descriptive data analysis Tables:(Frequencies and Percentages) and Inferential data analysis .The Contingency Coefficients test was employed to estimate the association between variables and identify correlations. The analysis involved the Chi-square (χ^2) Test.

RESULTS

As presented in Table 1, the mean age of the participants was 45.87 years, with a standard deviation of 18.39. Nearly two-thirds (64.7%) of the participants were over 35 years of age, 23.5% were between 25 and 35 years, and only 11.8% were under 25 years. Regarding educational attainment, 33.3% of the participants were illiterate, while 19.6% held degrees from an institute or university. The majority of participants (86.3%) were housewives, with a small percentage (2%) being retired. Additionally, 64.7% of the participants resided in urban areas, while rural residents constituted 3.9%.

As presented in Table 2, participants were classified as either overweight (47.1%) or of normal weight (31.4%). In terms of family history of gallstones, more than half of the patients (52.9%) reported a family history of gallstones, whereas 47.1% did not have such a history.

The results presented in Table 3 indicate that less than half (49%) of the patients had four or more children, while 21.6% had two or three children. Additionally, only 9.8% were nulliparous. Concerning the duration of contraceptive pill use, 64.7% of the patients utilized contraceptives for less than 10 years, whereas 41.2% used them for more than 10 years.

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Table 4 demonstrates a statistically significant association between the level of education and the use of oral contraceptives ($p\text{-value} < 0.005$). Conversely, no statistically significant association was found between age, occupation, and residence ($p\text{-value} > 0.05$).

According to the findings in the Table 5, indicated that there was no statistically significant association between BMI and family history of gallstones ($p\text{-value} > 0.05$).

DISCUSSION:

The study aimed to investigate the association between gallstone and oral contraceptive pills in the Teaching Hospital for Gastroenterology and Hepatology in Sulaymaniyah city. The study revealed that nearly two-thirds of the participants were over 35 years old. In terms of education, 33.3% of the patients were illiterate, while 19.6% were graduates of an institute or university. The majority of participants were housewives, with a few being retired. Additionally, nearly two-thirds of the patients

resided in urban areas. These sociodemographic characteristics align with the findings of Mousa et al. ⁽¹⁴⁾, who reported the highest prevalence of gallbladder disease (27.5%) in patients aged 35 years. Similarly, Shafique et al. ⁽¹⁵⁾ found that almost half (48.13%) of their patients were younger than 30 years.

In contrast, the study by Mehboob et al. ⁽¹⁶⁾ indicated that 49.3% of patients were under 40 years old, with a higher prevalence of gallstones observed among housewives compared to employed individuals (80.2% vs. 19.8%). Numerous studies have identified age as a significant risk factor for gallstones. As individuals grow older, the likelihood of developing gallstones increases due to several factors. Firstly, changes in bile composition can occur with age, leading to higher cholesterol levels that may promote the formation of cholesterol gallstones. Secondly, aging may reduce gallbladder motility, resulting in less efficient emptying and an increased frequency of gallstone formation due to stasis. Lastly, over time, exposure to various risk factors such as diabetes, obesity, and certain medications can further elevate the risk of developing gallstones ^(17, 18).

Furthermore, Shafique et al. ⁽¹⁵⁾ found that the highest percentage of patients with gallstones was among highly educated individuals (12.9%), whereas our study identified the highest percentage among illiterate patients (33.3%). Regarding occupation, the prevalence of gallstones was higher in housewives compared to employees (11.6% vs. 6.4%). There appears to be a complex and insufficiently defined relationship between education level and gallstone formation. Certain research indicates an indirect association influenced by factors such as diet, lifestyle, and access to healthcare, all of which may vary based on an individual's educational background. For example, individuals with higher levels of education may have better access to healthcare and a greater understanding of healthy lifestyles, potentially reducing their risk of developing gallstones. In contrast, lower education levels are

often linked to poorer dietary habits and higher rates of obesity, both of which serve as risk factors for gallstones (16, 19).

The association between obesity and an increased risk of developing gallstones is supported by epidemiologic studies, although these studies have shown conflicting results. Some studies propose that obesity may be associated with enhanced synthesis and excretion of cholesterol into bile, with the quantity of cholesterol generated directly correlated with overweight (19). Similarly, Mehboob et al. (16) showed that obesity is a major risk factor for gallbladder stone disease (GSD).

Additionally, Belal et al. (20) reported that the prevalence of overweight and obesity was higher among patients (75.6%) compared to controls (53.7%). The prevalence of cholelithiasis is anticipated to rise in conjunction with increasing obesity rates and its association with GSD.

With regard to family history of gallstones, the current study indicates that more than half of the patients reported a family history of gallstones, while 47.1% did not have such a history. This aligns with findings from a study conducted by Belal et al. (20), which noted a higher percentage of gallstones in patients with a family history of gallstones compared to the control group (12.2% vs. 0%).

The present study's findings regarding the relationship between gallstones and obstetrical history are consistent with those of Ahmed et al. (21), who observed that 37% of cases were multipara compared to 23% in the control group (p -value = 0.000). A similar study by Naeem et al. (22) conducted in Karachi reported a high incidence of parity among cholelithiasis patients. Additionally, Mousa et al. (14) found that 39.3% of women with a parity of four or more had gallbladder disease, demonstrating a significant association ($P = 0.001$).

In addition, Maruyama et al. (23) corroborated that women with multiple pregnancies are at an increased risk of developing gallstones. This is substantiated by the observed positive correlation

between elevated parity rates and the incidence of gallstones. Multiparous women are at a heightened risk of gallstone formation due to hormonal changes. Elevated levels of estrogen and progesterone during pregnancy can lead to increased cholesterol in bile and decreased gallbladder motility, thereby facilitating gallstone formation.

Regarding the association between sociodemographic variables and gallbladder disease (GBD), the present study identified a significant relationship between education level and cholelithiasis. However, Mousa et al. (14) reported a significant association between age and family history of gallbladder disease ($P = 0.001$) while finding no significant links between gallbladder disease and other variables such as occupation, residence, and educational level.

Furthermore, Wang et al. (8) confirmed that there was no significant relationship between oral contraceptive use and the risk of cholelithiasis, potentially attributable to variations in the types and doses of contraceptives. Thus, oral contraceptives did not demonstrate a significant increase in the risk of cholelithiasis.

CONCLUSIONS:

The findings of the present study found a statistically significant association between the level of education and the type of contraceptive used. However, there was no statistically significant association between BMI, family history of gallstones, and the use of oral contraceptive pills.

LIMITATION OF THE STUDY:

Our study was limited to female participants, given the higher prevalence of gallstones in women. Nevertheless, these findings warrant further analysis with a larger sample size.

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TABLES:

Table (1): Socio-demographic characteristics

Socio-demographic characteristics		Frequency (F)	Percentage (%)
Age (Years)	< 25	6	11.8
	25 – 35	12	23.5
	More than 35	33	64.7
Mean \pm S.D		45.87 \pm 18.39	
Level of education	Illiterate	17	33.3
	Primary	13	25.5
	Secondary	11	21.6
	Institute/University	10	19.6
Occupation	Housewife	44	86.3
	Employed	6	11.8
	Retired	1	2.0
Residence	Urban	33	64.7
	Sub-urban	16	31.4
	Rural	2	3.9
Total		51	100

Table (2): Clinical characteristics of patients

Clinical Characteristics		Frequency (F)	Percentage (%)
BMI	Under weight	2	3.9
	Normal	16	31.4
	Over weight	24	47.1
	Obese	9	17.6
Family history of gallstone	Yes	27	52.9
	No	24	47.1
Total		51	100

Reproductive history		Frequency (F)	Percentage (%)
Parity	Nulliparous	5	9.8
	1 child	10	19.6
	2-3 children	11	21.6
	4 and more	25	49
	How long using contraceptive?		
	< 10 years	10	64.7
	≥ 10 years	7	41.2
Total		51	100

Socio-demographic characteristics		Yes (N=17)		No (N=34)		Total		Significant test
		N	%	N	%	N	%	
Age	< 25 years	1	5.9	5	14.7	6	11.8	$\chi^2=0.886$ p=0.642
	25 – 35 years	4	23.5	8	23.5	12	23.5	
	More than 35 years	12	70.6	21	61.8	33	64.7	
Level of education	Illiterate	4	23.5	13	38.2	17	33.3	$\chi^2=10.21$ p=0.017
	Primary	9	52.9	4	11.8	13	25.5	
	Secondary	2	11.8	9	26.5	11	21.6	
	Institute/University	2	11.8	8	23.5	10	19.6	
Occupation	Housewife	16	94.1	28	82.4	44	86.3	$\chi^2=1.432$ p=0.489
	Employed	1	5.9	5	14.7	6	11.8	
	Retired	0	0.0	1	2.9	1	2	
Residence	Urban	12	70.6	21	61.8	33	64.7	$\chi^2=0.88$ p=0.643
	Sub-urban	4	23.5	12	35.3	16	31.4	
	Rural	1	5.9	1	2.9	2	3.9	
Total		17	100	34	100	51	100	

Significant Test at the level of significance 0.05. If (P-value < 0.05), it is significant.
The Significant Test is the Chi-Square Test.

Clinical Characteristics		Yes (N=17)		No (N=34)		Total		Significant test
		N	%	N	%	N	%	
BMI	Under weight	0	0	2	5.9	2	3.9	$\chi^2 = 1.219$ p=0.749
	Normal	5	29.4	11	32.4	16	31.4	
	Over weight	9	52.9	15	44.1	24	47.1	
	Obese	3	17.6	6	17.6	9	17.6	
Family history of Gallstone	Yes	9	52.9	15	44.1	27	52.9	$\chi^2 = 0.354$ p=0.552
	No	8	47.1	19	55.9	24	47.1	
Total		17	100	34	100	51	100	

Significant Test at the level of significance 0.05. If (P-value < 0.05), it is significant.
The Significant Test is the Chi-Square Test.