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# The effect of lipid levels on the development of gallstone disease and its role with age, blood type and body mass index

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**ABSTRACT:** Gallstone disease (GSD) is a prevalent and expensive biliary condition. Numerous studies have examined the correlations between blood lipid metabolism and the risk of GSD. Blood samples were collected from 75 people divided into three groups, First group: Healthy people were used as a control group (n=25), second group (2): Patients with gallstones (n=25), and third group (3): Cholecystectomy patients (n=25). The samples were females only, and their ages ranged between (20-60 years). Determine levels of Total Cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL), between healthy individuals, gallstone patients, and patients who underwent cholecystectomy. The results of the present study show significant differences in Total cholesterol concentration in cholecystectomy patients (208.88 ±6.09) compared to both healthy groups (175.92  $\pm$ 4.80) and gallstone patients (189.28  $\pm$ 8.70), significant increase in triglyceride levels in cholecystectomy patients (211.56  $\pm$ 17.57) compared with healthy controls (114.88  $\pm$ 8.70) and gallstone patients (101.08 ±9.91), the LDL level increased significantly in the group of gallstone patients compared to healthy subjects  $(95.60 \pm 5.36)$  at a probability level (P $\leq 0.05$ ). There was a significant increase in VLDL levels in cholecystectomy patients (42.31  $\pm$ 3.51) compared to healthy subjects (22.97  $\pm$ 1.74) and gallstone patients (20.21  $\pm$ 1.98), statistically significant differences at a significance level of (0.05) in the age group less than 40 years between the study groups. The study showed an association between dyslipidemia (elevated total cholesterol, triglycerides, and VLDL) and gallstone incidence and gallstone removal, with increased LDL levels in patients with gallstones. The incidence was also found to be more common in the age group below 40 years and was associated with blood group O+ and Rh+.

Keywords: Gallstones; cholecystitis; Cholecystectomy; cholesterol; Triglycerides



# **1. INTRODUCTION**

Gallstones are solid deposits of digestive fluid (bile) that form inside the gallbladder, and range in size from as small as a grain of sand to as large as a golf ball(1). This condition is a common digestive system disease, affecting 10% to 20% of adults. The primary treatment for gallstones is to remove the gallbladder, a procedure that is often accompanied by severe physical pain and can significantly affect the patient's life. Clinical research indicates that gallstones are associated with several factors, including age, gender, and body mass index, in addition to their association with obesity, diabetes, non-alcoholic fatty liver disease, and other diseases (2). The majority of gallstone disease (GSD). Numerous studies have assessed the correlation between serum lipid levels and the risk of GSD (2, 8). Nonetheless, a significant

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disparity exists among the findings. These are attributable to variations in study design, sample size, respondents' ethnicity, and the definition of dyslipidemia, hence constraining the robustness and applicability of this data. The etiology of this disease is related to the interaction of genetic and environmental factors, which include hypercholesterolemia in the liver, hypersaturation of bile and mucus, inflammatory changes, decreased intestinal motility, hyperabsorption of cholesterol in the intestine, and changes in the gut microbiota (3). The occurrence of gallstones is also associated with high levels of triglycerides and cholesterol in the blood (4). Also, a high body mass index is associated with an increased incidence of gallstones (5). The incidence rate increases with age (6). There are three main types of gallstones: cholesterol stones, pigment stones, and brown stones. Cholesterol stones are the most common due to the prevalence of associated risk factors in both developing and developed countries (7).

The study aimed to compare some biochemical indicators, such as cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL), between healthy individuals, gallstone patients, and patients who underwent cholecystectomy.

# 2. MATERIALS AND METHODS

#### 2.1Subjects

Blood samples were collected from (75) people divided into three groups, **Group (1)**: Healthy people were used as a control group (n=25), **Group (2)**: Patients with gallstones (n=25), **Group (3)**: Cholecystectomy patients (n=25), The comparative study was conducted in Ramadi Teaching Hospital for the period from 15/8/2024 to 20/10/2024. The samples consisted of females only, and their ages ranged between 20 and 60 years.

#### **2.2 Samples treatments**

(5 ml) of blood was drawn from the Median Cubital Vein through Disposable Syringes and then the sample was placed in a gel tube. Centrifugation was performed at 3000 rpm for 10 minutes, which led to the separation of the serum. The samples were preserved at -20°C until it was required for examination. Prior to assessing the biochemical parameters, such as T.C., HDL, T.G., LDL, and VLDL.

#### 2.4 Measurement of serum lipid markers

Serum lipid concentration was measured using the Chemistry Analyzer Smart-150 according to the instructions of the kit provided by GIESSE of Italy.

#### Ethics approval

The ethical approvals that are outlined in the Declaration of Helsinki were adhered to throughout this research project. Following the review and approval of the study protocol and subject's information by the local ethics committee in accordance with document number 19 and the date on 12/11/2024), the patient's informed written and verbal agreement was obtained prior to the collection of the sample.

#### 2. 5Statistical analysis

Statistical Packages for the Social Sciences (2019) application was utilized to determine the impact that different groups have on the parameters of the study. In order to make a meaningful comparison between the means, the least meaningful Difference (LSD) and the T-test were utilized. To make a statistically significant comparison between the

percentages (0.05 and 0.01 likelihood), the Chi-square test was utilized. Estimation of the coefficient of correlation between the variables in this investigation (8).

#### 3. RESULTS AND DISCUSSION

3.1 Comparison of lipid levels between healthy subjects, gallstone patients, and cholecystectomy patients.

3.1.1 Total Cholesterol levels in studied groups

The results of the current study (Figure 1) showed significant differences in Total cholesterol concentration in **cholecystectomy patients was (208.88 ±6.09 a)** compared to both healthy groups (175.92 ±4.80) and **gallstone patients** (189.28 ±8.70 b) at a probability level of (P $\leq$ 0.05). No significant differences were observed between healthy subjects and gallstone patients.



Figure 1: Comparison between difference groups in Total cholesterol

# 3.1.2 Triglycerides levels

The results in Figure 2 showed a significant increase in triglyceride levels in cholecystectomy patients  $(211.56 \pm 17.57 \text{ a})$  compared with healthy controls  $(114.88 \pm 8.70)$  and gallstone patients  $(101.08 \pm 9.91 \text{ b})$  at the probability level (P<0.01). While no statistically significant differences were observed in triglyceride levels between healthy groups and stone patients



#### 3.1.3 High-density lipoprotein (HDL) cholesterol levels

The study did not show any significant differences in HDL levels between the three groups (57.34  $\pm$ 3.42), (51.76  $\pm$ 2.14) and (58.64  $\pm$ 1.47) for control groups, cholecystectomy patients and gallstone patients respectively. As shown in Figure 3.



Figure 3: Comparison between difference groups in HDL

## 3.1.4. Low-density lipoprotein (LDL) cholesterol:

The LDL level increased significantly in the group of gallstone patients compared to healthy subjects (95.60  $\pm$ 5.36) at a probability level (P $\leq$ 0.05). No significant differences were observed in LDL levels between cholecystectomy patients

 $(107.93 \pm 5.11 \text{ ab})$  and healthy subjects, or between cholecystectomy patients and gallstone patients was  $(117.30 \pm 6.32 \text{ a})$ . As shown in Figure 4.



Figure 4: Comparison between difference groups in LDL

# 3.1.5. Very-low-density lipoprotein (VLDL) cholesterol:

There was a significant increase in VLDL levels in cholecystectomy patients ( $42.31 \pm 3.51$  a) compared to both healthy subjects ( $22.97 \pm 1.74$ ) and gallstone patients ( $20.21 \pm 1.98$  b) at a probability level (P $\leq 0.01$ ). The results did not show significant differences in VLDL levels between healthy subjects ( $22.97 \pm 1.74$ ) and gallstone patients ( $20.21 \pm 1.98$  b), as shown in Figure 5.





#### 3.2 Distribution of study samples according to age, blood type and Rh

The results of Table (1) showed statistically significant differences at a significance level of (0.05) in the age group less than 40 years between the study groups (gallstone patients, cholecystectomy patients, and healthy individuals). The percentage was higher in the group of gallstone patients compared to the groups of cholecystectomy patients and healthy

individuals. The results also showed statistically significant differences at a significance level of (0.01) regarding blood type (+O) between the study groups, as the percentage was higher in the groups of gallstone patients and cholecystectomy patients compared to the healthy group. In addition, statistically significant differences were observed at a significance level of (0.01) regarding the positive Rhesus factor (+Rh) between the study groups.

Factors		Control No (%)	Infection No (%)	Operation No (%)	P-value
Age groups (year)	<40 yr.	6 (24.00%)	13 (56.00%)	10 (40.00%)	0.0385 *
<b>v</b>	40-50 yr.	10 (40.00%)	9 (36.00%)	6 (24.00%)	
	>50 yr.	9 (36.00%)	3 (12.00%)	9 (36.00%)	
Blood groups	А	3 (12.00%)	4 (16.00%)	2 (8.00%)	0.0001 **
	В	2 (8.00%)	3 (12.00%)	0 (0.00%)	-
	AB	8 (32.00%)	1 (4.00%)	1 (4.00%)	-
	0	12 (48.00%)	17 (68.00%)	22 (88.00%)	-
Rh	+	22 (88.00%)	23 (92.00%)	(96.00%)	0.0001 **
	-	3 (12.00%)	2 (8.00%)	1 (4.00%)	
		* (P≤0.0	05), ** (P≤0.01).	1	

Table 1: Distribution of sample study according difference factors in difference groups

#### 3.3 Comparison of study groups of different ages and body mass index

The results of the current study, as shown in Table (2), indicate an increase in the average age of the healthy group and compared to the incidence rates of gallstones at a significance level ( $P \ge 0.01$ ). On the other hand, no significant differences were observed between the healthy group and RF cholecystectomy, while a significant increase in the average age was observed in cholecystectomy patients compared to gallstone patients.

There is a body mass index (BMI), as there are high results in the BMI in gallstones patients and compared to the healthy group at a significance level (P < 0.05). However, no significant differences were observed in the BMI between the cholecystectomy group and gallstone patients, and no significant differences were observed between the healthy group and gallstone patients.

Table 2: Comparison between difference groups in Age and BMI					
Group	Mean ±SE				
Group	Age (year)	BMI (kg/m <sup>2</sup> )			
Control	46.20 ±1.82 a	27.94 ±0.58 b			
Infection	37.24 ±2.05 b	30.12 ±0.71 ab			
Operation	43.44 ±2.13 a	31.33 ±1.10 a			
LSD	5.649 **	2.341 *			
P-value	0.0075	0.0178			
Means having with the different letters in same column differed significantly, * ( $P \le 0.05$ ), ** ( $P \le 0.01$ ).					

Cholesterol gallstones are one of the most common digestive diseases, and are closely related to the process of cholesterol metabolism in the liver. Evidence suggests that stone formation may be caused by disorders in hepatic cholesterol metabolism, such as increased cholesterol synthesis or disorders in its absorption or export from the liver (9). One study showed that gallstone disease is associated with abnormal levels of blood lipids, and that cholecystectomy can improve these levels (10). For example, one study indicated a decrease in total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels after cholecystectomy, while no significant changes were recorded in triglycerides and high-density lipoprotein cholesterol (HDL-C) levels (11). On the other hand, a positive association was found between triglyceride levels and gallstone disease, especially in women and individuals with obesity (12). A recent study by Singh (2024) also confirmed a significant reduction in total cholesterol and high-density lipoprotein cholesterol (HDL-C) levels decreased after surgery, while total cholesterol and HDL-C levels remained largely unchanged (14). These results suggest that cholecystectomy can have a positive effect on improving some blood lipid parameters, with varying effects depending on the type of lipid and the target patient population.

Gallstones are more common in women, with a four-fold higher incidence in women than men, especially in obese and fertile women over the age of 40. Although gallstones are rare before the age of 20, they can occur at any age (15). One study suggests that the incidence of gallstones increases with age (5). A previous study showed that individuals with blood type A were more likely to develop gallstones than those with blood types O and B (16). On the other hand, another study suggested that gallstones were more common in patients with blood type O (17). Other studies have confirmed a strong association between obesity, metabolic syndrome, premenopausal women, and advancing age with an increased incidence of gallstones (18). In a 2024 study, Prakash's findings showed a positive association between body mass index and gallstone development (19). Another study also showed that the incidence of gallstones is higher in women and obese patients, and this risk increases with age (20). In an additional study, a strong association was confirmed between body mass index and age with the risk of gallstones, while no association was found between gender and the risk (21).

#### 4. CONCLUSION

The study demonstrated an association between dyslipidemia-including elevated total cholesterol, triglycerides, and VLDL- and both gallstone incidence and removal, with increased LDL levels in patients with gallstones. The incidence was also found to be more common in the age group below 40 years and was associated with blood group O+ and Rh+. Obesity was found to be an additional risk factor as patients had a higher BMI. The results emphasize the importance of focusing on lipid control, obesity management, and early intervention to prevent the disease and its complications.

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