

Original Research Article

Physiological effect of cholecystectomy on lipid profile of patients with cholelithiasis

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ABSTRACT

Background: The association of cholecystectomy with alterations in lipid profile is well documented. Objectives of this study were to determine the effect of cholecystectomy on lipid profile of cholelithiasis patients.

Methods: This cross-sectional observational study was done on 170 patients admitted in general surgery department of Naz Memorial Hospital, Karachi from July 2018 to June 2019. Symptomatic cholelithiasis patients between 18 to 60 years, elective cholecystectomy was included while patients previously on lipid lowering agents, diagnosed renal failure, nephrotic syndrome, cardiac failure, pregnant mothers, hypothyroidism, pancreatitis and obstructive jaundice were excluded. For data analysis, SPSS was used. Wilcoxon signed ranked test was used to compare mean values of pre- and post-operative lipid profiles after cholecystectomy keeping p value of <0.05 as significant.

Results: 60% of patients were females with majority, 31% patients between 31-40 years while least, i.e. 11% were between 61-70 years. The mean pre-operative and post-operative difference of 52 ± 7.32 mg/dl was seen in total cholesterol levels ($p < 0.001$). The mean difference in high density lipoprotein (HDL) between pre and post-operative was of 13 ± 0.36 mg/dl ($p < 0.001$). The mean difference in low density lipoprotein (LDL) between pre and post-operative was 61 ± 10.45 mg/dl ($p < 0.001$). The mean difference in triglycerides levels between pre and post-operative was 46 ± 25.49 mg/dl ($p < 0.001$).

Conclusions: Cholecystectomy in gall stone disease patients elicited favorable response in significantly lowering levels of total serum cholesterol, LDL and triglycerides while substantially increasing levels of HDL cholesterol.

Keywords: Lipid profile, Cholecystectomy, Cholelithiasis, HDL, LDL, Triglycerides

INTRODUCTION

Cholelithiasis or gall stone disease is commonly observed throughout the world, with an incidence of around 1.4 per 100 people each year.¹ It is one of the most frequently observed disorders clinically reported. Nonetheless, many patients remain asymptomatic and/or are diagnosed on incidental finding at the time of abdominal ultrasonography for unrelated diseases.² Prevalence of

cholelithiasis varies from 6 to 10% in adult population, more so in females. Cholelithiasis is reported in populations having a rich diet in saturated fats and reduced intake of fiber content in foods. In addition, age, ethnicity, gender and a sedentary lifestyle all tend to be risk factors for the disease.³

Symptomatic gall stone disease is normally treated via cholecystectomy.⁴ The laparoscopic cholecystectomy is

regarded as the 'gold standard' for cholelithiasis. It is approximated that most of the cholecystectomies are carried out as laparoscopic surgeries since it has various benefits of early recovery in terms of early return of bowel functions, improved cosmesis, lesser post-operative pain, reduced duration of hospital stays and early returning towards daily routine activities.⁵ Linking gall stones in patients having alteration in lipid profile are well known. Over 50% patients having gall stones tend to have some type of lipid disorder. In routine per-operative check-ups, many clinicians find derangements in lipid profile of patients. Furthermore, strong links between alterations of lipid profile with increase in coronary artery disease risk and risk of stroke have suggested a strong association between them as well.⁶

Cholesterol levels in bile are higher as compared to other phospholipids in people having cholesterol stones. This gives a general picture that cholesterol stone pathogenesis involves alterations in lipid metabolism.⁷ Some researchers have reported improvements in patient's lipid profile after cholecystectomy.⁸ Hypothesis states that after cholecystectomy, a reduced level of bile acid pool's size coupled with increases in entero-hepatic circulation frequency tends to lower lipid levels by causing a reduction in the total cholesterol level as well as low-density lipoprotein (LDL) cholesterol levels as well.⁹

Gall stone formation is a complex process. Main factors which facilitate stone formation are: super saturation of the secreted bile, bile concentrations within gall bladder, nucleation and an abnormal emptying of gall bladder.¹⁰ It has been reported that females tend to be at a 2-3 times higher risk for gall stone disease in comparison to males probably owing to role of steroid hormones and pregnancy also increases the risk of formation of gall stones and the risk increases as the number of pregnancies increase.¹¹ A significant factor is the super saturation of bile via cholesterol which is water insoluble, secreted from uni-lamellar phospholipid vesicle through canalicular membrane. The solubility of cholesterol in bile require a sufficient level of bile salts as well as phospholipids (pre-dominantly phosphatidyl choline i.e. lecithin. Any excessive cholesterol or reduction in phospholipid level and/or bile acid content leads to nucleation of cholesterol which forms crystals leading to formation of cholesterol stone.¹² Secreted cholesterol gets super-saturated leads to dys-motility of gall bladder causing cholesterol crystal aggregation and delaying in large intestine's transit time period which favors re-absorption of deoxycholic acid, resecting ileum in depletion of the bile acid's secretary pool have been implicated in formation of gall stones.¹³

Studies have evidenced that over 50% of cholelithiasis patients do contain some or the other kind of lipid dysregulation.¹⁴ Hyperlipidemia is usually characterized via high levels of total serum cholesterol, LDL, triglycerides and low level of high-density lipoprotein (HDL). Cholelithiasis has been more often than not associated to

high triglyceride levels and low HDL level while results have been inconclusive with regards to total cholesterol and LDL levels.¹⁵ A pre-direction of cholelithiasis has been reported more commonly among hyperlipidemia type IV patients. Any abnormal function of lipid metabolism might arise from combination of different factors like high calorie diet, diabetes, obesity, drugs for example oral contraceptives and importantly, genetic predispositions.¹⁶

Metabolic factors are in relation to cholesterol solubility in bile acids. Bile acids are formed in the liver from cholesterol. Normal ratio of cholesterol to bile acid is 1:25 and the vital level of precipitation is 1:13.¹⁷ Level of bile salts present in bile is decreased by factors that cause interruption in the normal entero-hepatic circulation, e.g. ileal disease, biliary fistula resection or gastric bypass surgeries. All the disorders are linked to increase incidences of cholelithiasis.¹⁸

The objective of this study is to determine the physiological effect of cholecystectomy on lipid profile of patients with cholelithiasis.

METHODS

This cross-sectional observational study using non-probability convenient sampling technique was done at the department of surgery of Naz Memorial Hospital, Karachi for a period of 1 year from July 2018 to June 2019. After ethical approval from the Institutional Review Board of the respective hospital, a total of 175 patients were enrolled in the study. All patients having symptomatic gall stone disease admitted to the general surgery department of NMH, Karachi between ages 18 to 60 years, for elective cholecystectomy (either laparoscopic or open cholecystectomy) were included in the study. Patients that were previously on lipid lowering agents or patients with diagnosed renal failure, nephrotic syndrome, cardiac failure, pregnant mothers, hypothyroidism, and pancreatitis and with obstructive jaundice were excluded from the study. Patients undergoing emergency cholecystectomy were also excluded from the study.

After written and informed consent from the patients, a detailed history was recorded along with clinical examination and routine pre-operative investigations. Hematological variables involved fasting lipid profile pre-operatively as well as post-operatively. A post-operative lipid profile was done at 1 month follow up time period and compared with the pre-operative lipid profile. For lipid profile, ten ml blood sample was drawn on the morning of the day of surgery and at 1st month follow up after cholecystectomy.

Data analysis

For analysis of data, SPSS version 23 was used. Qualitative data was presented as frequency and

percentages while quantitative data was reported as mean and standard deviation. Wilcoxon signed ranked test was performed for comparison of the mean values of pre-operative and 1st month post-operative lipid profiles after cholecystectomy keeping a p value of <0.05 as statistically significant.

RESULTS

All 170 patients of elective cholecystectomy those were included in the study, a substantial decrease in the various lipid levels were observed in all of the patients. None of the patients showed any increase in lipid levels except levels of HDL which were as anticipated, found to be higher 1 month after cholecystectomy since HDL is good cholesterol and predictor of good lipid function.

From the 170 patients included in the study, 68 (40%) of the patients were reported to be males while majority 102 (60%) of the patients were females. The majority of the patients, i.e. 52 (31%) were between 31-40 years while least, i.e. 19 (11%) were between 61-70 years (Table 1).

Table 1: Baseline demographics of patients in the study.

Variables	Frequency	Percentage
Gender	Male	68
	Female	102
Age distribution (in years)		
21-30	37	22
31-40	52	31
41-50	35	21
51-60	27	16
61-70	19	11

The mean pre-operative total serum cholesterol of the patients was 196±29.79 mg/dl. Mean post-operative total serum cholesterol was 144±22.47 mg/dl with a mean

difference of 52±7.32 mg/dl. A significant difference of <0.001 existed between pre- and post-operative measurement of cholesterol. The mean high-density lipoprotein (HDL) of the patients at pre-operative checkup was 32±5.98 mg/dl while post-operatively, the mean HDL was 45±6.34 mg/dl with a mean difference of 13±0.36 mg/dl. A substantial difference of <0.001 was observed at pre- and post-operative HDL levels. The mean low-density lipoprotein (LDL) at pre-operative measurement was 172±27.77 mg/dl while mean post-operative LDL was 111±17.32 mg/dl with a mean difference of 61±10.45 mg/dl. A significant difference of <0.001 was reported between pre- and post-operative levels of LDL. The mean triglycerides levels at pre-operative checkup were 194±37.89 mg/dl while mean post-operative triglyceride level was 148±12.40 mg/dl with a mean difference of 46±25.49 mg/dl. A substantial difference of <0.001 was seen between pre- and post-operative level of triglycerides (Table 2 and Figure 1).

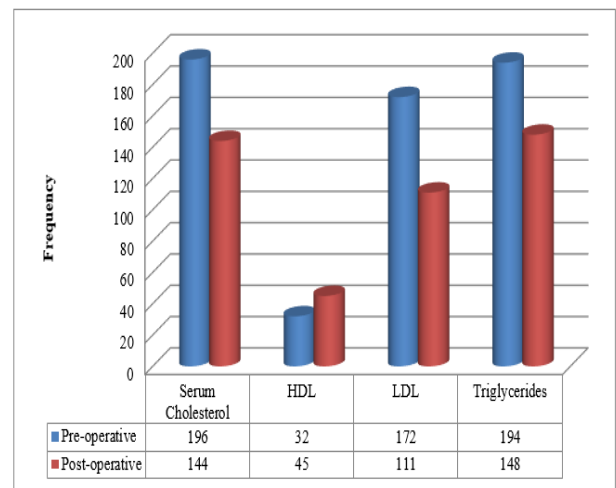


Figure 1: Serum lipid profiles at pre and post-operative follow up.

Table 2: Serum lipid profiles pre and post-operatively at 1 month.

Type of lipid	Pre-operative (mean±SD)	Post-operative (mean ±SD)	Mean difference	P value
Total serum cholesterol (mg/dl)	196±29.79	144±22.47	52±7.32	<0.001
High density lipoprotein (mg/dl)	32±5.98	45±6.34	13±0.36	<0.001
Low density lipoprotein (mg/dl)	172±27.77	111±17.32	61±10.45	<0.001
Triglycerides (mg/dl)	194±37.89	148±12.40	46±25.49	<0.001

DISCUSSION

The classic demographics, female, fatty, fertile, forty tend to be the prevalent dispositions for gall stone disease.¹⁹ Similarly, the above-mentioned demographic representations were also noticed in our study as well. Higher ratio of females as compared to male, highest percentage of patients being in the 40 years approximate group which is also the fertile age range, all point towards the phenomenon. Other age groups in our study,

the 21-30 years, 41-50 years and 51-60 years were more or less similar in respect of the patient distribution, being at 22%, 21% and 16% respectively. However, least frequencies were observed in the 61-70 years age group. All of the patients in this study were observed to have derangements in their pre-operative lipid profiles. Hypercholesterolemia, hypertriglyceridemia and lower HDL-cholesterol levels were the abnormalities reported in the study.

Effects of cholecystectomy on lipid profiles of patients in various studies have reported a significant decrease post-operatively at subsequent follow ups. Theoretically speaking, cholecystectomy leads to a favorable change in lipid profile.²⁰ The changes are attributed to lipid levels which are in part because of enhancements in phospholipid secretion as well as bile acids into the bile after under-going cholecystectomy. This in turn causes increase in its frequency of circulation in entero-hepatic that leads to increased excretion of lipids therefore causing an effective reduction in the total pool of bile acid.²¹

Several studies have reported a substantial decrease in the total cholesterol levels, LDL, triglycerides and a significant increase in HDL following cholecystectomy. A study by Katahan et al on patients with gall stone disease reported an insignificant difference ($p > 0.10$) of serum cholesterol and HDL ($p > 0.01$) in between cases and controls while phospholipids, LDL and triglycerides were observed to have a significant difference ($p < 0.01$) between cases and controls.²²

A study by Ahi et al reported a similar result to our study in which most patients having lipid alterations in cholelithiasis being females and between 31-40 years of age and same pattern of lipid level lowering as seen in our study.²³ Singh et al in their study attributed gall stone formation and lipid dysregulation to estrogens as well as HDL might cause inhibitions of hepatic cholesterol synthesis. It is reported that progesterone also aids in promoting formation of saturated bile through smooth muscle relaxation and impairment of gall bladder emptying.²⁴ Likewise, in a study by Singletary et al, the presence of progesterone and estrogen receptor on gall bladder concluded that they must have an effect on the gall bladder's function.²⁵

Another study similar to ours, by Katahan et al and Erpecum et al found a higher level of cholesterol in patients having cholelithiasis.^{22,26} In accordance with our study, another study also reported a higher lipid levels in gall stone diseases patients.²⁷ Channa et al observed in their study that increased steroid synthesis because of free cholesterol led to lower bile acid production which caused hyper saturation of bile with cholesterol.²⁹

Another study reported that patients with cholelithiasis tend to show lower levels of HDL while higher LDL levels.³⁰ On the contrary, a study found an inverse relationship of HDL with bile cholesterol saturation.³¹ Most researchers recorded high HDL levels to be a cause of higher cholesterol delivery into hepatic tissues which was seen in their studies.³² Yet another study also found a correlation between HDL and bile acids in cholecystectomy patients.³³ A study by Helvacı et al concluded low HDL levels among cholelithiasis patients.³⁴ Shiina et al found substantial increase in cholesterol, triglycerides and LDL in cardiac patients that had cholelithiasis following cardiac surgery.³⁵

Triglycerides also showed a steep decrease after cholecystectomy in our study; likewise, other studies also reported the same, regardless of the state of obesity. Weerakoon et al found a higher triglyceride level in gall stone disease patients than in controls. Increased levels of triglycerides have been reported to cause hypo motility in gall bladder via decreases in gall bladder's sensitivity to cytokines which may cause cholesterol crystallization leading to the formation of cholesterol stones.

Limitations and recommendation of the study

Although we have determined the different lipid levels in gall stone diseased patients before and after undergoing cholecystectomy, however the study was not immune from observer, selection bias and the fact that the study was carried out at a single center with limited sample size. Furthermore, only symptomatic cholelithiasis patients were included in the study. Asymptomatic patients that must have had altered lipid profiles were left out. Therefore, application of the results of this study to the general population is yet to be done. Additionally, shorter follow up time period could also have been a source of bias in the study, since longer follow up time period are associated with lack of patient compliance in regular follow up visits, especially at the low resourced, under-developed population. Future, multi-centered studies on larger scales involving cholelithiasis patients of different symptomatic, asymptomatic variety with the type of gall stone present would be enlightening in determining a more accurate interpretation of results.

CONCLUSION

According to the results of the study, cholecystectomy in gall stone diseased patients elicited a favorable response in significantly lowering the levels of total serum cholesterol, LDL and triglycerides while substantially increasing the levels of HDL cholesterol.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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