Original Research Article

COMPARATIVE STUDY ON EFFECT OF CHOLECYSTECTOMY ON SERUM LIPID PROFILE IN GALLSTONE PATIENTS

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Abstract

Background: Cholelithiasis or gall stone disease is commonly observed throughout the world, with incidence of around 1.4 per 100 people each year. Women are more common victims of the gall stone disease. The process of gall stone formation is multiplex. Cholesterol super saturation of bile is the most crucial factor. There is strong association between altered lipid profile and increase in risk of coronary artery disease and stroke. Hypothesis states that after cholecystectomy, reduced level of bile acid pool size coupled with increases in enterohepatic circulation frequency tends to lower lipid levels by causing a reduction in total cholesterol level as well as low density lipoprotein (LDL) cholesterol levels. This is study to know the beneficial effects of cholecystectomy due to change in lipid profile in patients of gall stone disease. To determine the changes in lipid profile parameters after cholecystectomy **Materials and Methods:** This was an observational study done for a period of 1 year in the Dept. of general Surgery, RIMS, Ranchi on all patients undergoing open/laparoscopic cholecystectomy. The pre-operative fasting lipid profile sample was taken one day prior to the surgery and one month after the surgery. **Result:** There was a significant improvement in the lipid profiles of study subjects post cholecystectomy. Total cholesterol, low density lipoprotein cholesterol, and triglycerides decreased significantly post cholecystectomy. Simultaneously, there was a significant increase in the high-density lipoprotein cholesterol levels post-surgery. **Conclusion:** Cholecystectomy has a favourable effect on the lipid profile of patients.

INTRODUCTION

Gall stone disease is commonly observed throughout the world, with an incidence of around 1.4 per 100 people each year.[1] Women are more common victims of the gall stone disease as compared to men.[2] Patients with symptomatic gall stone disease is normally treated via cholecystectomy.[3] Gallstones are basically classified into three main types: cholesterol, pigment, and mixed gallstones. Cholesterol gallstones contain 51%–99% of pure cholesterol. Mixed gallstones have cholesterol as well as calcium salts, bile acids, phospholipids and bile pigments. In about 70–80% of the cases, gallstones are mixed stones.[4] The process of gall stone formation is multifactorial. Major factors that govern the stone formation are: super saturation of the bile, concentration of bile within the gall bladder, nucleation, and abnormal gall bladder emptying.[5] Cholesterol super saturation of the bile is the most crucial factor.[6,7]

Cholesterol is not soluble in water; it is secreted from the canalicular membrane in unilamellar phospholipid vesicle. Cholesterol solubility in the bile requires adequate bile salts and phospholipids, predominantly phosphatidylcholine. If there is an excess of cholesterol or reduced phospholipids and/or bile acid, multi lamellar vesicles are formed causing nucleation of the cholesterol crystals which leads to the formation of stone. The secretion of cholesterol supersaturated lithogenic bile, decreased concentration of phospholipids, gallbladder dysmotility, delayed large bowel transit times (favouring reabsorption of deoxy- cholic acid), and the resection of ileum (depleting the acid pool) have all been involved in the formation of gall stone.[8]

Hyperlipidemia is usually characterized by high serum levels of total cholesterol, triglycerides, low density lipoproteins (LDL), and low levels of high-density lipoprotein (HDL). Based on the evidence, more than 50% of patients with gall stones have some sort of lipid disorder.[9] Though lipid and bile acids metabolisms are functionally correlated, how cholecystectomy affects lipid profile is not well understood. High lipid profile levels, consisting of elevations in chylomicron, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and intermediate-density lipoprotein (IDL) levels, are becoming on the rise, specially with the factors, such as urban residence, advancing age, specially 40 years and above; inadequate physical inactivity, overweight and obesity, diabetes mellitus, frequent fast food consumption, and so on.[10] This, in turn, raises concerns about the effective management of such conditions. Cholecystectomy, which is considered the most definitive management of symptomatic gallbladder diseases, for example, cholecystitis, biliary colic, gallbladder stones, and so on, was shown to decrease total serum lipids, serum cholesterol, serum LDL cholesterol, and serum triglycerides, and increase serum HDL cholesterol post- cholecystectomy after one day, one week, one month, and one year, according to Ali etal., Jindal et al., and Shen et al.[9,11-13] There is also a strong relation between deranged lipid profile and increase in risk of coronary artery disease and stroke.[14] Hypothesis states that after cholecystectomy, a reduced level of bile acid pool 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.[15] Current data suggest that 40 mg/dl decrease in LDL levels can be translated to 10% decrease in all-cause mortality, 24% reduction in major coronary events and 15% in stroke.[16] Since the relationship between cholecystectomy and serum lipid profile has not been established yet, this study will investigate the serum lipid profiles of patients up to 1 month post- cholecystectomy.

MATERIALS AND METHODS

A complete history of all patients with acute cholecystitis/right upper quadrant pain was taken followed by complete physical examination. Symptoms suggestive of acute cholecystitis was noted as follows: -

- Right upper quadrant/epigastric post prandial pain lasting longer than 24 hours,
- fever,
- nausea and
- vomiting.

Physical examinations suggestive of acute cholecystitis was noted as follows: -

- Tenderness noted on palpation of the right upper quadrant,
- voluntary cessation of respiration when the examiner exerts constant pressure under the right costal margin (Murphy's sign),
- guarding in the right upper quadrant,
- fever,
- tachycardia.

Along with serum Lipid Profile (HDL, LDL, Triglycerides, Total cholesterol), they were subjected to standard blood examinations including complete blood count, PT-INR, liver function tests including bilirubin levels, gamma glutamyl transferase, alkaline phosphatase, alanine transaminase, aspartate transaminase, renal function test, serum amylase, serum lipase.

Blood investigations supporting diagnosis of acute cholecystitis were observed as follows:

- Mild elevations of alkaline phosphatase,
- transaminase levels,
- amylase,
- leukocytosis and
- direct bilirubin should be relatively normal.

Ultrasound findings suggestive of acute cholecystitis: thickening of the gallbladder wall to greater than 4 mm and pericholecystic fluid and sonographic Murphy sign documenting tenderness specifically over the gallbladder. Additional USG findings suggestive of gallstones are: - echogenic focus with a characteristic shadowing behind the stone which moves on positional changes of the patient is suggestive of presence of calculus.

The lipid profile was evaluated on the day of surgery pre-operatively and post-operatively one month later.

RESULTS

The present study was conducted in the Department of General Surgery, Rajendra Institute of Medical Sciences, RIMS, Ranchi. A total of 112 patients who were diagnosed with cholelithiasis were included in the study.

1. **Age Distribution:**

- The table categorizes individuals into different age groups.
- The largest age group is 41–50 years, comprising 46 individuals, which represents 41.07% of the total.
- The next largest group is 31–40 years, with 30 individuals, accounting for 26.78%.
- The smallest groups are >70 years (1 individual, 0.90%) and 21–30 years (4 individuals, 3.57%).

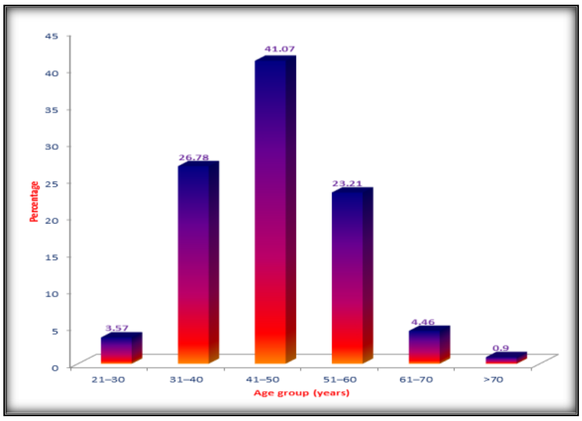
2. **Percentage Distribution:**

- The table shows the percentage of each age group relative to the total population of 112 individuals.

- This percentage distribution provides insight into the demographic composition in terms of age.

3. **Insights:**

- The data indicates a relatively balanced distribution among the middle-aged groups (31–60 years).
- There are fewer individuals in the younger (<30 years) and older (>60 years) age brackets.
- The majority of individuals (over 64%) fall within the age range of 31–60 years.



Analysis:

1. **Mean and Standard Deviation:**

○ **Pre-operative:**

- Mean total cholesterol level before the operation: 186.46 mg/dL.
- Standard deviation (SD) of total cholesterol before the operation: 21.30 mg/dL.

○ **Post-operative:**

- Mean total cholesterol level after the operation: 155.9 mg/dL.
- Standard deviation (SD) of total cholesterol after the operation: 23.79 mg/dL.

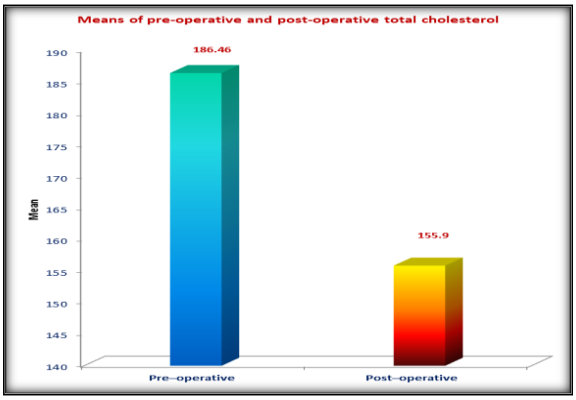
2. **Comparison (p value):**

○ The table indicates a statistically significant difference in total cholesterol levels before and after the operation.

○ The p value provided (<0.0001) suggests that the difference is highly significant.

Interpretation

Significant Change: The mean total cholesterol level has decreased from 186.46 mg/dL pre-operatively to 155.9 mg/dL post-operatively. This difference is statistically significant, indicating that the operation has had a notable impact on reducing total cholesterol levels.



Analysis:

1. **Mean and Standard Deviation:**

○ **Pre-operative**

- Mean HDL level before the operation: 39.39 mg/dL.
- Standard deviation (SD) of HDL before the operation: 11.23 mg/dL.

○ **Post-operative**

- Mean HDL level after the operation: 50.58 mg/dL.
- Standard deviation (SD) of HDL after the operation: 8.52 mg/dL.

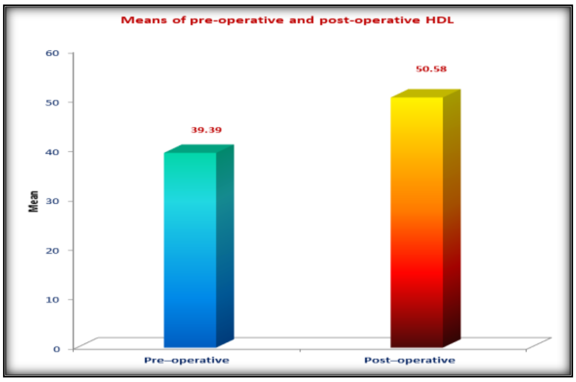
2. **Comparison (p value)**

○ The table indicates a statistically significant difference in HDL levels before and after the operation.

○ The p value provided (<0.0001) suggests that the observed difference is highly significant.

Interpretation

Increase in HDL Levels: The mean HDL level has increased from 39.39 mg/dL pre-operatively to 50.58 mg/dL post-operatively. This difference is statistically significant, indicating that the operation has had a notable impact on increasing HDL levels.



Analysis

1. **Mean and Standard Deviation:**

○ **Pre-operative:**

- Mean LDL level before the operation: 120.83 mg/dL.
- Standard deviation (SD) of LDL before the operation: 20.77 mg/dL.

○ **Post-operative:**

- Mean LDL level after the operation: 100.37 mg/dL.

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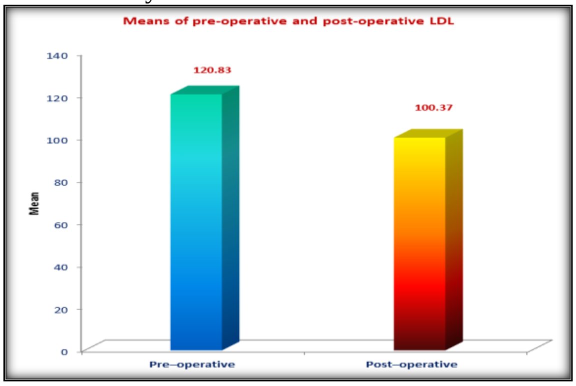
- Standard deviation (SD) of LDL after the operation: 14.61 mg/dL.

2. **Comparison (p value):**

- ○ The table indicates a statistically significant difference in LDL levels before and after the operation.
- ○ The p value provided (<0.0001) suggests that the observed difference is highly significant.

Interpretation:

Decrease in LDL Levels: The mean LDL level has decreased from 120.83 mg/dL pre-operatively to 100.37 mg/dL post-operatively. This difference is statistically significant, indicating that the operation has effectively reduced LDL levels.



Analysis:

1. **Mean and Standard Deviation**

- ○ **Pre-operative:**
- Mean triglyceride level before the operation: 143.56 mg/dL.
- Standard deviation (SD) of triglycerides before the operation: 26.54 mg/dL.
- ○ **Post-operative**
- Mean triglyceride level after the operation: 122.26 mg/dL.
- Standard deviation (SD) of triglycerides after the operation: 22.99 mg/dL.

2. **Comparison (p value)**

- ○ The table indicates a statistically significant difference in triglyceride levels before and after the operation.
- ○ The p value provided (<0.0001) suggests that the observed difference is highly significant.

Interpretation

Decrease in Triglyceride Levels: The mean triglyceride level has decreased from 143.56 mg/dL pre-operatively to 122.26 mg/dL post-operatively. This difference is statistically significant, indicating that the operation has effectively reduced triglyceride levels.

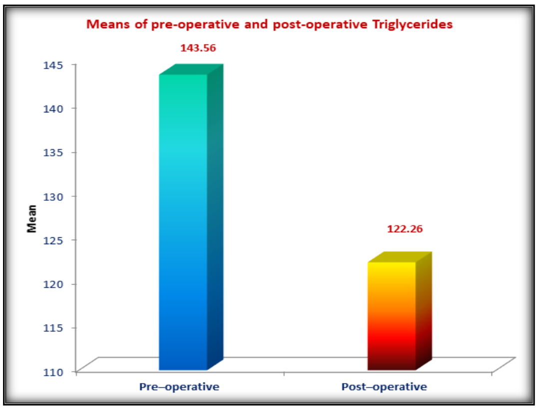


Table 1: Description of the age distribution.

Age group (Years)	Number	Percentage (%)
21–30	4	3.57
31–40	30	26.78
41–50	46	41.07
51–60	26	23.21
61–70	5	4.46
>70	1	0.90
Total	112	100.00

Table 2: Comparison between means of pre-operative and post-operative total cholesterol (n=112)

Parameter	Pre–operative		Post–operative		p value
	Mean	SD	Mean	SD	
Total cholesterol (mg/dL)	186.46	21.30	155.9	23.79	<0.0001

Table 3: Comparison between means of pre-operative and post-operative HDL (n=112)

Parameter	Pre–operative		Post–operative		p value
	Mean	SD	Mean	SD	
HDL (mg/dL)	39.39	11.23	50.58	8.52	<0.0001

Table 4: Comparison between means of pre-operative and lost-operative LDL (n=112)

Parameter	Pre–operative		Post–operative		p value
	Mean	SD	Mean	SD	
LDL(mg/dL)	120.83	20.77	100.37	14.61	<0.0001

Table 5: Comparison between means of pre-operative and post-operative Triglycerides (n=112)

Parameter	Pre–operative		Post–operative		p value
	Mean	SD	Mean	SD	
Triglycerides (mg/dL)	143.56	26.54	122.26	22.99	<0.0001

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DISCUSSION

Cholelithiasis is a common disease, affecting adults all over the world and represents one of the most common causes of morbidity. In India, the prevalence of cholelithiasis varies in different region. Gall stone disease is one of the most common and most expensive conditions to treat of all digestive disorders requiring admission to hospital.[17] Of all gallstones found during cholecystectomy, cholesterol gallstones account for 80-90%.[18] Cholesterol gallstones are primarily made up of cholesterol crystals (70%) which are held together in an organic matrix of glycoproteins, calcium salts, and bile pigments. They could be present either singly or multiply, in various sizes, shapes and surfaces.[19]

In the above observational study, the results reveal significant findings related to the age distribution and lipid profile changes pre- and post-operatively among the sample population. The age distribution indicates that the largest age group comprises individuals aged 41–50 years, representing 41.07% of the total sample, followed by those aged 31–40 years, accounting for 26.78%. The smallest groups are those aged over 70 years (0.90%) and those aged 21–30 years (3.57%). This demographic breakdown shows a relatively balanced distribution among the middle-aged groups (31–60 years), with fewer individuals in the younger and older age brackets. Notably, over 64% of the participants fall within the 31–60 years' age range.

In terms of lipid profiles, the study demonstrates statistically significant improvements post-operatively. The mean total cholesterol levels decreased from 186.46 mg/dL (SD = 21.30) pre-operatively to 155.9 mg/dL (SD = 23.79) post-operatively, with a highly significant p-value of <0.0001. High-density lipoprotein (HDL) levels increased from a mean of 39.39 mg/dL (SD = 11.23) to 50.58 mg/dL (SD = 8.52), also showing a significant p-value of <0.0001. Low-density lipoprotein (LDL) levels reduced significantly from a pre-operative mean of 120.83 mg/dL (SD = 20.77) to a post-operative mean of 100.37 mg/dL (SD = 14.61), with a p-value of <0.0001. Similarly, triglyceride levels decreased from 143.56 mg/dL (SD = 26.54) to 122.26 mg/dL (SD = 22.99), again with a significant p-value of <0.0001.

These findings indicate that the operation had a notable positive impact on the participants' lipid profiles, effectively reducing total cholesterol, LDL, and triglyceride levels while increasing HDL levels. This suggests substantial cardiovascular health benefits post-operation, highlighting the procedure's effectiveness in improving lipid-related health outcomes.

The primary objective of this study was to evaluate the impact of a surgical operation on lipid profiles, specifically total cholesterol, HDL, LDL, and triglycerides, across a sample population of various age groups.

In comparison, the study by Kuldip Singh Ahi et al. (2017),[20] focused on the lipid profile changes pre- and post-cholecystectomy. Pre-operatively, the total serum cholesterol level ranged from 111-298 mg% with a mean value of 193.17±58.84 mg%. On the 7th post-operative day, the mean total cholesterol level was 186.3±56.71 mg%, and one month after cholecystectomy, it further decreased to 166.95±48.08 mg%. This demonstrates a significant reduction in total cholesterol levels, which is consistent with our findings, although our observed decrease was more pronounced immediately post-operation.

Regarding HDL cholesterol, Kuldip Singh Ahi et al. (2017),[20] reported a pre-operative mean of 41.35±5.4 mg%, which increased to 43.27±6.3 mg% on the 7th post-operative day and further to 54.10±8.5 mg% one month post-operation. Our study similarly found an increase in HDL levels, though our post-operative mean was slightly higher at 50.58 mg/dL, indicating a significant improvement akin to the Kuldip Singh Ahi et al. (2017),[20] study.

For LDL cholesterol, Kuldip Singh Ahi et al. (2017),[20] noted a pre-operative mean of 120.90±43.44 mg%, decreasing to 132.08±36.93 mg% on the 7th day and 117.52±29 mg% one month post-operation. This aligns well with our findings of a reduction from 120.83 mg/dL to 100.37 mg/dL post-operatively, reinforcing the efficacy of surgical intervention in lowering LDL levels.

In terms of triglycerides, Kuldip Singh Ahi et al. (2017),[20] observed a pre-operative mean of 143.63±69.05 mg%, which increased to 159.47±43.32 mg% on the 7th day but decreased to 139.60±60 mg% one month post-operation. Contrarily, our study found a consistent decrease in triglyceride levels from 143.56 mg/dL to 122.26 mg/dL post-operatively. This discrepancy might be attributed to differences in the surgical procedures, patient demographics, or post-operative care protocols.

The significant reduction in total cholesterol and LDL levels observed in both studies suggests that surgical interventions effectively mitigate key cardiovascular risk factors. The increase in HDL levels further supports the cardiovascular benefits of such operations, given HDL's role in reverse cholesterol transport and cardiovascular protection. The consistent decrease in triglycerides in our study, compared to the initial increase observed by Kuldip Singh Ahi et al., highlights the variability that may arise from different clinical settings or patient populations.

In another study conducted by Mohammad Moazeni-Bistgani, Soleiman Kheiri2, Koorosh Ghorbanpour (2014),[21] the study had a predominantly female cohort (64 females out of 72 patients) as compared to my study included a total of 112 participants with a more balanced gender distribution. The age range in the comparative study was from 21 to 85 years with a mean age of 49.7 years, slightly older on average compared to the largest age group in my study, which was 41-50 years (41.07%). This suggests that the comparative study had a broader age distribution. In

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my study, the mean total cholesterol level significantly decreased from 186.46 mg/dL pre-operatively to 155.9 mg/dL post-operatively ($P < 0.0001$). This significant reduction indicates a notable improvement in total cholesterol levels post-surgery. In contrast, the comparative study showed a significant decrease in total cholesterol levels three days' post-operation ($P = 0.046$) but observed no significant differences at the 30-day and one-year follow-ups compared to pre-operative levels. This suggests that while the immediate post-operative period shows a decrease, the long-term effect on total cholesterol might not be as pronounced in the comparative study. My study found a significant increase in HDL levels from 39.39 mg/dL pre-operatively to 50.58 mg/dL post-operatively ($P < 0.0001$), indicating a positive impact of the surgery on raising HDL levels. Conversely, the comparative study reported a significant decrease in HDL levels three days' post-operation ($P = 0.030$) but found no significant changes at the 30-day and one-year marks. This contrast suggests a difference in how HDL levels respond over time between the two studies, with my study showing sustained improvement post-operatively. In my study, LDL levels significantly decreased from 120.83 mg/dL pre-operatively to 100.37 mg/dL post-operatively ($P < 0.0001$). This indicates a substantial reduction in LDL levels post-surgery. The comparative study also showed a significant decrease in LDL levels three days' post-operation ($P = 0.007$) but, similar to HDL and total cholesterol, found no significant differences at the 30-day and one-year follow-ups. This pattern suggests that while the immediate post-operative period reduces LDL levels, the long-term effect may vary between studies. For triglycerides, my study demonstrated a significant reduction from 143.56 mg/dL pre-operatively to 122.26 mg/dL post-operatively ($P < 0.0001$). The comparative study, however, observed an increase in triglycerides three days' post-operation ($P < 0.001$) and, despite a slight decrease after one month, the levels were still significantly higher compared to pre-operative values ($P = 0.001$). This increase persisted at the one-year follow-up. This stark difference highlights a divergent response in triglyceride levels post-surgery between the two studies, with my study indicating a consistent decrease while the comparative study noted an increase.

The results of my thesis demonstrate significant improvements in lipid profiles following surgery, which are consistent with findings from the study conducted by Jose V. Francisco Menezes, Rewanth R. Katamreddy (2019).[22] In my thesis, it was observed that the mean total cholesterol levels decreased significantly from 186.46 mg/dL pre-operatively to 155.9 mg/dL post-operatively ($p<0.0001$). This finding is in line with Menezes and Katamreddy's study, which reported a significant reduction in total cholesterol levels post-cholecystectomy, with a p-value of less than 0.001.

Similarly, my thesis showed a significant increase in HDL cholesterol levels from 39.39 mg/dL pre-operatively to 50.58 mg/dL post-operatively ($p<0.0001$). This is corroborated by the Jose V. Francisco Menezes, Rewanth R. Katamreddy (2019),[22] study, which also noted a statistically significant elevation in HDL cholesterol levels post-surgery ($p<0.001$).

Furthermore, the LDL cholesterol levels in my study decreased from 120.83 mg/dL to 100.37 mg/dL post-operatively ($p<0.0001$). The study by Jose V. Francisco Menezes, Rewanth R. Katamreddy (2019),[22] also found a significant reduction in LDL cholesterol levels ($p<0.001$), indicating a consistent trend across both studies in terms of LDL reduction post-cholecystectomy.

Triglyceride levels in my study decreased significantly from 143.56 mg/dL to 122.26 mg/dL post-operatively ($p<0.0001$). This finding aligns with the results from Menezes and Katamreddy, who reported a significant decrease in triglyceride levels post-surgery ($p<0.001$).

A key observation from the study by Jose V. Francisco Menezes, Rewanth R. Katamreddy (2019),[22] is the categorization of gallstones, with cholesterol stones accounting for 51% of the cases, pigment stones for 6%, and mixed stones for 43%. While my thesis did not delve into the types of gallstones, this information provides a broader context for understanding the lipid profile improvements post-cholecystectomy, especially given the predominance of cholesterol stones.

Overall, the consistency in findings between my thesis and the study by Jose V. Francisco Menezes, Rewanth R. Katamreddy (2019),[22] reinforces the positive impact of cholecystectomy on lipid profiles. Both studies demonstrate significant reductions in total cholesterol, LDL, and triglycerides, along with an increase in HDL levels, highlighting the surgical procedure's efficacy in improving lipid metabolism.

CONCLUSION

In conclusion, this study has explored the demographic characteristics and lipid profile changes among individuals undergoing surgical intervention. The age distribution analysis highlighted a predominant representation in the 41-50 years' age group, reflecting a diverse demographic composition. Importantly, the study demonstrated significant improvements in lipid profiles post-surgery, including reductions in total cholesterol, LDL, and triglycerides, alongside an increase in HDL levels. These findings underscore the beneficial impact of surgical procedures on lipid metabolism. Moving forward, further research is recommended to elucidate the underlying mechanisms driving these changes and to optimize post-operative care strategies aimed at enhancing patient outcomes in lipid management. Ultimately, this study contributes valuable insights into the intersection of surgical interventions, demographic factors, and lipid health, paving the way for targeted approaches to improve cardiovascular health in clinical practice.

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