

## Article

# Relationship between serum lipid profile and biochemical analysis of gallstones in patients with Cholelithiasis

Balaji Patil<sup>1</sup>, Sandesh Gawade<sup>2</sup>, Rishabh Gandhi<sup>3</sup>, Ajinkya Patil<sup>3,\*</sup> and Pratik Bamane<sup>3,\*</sup>

<sup>1</sup> General Surgeon, Department of General Surgery, MIMER Medical College, Talegoan Dabhade Pune, Maharashtra, India.

<sup>2</sup> Professor, Department of General Surgery, MIMER Medical College, Talegoan Dabhade Pune, Maharashtra, India.

<sup>3</sup> PG 3rd Year, Department of General Surgery, MIMER Medical College, Talegoan Dabhade Pune, Maharashtra, India.

\* Correspondence: ajinkyapatil1613@gmail.com

Received: 1 February 2023; Accepted: 5 May 2023; Published: 14 May 2023.

**Abstract:** Gallstone disease is a prevalent condition affecting 3-20% of the global population. While the majority of gallstones are asymptomatic, a small percentage of patients develop symptoms requiring cholecystectomy. The classification of gallstones includes cholesterol, pigment, and mixed types, with ongoing debates regarding the association of hyperlipidemia with gallstone formation. However, there is a lack of information regarding the relationship between abnormal lipid profiles and the biochemical analysis of gallstones. Therefore, this study aimed to assess the association between serum lipid profiles and the biochemical analysis of gallstones in patients with cholelithiasis. A total of 100 patients diagnosed with gallbladder stones were included in the study, and preoperative samples were collected for lipid profile analysis. The patients underwent either open or laparoscopic surgery, and their gallstones were sent for biochemical analysis. The findings revealed that cholesterol stones were the most common type observed. The overall prevalence of hyperlipidemia was 48%, and a significant association was found between hyperlipidemia and the cholesterol content of stones. In particular, the prevalence of hyperlipidemia was 54.3% in pure cholesterol stones, 48.8% in mixed stones, and 23.1% in pigmented stones. Moreover, there was a significant association between blood cholesterol levels and cholesterol stones, with a prevalence of 39.1% in pure cholesterol stones, 19.5% in mixed stones, and 7.7% in pigmented stones. However, no association was observed between triglyceride, LDL, and HDL levels with the composition of stones in cholelithiasis cases. In conclusion, this study highlights a significant association between blood cholesterol levels, hyperlipidemia, and the cholesterol content of gallstones, suggesting that hyperlipidemia, particularly raised cholesterol levels, can be considered a major risk factor in cholelithiasis.

**Keywords:** Hyperlipidaemia; Blood cholesterol; Type of gallstones.

## 1. Introduction

The prevalence of gallstone disease in the general population ranges from 3% to 20% worldwide [1–10]. In India, the prevalence of gallstones in the adult population is approximately 4% [5]. It is noteworthy that over 80% of gallstones are asymptomatic [1]. However, 1-2% of asymptomatic patients will develop symptoms requiring cholecystectomy each year, making it one of the most commonly performed operations by general surgeons [1].

Gallstones are classified into three main types: cholesterol, pigment, and mixed gallstones. Cholesterol gallstones contain 51-99% pure cholesterol, while mixed gallstones consist of cholesterol, calcium salts, bile acids, phospholipids, and bile pigments. The majority of gallstones, about 70-80% of cases, are mixed stones [1]. Cholesterol is insoluble in water and is secreted from the canalicular membrane in unilamellar phospholipid vesicles. Solubility of cholesterol in bile requires sufficient bile salts and phospholipids, particularly phosphatidylcholine.

The process of gallstone formation is complex, involving various factors. Major factors implicated in gallstone formation include the secretion of cholesterol supersaturated lithogenic bile, decreased concentration

of phospholipids, gallbladder dysmotility, delayed large bowel transit times favoring reabsorption of deoxycholic acid, and resection of the ileum depleting the acid pool [1].

Controversies exist regarding the association between hyperlipidemia and gallstones. Some studies have shown a significant association between hyperlipidemia, especially hypertriglyceridemia and increased LDL levels, and gallstones [7,8,10]. However, other studies have found no significant association between hyperlipidemia and gallstones [2,4]. Information regarding the association of abnormal lipid profile parameters with the biochemical analysis of gallstones, particularly in this region of India, is limited. Therefore, this study aimed to assess the relationship between serum lipid profile and biochemical analysis of gallstones in patients with cholelithiasis.

## 2. Material and methods

This single centric prospective analytical study was conducted from January 2020 to July 2021 for the patients in the department of general surgery at a tertiary care centre. A total of 100 patients with symptomatic cholelithiasis undergoing cholecystectomy were enrolled. The confirmation of cholelithiasis was done by imaging techniques (USG/CT-SCAN/MRI). Thorough clinical examination and preoperative evaluation was done.

Samples for lipid profile were collected after an overnight fasting in a 5 ml syringe. After collection, the sample was allowed to clot for half hour and then the serum was analysed for lipid profile using commercially available kits on fully automated analyser in the biochemistry laboratory. Cases were then taken up for surgery (Open/ Laparoscopic). After the surgery, gallstones were sent for biochemical analysis. Biochemical analysis of stones were correlated with the serum lipid profile of the patient.

### 2.1. Inclusion criteria

1. Patients with age above 18 yrs.
2. Patients with confirmed diagnosis of gall stones on imaging techniques and advised surgery for the same.

### 2.2. Exclusion criteria

1. Patients on lipid lowering agents for medical conditions.
2. Pregnant and lactating females.
3. Immunologically compromised patients (HIV/ Patients on chemotherapy, etc.)

### 2.3. Statistical Analysis

All the data was noted down in a pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test with Continuity Correction for all 2 X 2 tables and Fisher's exact test for all 2 X 2 tables. Quantitative data was represented using Mean  $\pm$  SD. Analysis of Quantitative data between the two groups was done using unpaired t-test if data passed 'Normality test' and by Mann-Whitney Test if data failed 'Normality test'. A p-value < 0.05 was taken as level of significance. Results were graphically represented where deemed necessary. SPSS Version 21.0 was used for most analysis and Microsoft Excel 2010 for graphical representation.

## 3. Results

Mean age of the study groups was 54 years with over half (55%) of the cases were over 50 years of age. Overall female predominance was seen among cases of cholelithiasis with 64% females to 36% males. Obesity was observed among 33% cases of cholelithiasis. Out of the total 100 cases of cholelithiasis, 46% cases had pure cholesterol stones while mixed and pigmented stones were seen in 41% and 13% cases respectively.

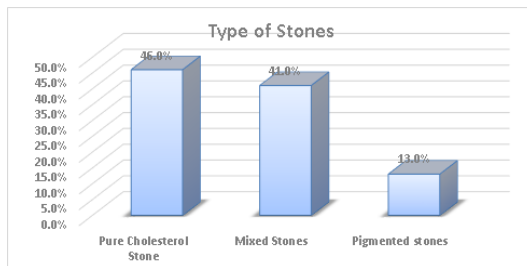


Figure 1. Type of Stones

Raised cholesterol levels were seen among 27% cases while raised triglyceride and LDL levels were seen among 24% and 36% cases respectively. Low HDL levels were seen among 22% cases.

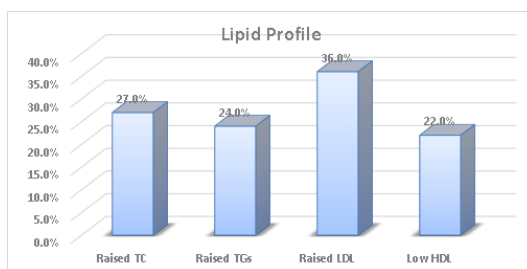


Figure 2. Lipid Profile

A significant association was observed between hyperlipidaemia with cholesterol content of stones. Prevalence of hyperlipidaemia was 54.3% in pure cholesterol stones while its prevalence was 48.8% in mixed stones and 23.1% in pigmented stones ( $p < 0.05$ ).

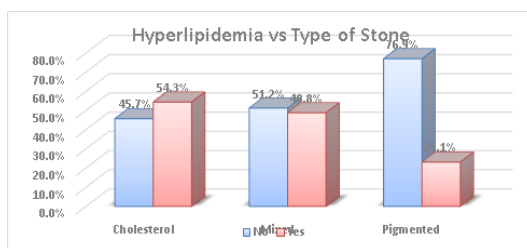


Figure 3. Hyperlipidemia vs Type of Stone

A significant association was observed between blood cholesterol levels with cholesterol content of stones. Prevalence of raised cholesterol levels was 39.1% in pure cholesterol stones while its prevalence was 19.5% in mixed stones and 7.7% in pigmented stones ( $p < 0.05$ ).

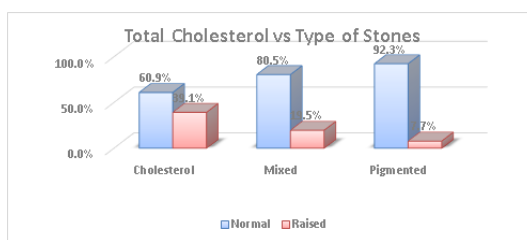


Figure 4. Total Cholesterol vs Type of Stones

Overall prevalence of hyperlipidaemia among cholelithiasis cases was 48%. No association was observed between triglyceride levels with composition of stones in cholelithiasis cases ( $p = 0.19$ ). No association was observed between LDL levels with composition of stones in cholelithiasis cases ( $p = 0.19$ ). No association was observed between HDL levels with composition of stones in cholelithiasis cases ( $p = 0.19$ ).

#### 4. Discussion

Cholecystitis is inflammation of the gall bladder that occurs most commonly because of an obstruction of the cystic duct due to cholelithiasis (Nagaraj et al., 2012)[9]. Cholesterol super saturation of the bile is the most crucial factor in process of gall stone formation [6,7]. There are controversies that hyperlipidemias are associated with the gallstones. Some studies have showed a significant association of hyperlipidemias with gallstones (Dhamnetiya et al., 2018)[4] while others showed no significant association. Present hospital based observational study thus aimed to assess the relationship between serum lipid profile and biochemical analysis of gallstones in patients with cholelithiasis. Study included 100 cases of symptomatic cholelithiasis undergoing cholecystectomy.

Mean age of the study groups was 54.06 years with over half (55%) of the cases were over 50 years of age. Overall female predominance was seen among cases of cholelithiasis with 64% females to 36% males. (Nagaraj et al., 2012)[9] observed the highest incidence in patients in the age group of 41-50 years with mean age of 48.7 years and female to male ratio was 2.57:1. (Mammad Asfak Ahmed, Bhupati Bhushan Das, Shushanta Kumar Das, Niranjana Sahoo, Laxmidhar Padhy, 2015)[8] also observed highest age group of the presentation of cholelithiasis as 41 to 50 years, the incidence in females being more common than males. (Kumar et al., 2016)[7] in their study observed that maximum of 38% were in their 4th decade with females constituting 82% of total.

Gallstones are classified into three main types: cholesterol, pigment, and mixed gallstones. Cholesterol gallstones contain 51%–99% of pure cholesterol. Mixed gallstones have cholesterol plus calcium salts, bile acids, phospholipids and bile pigments. In about 70–80% of the cases, gallstones are mixed stones [4].

In present study, out of the total 100 cases of cholelithiasis, 46% cases have pure cholesterol stones while mixed and pigmented stones were seen in 41% and 13% cases respectively. Among mixed stones, 14% cases had bilirubin along with cholesterol while 10% each had calcium and triglycerides. Pigmented stones included: dolomite (7%) and calcium bilirubinate (6%).

The biochemical analysis of stones in the (Gill & Gupta, 2017)[5] study revealed that maximum stones were cholesterol stones (36, 72%) followed by mixed (8, 16%) and pigment stones (6, 12%). (Nagaraj et al., 2012)[9] in their study showed that 68% patients to have mixed stones while 28% were pure cholesterol stones, with bilirubin being the major constituent of these stones apart from cholesterol. (Batajoo & Hazra, 2013)[3] observed that out of the total 50 cases with cholelithiasis, 38 patients (76%) had mixed stones, followed by pigment stones in 8 cases (16%) followed by cholesterol stones in remaining 4 cases (8%). Raised cholesterol levels were seen among 27% cases while raised triglyceride and LDL levels were seen among 24% and 36% cases respectively. Low HDL levels were seen among 22% cases. Overall prevalence of dyslipidemia among cholelithiasis cases was 48%.

(Nagaraj et al., 2012)[9] observed hyperlipidaemia in 64% of the cases of cholelithiasis. (Gill & Gupta, 2017)[5] observed dyslipidemia in 52% cases of cholelithiasis. The Mean levels of TC, TGs, and VLDL-C were observed to be significantly elevated and that of HDL was significantly lowered in patients with cholelithiasis as compared to controls.

The major understanding to the formation of stones came from the concept of physico-chemical properties of the lipid in the bile pursued by Admirend and Small. They demonstrated that the solubility of cholesterol in bile could be described by the molar concentration of cholesterol, bile salts and lecithin. If the concentration of bile salts and lecithin falls below a critical level, cholesterol precipitates from bile.

In present study too, we observed a significant association between dyslipidemia with cholesterol content of stones. Prevalence of dyslipidemia was 54.3% in pure cholesterol stones while its prevalence was 48.8% in mixed stones and 23.1% in pigmented stones ( $p < 0.05$ ). We also observed a similar significant association with cholesterol levels. Prevalence of raised cholesterol levels was 39.1% in pure cholesterol stones while its prevalence was 19.5% in mixed stones and 7.7% in pigmented stones ( $p < 0.05$ ). No association was observed between triglyceride, LDL and HDL levels with composition of stones in cholelithiasis cases ( $p = 0.19$ ).

(Kumar et al., 2016)[7] in their study observed Serum total cholesterol, triglycerides and low density lipoprotein cholesterol were found to be higher and statistically significant in patients with gallstone compared to controls ( $p$  value 0.024,  $< 0.01$  and 0.016 respectively). Serum High density lipoprotein cholesterol was lower in gallstone patient than in control but not statistically significant ( $p$  value - 0.23). (Gupta et al., 2018)[6] observed correlation between gall stones and levels of serum cholesterol, triglyceride and levels of VLDL

( $p < 0.05$ ). Thus to summarize, cholesterol stone are the most common type of stone observed among the patients and a significant observation was observed between cholesterol stones and dyslipidemia especially serum cholesterol levels. Hence, raised cholesterol levels should be regarded as a major key in controlling cholelithiasis and due preventive measures for controlling the same should be taken.

## 5. Conclusion

It is apparent from the findings of the present investigation that the most common gallstone was cholesterol stone. The age group at risk of having gallstones was the fourth and fifth decade of life, with a higher risk for females than males. High prevalence of dyslipidaemia was observed among cases with gall stones. A significant observation was observed between cholesterol stones and raised serum cholesterol levels. Hence hyperlipidaemia, especially raised cholesterol levels can be regarded as a major key in controlling cholelithiasis. However, this observation needs further randomized studies to confirm it.

**Author Contributions:** All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

**Conflicts of Interest:** The authors declare that they do not have any conflict of interests.

## References

- [1] Atamanalp, S. S., Keles, M. S., Atamanalp, R. S., Acemoglu, H., & Laloglu, E. (2013). The effects of serum cholesterol, LDL, and HDL levels on gallstone cholesterol concentration. *Pakistan Journal of Medical Sciences*, 29(1), 187.
- [2] Aulakh, R., Mohan, H., Attri, A. K., Kaur, J., & Punia, R. P. (2007). A comparative study of serum lipid profile and gallstone disease. *Indian Journal of Pathology & Microbiology*, 50(2), 308–312.
- [3] Batajoo, H., & Hazra, N. K. (2013). Analysis of serum lipid profile in cholelithiasis patients. *Journal of Nepal Health Research Council*.
- [4] Dhamnetiya, D., Goel, M. K., Dhiman, B., & Pathania, O. P. (2018). Gallstone disease and quantitative analysis of independent biochemical parameters: Study in a tertiary care hospital of India. *Journal of Laboratory Physicians*, 10(04), 448–452.
- [5] Gill, G. S., & Gupta, K. (2017). Pre-and post-operative comparative analysis of serum lipid profile in patients with cholelithiasis. *International Journal of Applied and Basic Medical Research*, 7(3), 186.
- [6] Gupta, M., Singh, V., Gupta, P., & Gupta, P. (2018). To study the assessment of lipid abnormalities in patients suffering from gallstones. *Journal of Evolution of Medical and Dental Sciences*, 7(21), 2572–2576.
- [7] Kumar, J., Chatterjee, S., Dinda, S., Ghosh, A., Mallick, N. R., & Rahman, Q. M. (2016). Dyslipidemia and gall stone disease; A search for their causal relationship. *Journal of Surgical Arts*, 9(2), 67–70.
- [8] Mammad Asfak Ahmed, Bhupati Bhushan Das, Shushanta Kumar Das, Niranjana Sahoo, Laxmidhar Padhy, S. K. R. (2015). Qualitative analysis of serum lipid profile in patients with gall stone disease. *J of Evidence Based Med & Healthcare*.
- [9] Nagaraj, S. K., Paul, P., Kumar, M. K., Muninarayanapp, S., & Anantharamaiah, H. (2012). Risk factors and the biochemical evaluation of biliary calculi in rural Kolar, Karnataka, India: a rural perspective of an urban disease. *JCDR*, 6(3), 364–368.
- [10] Weerakoon, H. T. W., Ranasinghe, S., Navaratne, A., Sivakanesan, R., Galketiya, K. B., & Rosairo, S. (2014). Serum lipid concentrations in patients with cholesterol and pigment gallstones. *BMC Research Notes*, 7, 1–5.



© 2023 by the authors; licensee PSRP, Lahore, Pakistan. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license (<http://creativecommons.org/licenses/by/4.0/>).