

A Prospective Study on the Pattern and Association of Hyperlipidemia in Patients with Cholelithiasis

Dr. Vijay Tara^{1*}

^{1*} Associate Professor, Department of Pathology, M.G.M Medical College, Jamshedpur, East Singhbhum, Jharkhand.

Corresponding Author: Dr. Vijay Tara

Abstract

Introduction: Gallstones are formed because of abnormal bile composition. Cholesterol is essentially water insoluble and requires aqueous dispersion into either micelles or vesicles, both of which require the presence of a second lipid to solubilise the cholesterol. Cholesterol and phospholipids are secreted into bile as uni-lamellar bilayered vesicles, which are converted into mixed micelles consisting of bile acids, phospholipids, and cholesterol by the action of bile acids.

Materials and methods: The study was conducted in department of Pathology, M.G.M medical College and Hospital, Jamshedpur from January 2018 to December 2018. For the study purpose patients admitted in the General Surgery ward were selected according to below mentioned inclusion and exclusion criteria. A proforma was used to record the history, clinical findings, investigations carried out for each case. Patient consent form mentioned the name of the study, name of the participant, age, sex, address and telephone number, annual registration number and Date. After taking informed consent, patient or her relatives (next of kin) will be asked a structured questionnaire. Participation in this study is not obligatory, but optional. If the patient wishes He/she may withdraw himself/herself from the study at any time. Participant's name, particulars & data collected will be kept confidential & will not be used for any purpose other than this study.

Results: Gallstone disease is common in the age group of 31-40 years. There is a female preponderance. Cholesterol stones constitute the majority among the two main types of stones. There was a statistically significant increase in the serum total cholesterol and serum LDL levels, but no significant change in the serum triglycerides, HDL and VLDL levels in cholelithiasis patients compared to the control group.

Conclusion: There was a significant association of cholelithiasis with high serum cholesterol (>200 mg/dl) and LDL (>130 mg/dl) levels and, but no such association was found with high serum triglycerides (\geq 150 mg/dl) or low serum HDL (<40 mg/dl) levels.

Key Words: HDL, VLDL, LDL, Gallstones

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I. Introduction

Gallstones are formed because of abnormal bile composition. Cholesterol is essentially water insoluble and requires aqueous dispersion into either micelles or vesicles, both of which require the presence of a second lipid to solubilise the cholesterol.¹ Cholesterol and phospholipids are secreted into bile as uni-lamellar bilayered vesicles, which are converted into mixed micelles consisting of bile acids, phospholipids, and cholesterol by the action of bile acids. If there is an excess of cholesterol in relation to phospholipids and bile acids, unstable, cholesterol-rich vesicles remain, which aggregate to form large multilamellar vesicle. Cholesterol gallstone disease occurs because of several defects, which include (1) bile super-saturation with cholesterol, (2) nucleation of cholesterol monohydrate with subsequent crystal retention and stone growth, and (3) abnormal gallbladder motor function with delayed emptying and stasis from which cholesterol crystals precipitate. Gall stones are formed because of abnormal bile composition. They are divided into two major types: Cholesterol stones - more than 80% of the total.² They usually contain >50% cholesterol monohydrate plus an admixture of calcium salts, bile pigments, and proteins. Pigment stones - less than 20%. They are composed primarily of calcium bilirubinate; they contain <20% cholesterol and are classified into "black" and "brown" types, the latter forming secondary to chronic biliary infection. There is a female preponderance.³ Cholesterol stones constitute the majority among the main two types of stones. The aim of the present study was to find out the association between serum lipid profile and gall stones and to compare the lipid profiles of cholelithiasis patients with a control group. Specific objectives of this study were to study the patterns of different types of stones in the surgically removed gallbladders in M.G.M Medical College, to analyse the association of Cholelithiasis with serum lipid profile, to compare the association of abnormal lipid profile of cholelithiasis patients with a control

group and to study the histopathological changes in gallbladder in the study population, with special reference to cholesterosis and their association with serum lipid profile.

II. Materials And Methods

The study was conducted in department of Pathology, M.G.M medical College and Hospital, Jamshedpur from January 2018 to December 2018. For the study purpose patients admitted in the General Surgery ward were selected according to below mentioned inclusion and exclusion criteria. A proforma was used to record the history, clinical findings, investigations carried out for each case. Patient consent form mentioned the name of the study, name of the participant, age, sex, address and telephone number, annual registration number and Date. After taking informed consent, patient or her relatives (next of kin) will be asked a structured questionnaire. Participation in this study is not obligatory, but optional. If the patient wishes He/she may withdraw himself/herself from the study at any time. Participant's name, particulars & data collected will be kept confidential & will not be used for any purpose other than this study. Participants will not have to bear any expenses for participating in this study. This is across sectional study on the distribution of different types of gallstones in patients attending M.G.M Medical College & Hospital with study area of Department of Pathology, Department of General Surgery & Department of Biochemistry. Study population included 54 calculous Cholecystitis patients who would undergo cholecystectomy for calculous cholecystitis in Department of General Surgery, M.G.M Medical College During the study period number of Cholecystectomy cases were recorded, and on the basis of that, sample size selected. 51 age and sex related control was selected. Age and gender matched non-cholecystectomy patients without hyperlipidaemia who were admitted and were willing to participate in the study were selected as control. Not more than 51 could be obtained who fulfilled all those criteria. In the present study, all the calculous cholecystitis cases undergoing cholecystectomy were selected following the inclusion and exclusion criteria fixed for this study. Inclusion Criteria Sonologically diagnosed calculous cholecystitis cases among those who attended OPD, M.G.M Medical College & Hospital. Exclusion Criteria Those with coronary heart disease, diabetes mellitus, HIV infection and carcinoma gall bladder were excluded from the study. Patients with coronary heart disease and diabetes mellitus were excluded from the study because these patients have deranged serum lipid profile as either a cause or consequence of their primary diseases only. Hence any abnormality in serum lipid profiles in these patients could not be associated with cholecystitis directly, without elimination of these factors. Patients with HIV infection were excluded because sometimes they were not operated. Those with associated carcinoma of gall bladder were also not taken in the study population because they also have correlation with serum lipid profile which might have shown a spurious correlation with cholelithiasis. Study design: hospital-based cross-sectional study. Sampling design: All samples of surgically removed gallbladder masses fulfilling the above-mentioned inclusion criteria were chosen randomly. Detailed clinical history will be taken from the patients.

Parameters studied: detailed history taking pre-operative imaging study by ultrasonography, preoperative blood test for Glucose, HIV Serology and ECG. Serum lipid profile, gross appearance of the specimens, Histopathological examination after H & E staining. Detailed history started with identification of the patient including name, age, religion, address, occupation followed by chief complaints. Following completion of history, complete general and systemic examinations were done. Routine investigations like total blood count, differential count of W.B.C., haemoglobin estimation, erythrocyte sedimentation rate, platelet count were done. USG of the whole abdomen was done as a routine first line investigation. Patients having sonological evidence of gall bladder stones were considered in the study population. Sample collection for biochemical examination: 2-3 ml of venous blood was drawn in plain vials from the patients after overnight fasting and sent to the Department of Biochemistry, M.G.M Medical College.

Measurement of serum lipid profile: By the use of the autoanalyser machine, following five parameters were measured-Total cholesterol, Triglycerides, High-density cholesterol, Low density cholesterol, Very low-density cholesterol. Sample collection for histopathological examination: Depending on the patients' age and anaesthetic fitness, either open cholecystectomy or laparoscopic cholecystectomy was done. All the specimens for histopathological examination were collected and sent to the Department of Pathology, M.G.M Medical College in formalin-filled containers.

Statistical Analysis: Data entry was done right after capture of relevant data for a given subject was complete. Statistical evaluation was done by appropriate statistical method using 'SPSS software for WINDOWS'. The mean value of the serum total cholesterol, triglyceride, HDL, LDL and VLDL of cholelithiasis patients were compared with those of the control groups using student's t-test for statistical analysis.

III. Results

Among 105 patients, 54 patients (51.92%) had cholelithiasis and 51 patients (48.57%) who were admitted with some illnesses other than gallstones were selected as controls after application of exclusion criteria. Among 54 cases, maximum patients (29.6%) were between 31 to 40 years of age [Fig. 1]. Only one patient was above 70 years of age. Mean age was 41.72 years. In our study, only 1 patient had pigment stone and the rest (i.e. 53 patients) had cholesterol stones [Fig. 3]. In the present series there were 75.9% females and 24.1% males. The male: female ratio was around 1:3. [Fig. 2] Mean serum total cholesterol in the control subjects was 187.06 mg/dl with a SD of 40.97. Mean serum total cholesterol in the cholelithiasis patients overall was 216.43 mg/dl with a SD of 51.31. The result showed that there was a significant increase in the serum total cholesterol [p value 0.002 (<0.05)] in the patients with cholelithiasis in comparison to the control group. As per the NCEP guidelines, 200 mg/dl was taken as the cut-off value of serum levels of total cholesterol. 15 out of the 51 controls (i.e., 29.4% of the controls) had serum total cholesterol level more than 200mg/dl. Whereas, 32 out of the 54 cases (i.e., 59.3% of the cases) had serum total cholesterol level more than 200mg/dl [Table 1]. By chi-square test, there was significant association between high serum total cholesterol levels and cholelithiasis. [p value <0.05] The mean value of the serum total cholesterol, triglyceride, HDL, LDL and VLDL of cholelithiasis patients were compared with those of the control groups using student's t-test for statistical analysis. The results showed that there was an overall increase in the serum total cholesterol (p value 0.002) and serum LDL (p value 0.001), but no significant change in the serum triglycerides (0.617), HDL (0.663) and VLDL (0.564) levels in cholelithiasis patients compared to the control group. Comparison of the mean serum levels of total Cholesterol, TG, HDL, LDL AND VLDL of the cases with cholesterosis and those without were made. The results showed that there was no significant difference in any of the parameters in those cases showing cholesterosis compared to those not showing cholesterosis.

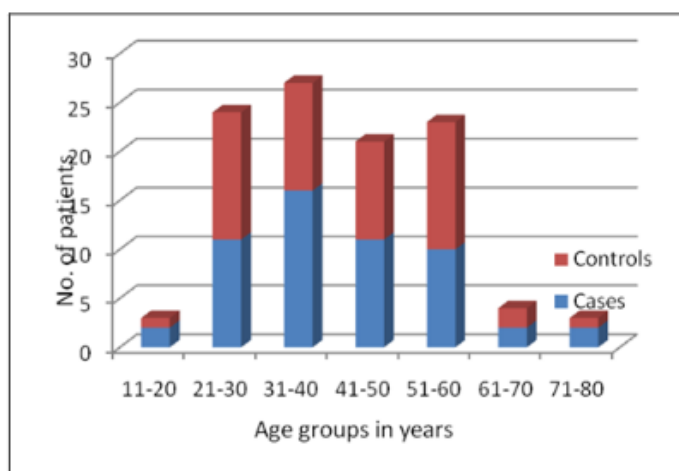


Figure 1. Frequency Distribution of Cases and Controls according to Age Group. (n=105)

Age incidence- In the present study maximum number of cases were encountered in the age group of 31-40 years (29.6%). Least number of cases were in the age group below 20 years, that between 21-30 years and that between 71-80 years (3.7% each).

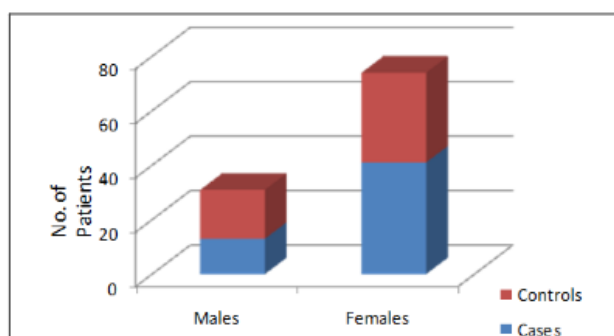


Figure 2. Frequency Distribution of Cases and Controls According to Sex (n=105)

In the present series there were 75.9% females and 24.1% males. The male: female ratio was around 1:3

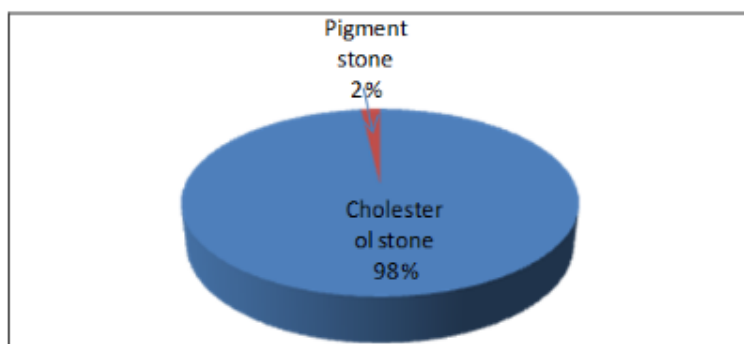


Figure 3. Frequency Distribution of Cases according to the Types of Stone.: (n=54)

In our study, only 1 patient had pigment stone and the rest (i.e. 53 patients) had cholesterol stones.

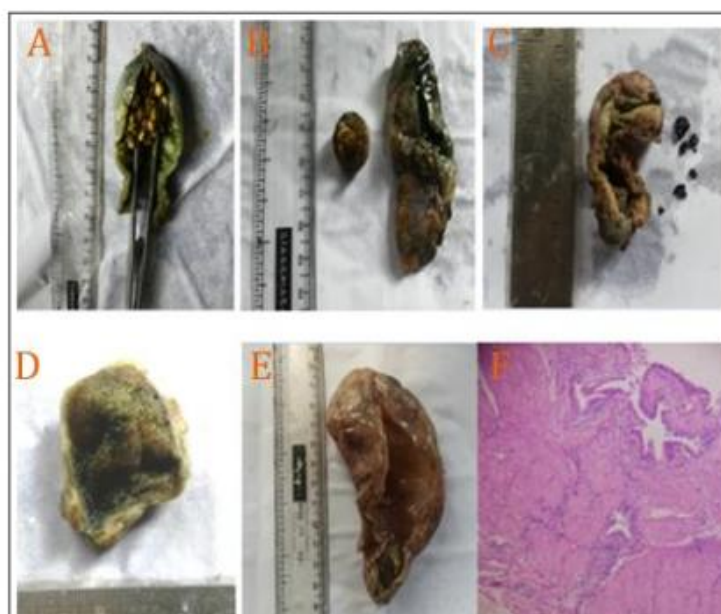


Figure 4. A Cut-Open Specimen of Gall Bladder Showing Multiple Yellowish Cholesterol Stones. B: Showing a Single Large Mixed Cholesterol Stone. C: Showing Multiple Black Pigment Stones D: Gross Features of Cholesterolosis. E: One Large Stone Obstructing the Neck of the Gall Bladder Resulting in a Mucocoele. F: Chronic Cholecystitis with RA-Sinus (H & E stain, 100 \times)

Parameter	With Cholesterol Stones (Mean \pm SD)	With Pigment Stone	Control (Mean \pm SD)	p Value
Serum total cholesterol(mg/dl)	218.45 \pm 50.10	139	187.06 \pm 40.97	0.002
Serum triglyceride(mg/dl)	174.72 \pm 52.35	141	168.51 \pm 61.73	0.617
Serum HDL(mg/dl)	46.08 \pm 5.48	45	47.22 \pm 18.72	0.663
Serum LDL(mg/dl)	135.43 \pm 49.28	74	104.65 \pm 42.85	0.001
Serum VLDL(mg/dl)	34.91 \pm 10.44	28	33.49 \pm 12.37	0.564

Table 1. Serum Lipid Profile of Cases with Cholesterol Stone (n=53): and Pigment Stone (n=1) Comparison of the Parameters with Controls

The mean value of the serum total cholesterol, triglyceride, HDL, LDL and VLDL of cholelithiasis patients were compared with those of the control groups using student's t-test for statistical analysis. The results showed that there was an overall increase in the serum total cholesterol (p value 0.002) and serum LDL (p value 0.001), but no significant change in the serum triglycerides (0.617), HDL (0.663) and VLDL (0.564) levels in cholelithiasis patients compared to the control group.

The results showed that there was no significant difference in any of the parameters in those cases showing cholesterosis compared to those not showing cholesterosis.

IV. Discussion

The majority of patients in the present study was in the age group of 31-40 years, whereas in the Brazilian series was >60 years old and 41-50 years in the study by Nagaraj et al. Series by Herman et al showed peak incidence in 41-50 years age group. In western studies the peak incidence is in the 5th and 6th decades.⁴ The rise in the peak age of incidence is due to change in the dietary factor. Similar findings are noted in the studies of Ganey et al and Moreaux et al. Cholelithiasis was uncommon in the first two decades of life, with only 2 cases in our study being below 20 years. In the series of Ghosh SK et al and Shenoy et al series the highest incidence was found in the age group of 41-50 years.⁵ Tyagi et al showed highest incidence in 31-40 years while Bhansali et al showed highest incidence in 51-60 years. In the present series there were 75.9% females and 24.1% males. The male: female ratio was around 1:3. Sex distribution in the study by Nagaraj et al showed a female to male ratio 2.57:1 while in Bockus et al study was 2.84:1.⁶ In Ghosh SK et al series, the ratio was 1.5:9, in Goswami series it was 1:2.5 and in Sharma LB series it was 1:1.7. Malhotra series showed sex distribution of 1:1.5.⁷ Framingham study concluded that the overall incidence of gallbladder disease was about twice as high in women as in men, and it increased with age in both sexes without any evidence of an excess in the forties. In the present study 53 patients (98.15%) had cholesterol stones (including both pure and mixed types) whereas only 1 patient (1.85%) had pigment stones. Other studies too showed a higher percentage of cholesterol stones and a much lower percentage of pigment stones.⁸

Only the study by Rakesh B et al showed a higher percentage of pigment stones than cholesterol ones.⁹ In the present study there was a statistically significant increase in the serum total cholesterol and serum LDL levels, but no significant change in the serum triglycerides, HDL and VLDL levels in cholelithiasis patients compared to the control group. This was in contrast with the observations of the study by Peela Jagannadha Rao where the triglycerides in serum were not altered in the cholelithiasis patients, but the serum high density lipoprotein (HDL) and low-density lipoprotein (LDL) were increased (p<0.01) when compared with controls.¹⁰ In the population-based study in China by Gabriella Andreotti et al, compared to controls (n=858), biliary stone cases (n=981) had significantly lower mean levels of total cholesterol, HDL and LDL, but a significantly higher mean level of triglycerides.¹¹

V. Conclusion

Gallstone disease is common in the age group of 31-40 years. There is a female preponderance. Cholesterol stones constitute the majority among the main two types of stones. There was a statistically significant increase in the serum total cholesterol and serum LDL levels, but no significant change in the serum triglycerides, HDL and VLDL levels in cholelithiasis patients compared to the control group. There was a significant association of cholelithiasis with high serum cholesterol (>200 mg/dl) and LDL (>130 mg/dl) levels and, but no such association was found with high serum triglycerides (≥150 mg/dl) or low serum HDL (<40 mg/dl) levels. There was no significant change in serum lipid profile of the patients with cholesterosis compared to those without. But many other risk factors, like weight, body-mass index, waist-hip ratio, socio-economic status and dietary habit were not taken into consideration in this study, which might have contributed to the differences in observation from some other related studies as mentioned. However, it can be concluded that gallstones should not only be regarded as the condition requiring cholecystectomy, but also as a marker of an underlying metabolic disorder that has to be investigated and treated accordingly. All patients who have cholelithiasis should now have a full serum lipid profile as a routine part of their clinical assessment. Considering the major role of LDL in coronary artery disease, it would be prudent to screen all patients with cholelithiasis for dyslipidaemia. This might help in instituting primary preventive measures.

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