Original Article

Cholelithiasis and its Relationship with Serum Lipids in a Tertiary Care Hospital of Rajshahi

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Abstract:

Background: Gallstone disease (GD) is one of the most prevalent gastrointestinal disease in worldwide and also in Bangladesh. High triglyceride and low HDL (high density lipoprotein) are associated with cholelithiasis whereas total cholesterol and LDL (low density lipoprotein) have less association.

Objectives: To find out the association of cholelithiasis and lipid profile.

Material and Methods: This case-control study was conducted on 300 patients in the department of surgery, Rajshahi Medical College Hospital from September, 2018 to August, 2019. Participants were divided into two groups; group A (case group- 150 patients) and group B (control group-150 patients). After overnight fasting 5 ml venous blood was collected and serum lipid profile was measured. Outcomes were expressed in the form of figures and tables.

Result: The mean age in case group were 39.79±8.16 years and in control group 38.67±7.99 years respectively with female predominance (72%) and male to female ratio was 1:2.57. out of 150 participants in case group 61% (91) had cholesterol stone. TG level was high both in cholesterol stone 57 (62.62%) and mixed stone 35 (59.32%) in case group. The mean BMI (25.73±2.10) in case group were significantly higher. Post-operative histopathology shown 2 (1.33%) patients associated with malignancy.

Conclusion: The increased lipid profile can be good indicator for gall stone diseases and female are more susceptible to form gallstone who have high cholesterol level. Obesity is a risk factor for gallstone so people should maintain an ideal body weight. Gallstones are predisposing factor for malignancy.

Introduction:

Gall stones disease (GD) or cholelithiasis is one of the most prevalent gastrointestinal diseases, with a substantial burden to health care systems.[1] In Western countries, the prevalence of gallstone disease reportedly ranges from approximately 7.9% in men to 16.6% in women. In Asians, it ranges from approximately 3% to 15%. With an overall prevalence of 10-20%, GD represents one of the most frequent and economically relevant health problems of industrialized countries.[2] The prevalence of cholesterol gallstones is increased in obese persons. The risk is especially high in those with the highest body mass index.[3] The incidence of gallstones increases with age.[4]

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Gallstones are classified into three types according to their chemical composition such as cholesterol, pigment, and mixed stones. Most Cholelithiasis are made up of cholesterol, calcium carbonate, calcium bilirubinate or a mixture of these. Cholesterol gallstones result from the secretion of bile by the liver supersaturated with cholesterol. This results in cholesterol crystallization and stone grows within the gallbladder, which can be exacerbated by gallbladder stasis. This may occur in association with obesity, high-caloric and cholesterol-rich diets, or drugs. In patients with gallstones, dietary cholesterol increases biliary cholesterol secretion.[5]

High triglycerides (TG) and low high density lipoprotein (HDL) have been most consistently associated with gallstones, whereas the associations of total cholesterol (TC) and low density lipoprotein (LDL) with gallstones are less consistent.[6] Etiology of the gallstone is probably multifactorial. The implicated factors are: metabolic, infection and bile stasis. Pathogenesis of black and pigment stone is due to hemolytic, e.g. hereditary spherocytosis, sickle cell anemia, thalassemia and malaria, in which bilirubin production is increased. Brown pigment stones occurs only in the biliary systems mainly in the intra or extra hepatic duct. Their pathogenesis may be due to stasis and infection by gram negative bacteria.[7] Elevation of serum TC, LDL cholesterol, tri-acyl glycerol and reduction of HDL cholesterol level seem to play a major contributing role in the pathogenesis of gallstones, especially in females.[8]

The aim of this study was to assess lipid profile status of cholelithiasis patient and control group.

Material and methods:
This case-control study was conducted on 300 patients in the department of surgery, Rajshahi Medical College Hospital from September, 2018 to August, 2019. Adult patient of both genders, with the diagnosis of cholelithiasis and absence of cholelithiasis based on ultrasonography were included in the study. First 150 patients with gallstone admitted for cholecystectomy formed the Group-A (i.e. case group) whereas Group-B (i.e. control group) constituted by another 150 patients without gallstone having an intact gallbladder.

Inclusion Criteria: 1) Adult patient who was diagnosed to have gallstone disease, 2) Both sexes, 3) Control was healthy volunteer from medical stuff & patient's relative who gave consent.

Exclusion Criteria: 1) Patients under 18 years, 2) Patient with gallbladder malignancy diagnosed by ultrasonography and histopathology, liver cirrhosis, cholangitis, pancreatitis. 3) Patients on current anti-cholesterol medication, 4) Hemolytic disorders e.g. sickle cell disease, hereditary spherocytosis, 5) Diabetes Mellitus, 6) pregnancy, 7) Cardiac (Myocardial infarction, CHD, Angina pectoris) and 8) Renal disease and others with serious illness.

Procedure:
On admission, 5ml of venous blood were collected after overnight fasting from all the subjects in serum separator vacutainer tubes and sent to pathology dept. of RMC for examination. The level of serum TC, LDL-C, HDL-C and TG were analyzed using an auto-analyzer. Fasting lipid profiles value more than the following considered as high; TC>200mg%, LDL>130mg%, HDL> 40mg%, TG>150mg% respectively. These data was entered into the computer using SPSS and Microsoft Excel Software. Statistical analysis was done by statistical students t-test. A 95% confidence interval was taken and p-value less than 0.05 was termed as statistically significant. Data were expressed in the form of tables and figures where feasible.

Result:
The mean age of presentation group in case group was 39.79±8.16 years and in control was 38.67±7.99 years respectively. The commonest (40%) age group is 35-45 years. In our study shown a female predominance with 72% female and 28% male with a ratio male to female was 1:2.57 in both case and control group (Table 1). Among the case group 48% patients suffering with chronic calculus cholecystitis (Figure I). Out of 150 participant in case group 61% (91) had cholesterol stone and 39% (59) had mixed stone respectively. TG level was high both in cholesterol stone 57 (62.62%) and mixed stone 35 (59.32%) in case group (Table 2). The mean BMI in case group were significantly higher than controls as these values were 25.73±2.10 and 22.38±1.82 respectively that was statistically significant. (Table 3). The serum TC, LDL-C, TG were all statistically higher and HDL-C was significantly lower in study case group than control group (Table-IV). Post-operative histopathological findings of case group shown only 2 (1.33%) patients associated with malignancy.

Table-I. *Distribution of patients according to demographic variables (n=300)*

Demographic variables	Case(150)	Control(150)	P-value
Mean age (±SD) (in years)	39.79±8.16	38.67±7.99	0.43[NS]
Sex Distribution			
M:F	1:2.57	1:2.57	
M	42 (28%)	42 (28%)	——
F	108 (72%)	108 (72%)	

P-value was calculated by student's t-test
S: Significant.
NS: Not significant.
P-value was significant at <0.05

Table-I shows that the overall demographic profile of the case and control groups where it was portrayed that the mean age of both the groups were 39.79±8.16 years and 38.67±7.99 years respectively. The male to female ratio in both the groups were same 1:2.57 as it was an age and sex matched case control study. In this study showed a female predominance with 72% female and 28% male with a ratio male to female was 1:2.57.

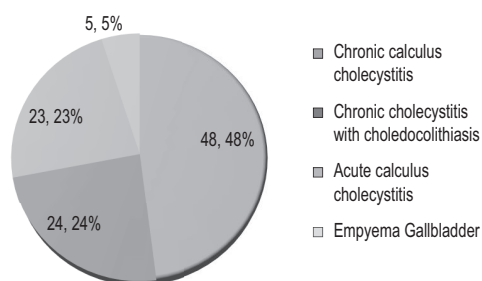**Presentation of gall stone disease of case group (n=150)**

Fig.-1: *Distribution of case according to gall stone diseases (n=150) (Ultrasonographic finding)*

Figure-1 shows that out of 150 participants in study group 48%, 24%, 23% and 5% were suffering from Chronic calculus cholecystitis, Chronic cholecystitis with choledocholithiasis, acute calculus cholecystitis and Empyema gallbladder with cholelithiasis respectively diagnosed by ultrasonography.

Table-II. *Dyslipidaemia in cases with cholesterol gallstone and mixed gallstone (n=150)*

Serum lipid parameter	Cholesterol stone 91 (61%)	Mixed stone 59 (39%)
TG	57 (62.62%)	35 (59.32%)
HDL-C	55 (60.63%)	31 (52.84%)
TC	32 (35.16%)	17 (28.81%)
LDL-C	29 (31.18%)	15 (25.42%)

Table-II shown that out of 150 participants in study case group 61% (91) had cholesterol stone among them triglyceride, HDL-C, total cholesterol, LDL-C were 63%,60%,45% and 40% respectively. Also 39% (59) had mixed stone among them triglyceride, HDL-C, total cholesterol, LDL-C were 59.32%, 52.84%, 28.81% and 25.42% respectively.

Table-III. *Distribution of participants according to BMI (n=300)*

BMI category	Case (n=150)	Control (n=150)	p-value
Underweight (<18.5)	0 (0%)	0(0%)	<0.001[S]
Normal weight (18.5-24.9)	48 (32%)	141 (94%)	
Overweight (25.0 -29.9)	67 (44.66%)	9 (6%)	
Obese (>30)	35 (23.33%)	0 (0%)	
Mean BMI ± SD	25.73±2.10	22.38±1.82	

p-value was calculated by student's t-test, S: Significant, NS: Not significant,p- value was significant at <0.05.

Table-III Shown that the mean BMI of case were significantly higher than controls as these values were 25.73±2.10 and 22.38±1.82 respectively. (p-<0.001)

Table-IV: *Distribution of participants according to mean lipid profile distribution (n=300)*

Lipid profile (Mean±SD)	Case (n=150)	Control (n=150)	P-value
TC (mg/dL)	191.78±15.66	123±10.04	<0.031[S]
HDL-C (mg/dL)	35.46±2.89	48.79±3.98	<0.049[S]
LDL-C (mg/dL)	128.13±10.48	92.35±7.54	<0.001[S]
TG (mg/dL)	146.59±11.97	137.37±11.22	<0.036[S]

p-value was calculated by student's t-test, S: Significant, NS: Not significantp-value was significant at <0.05.

Table-IV shown that the serum TC, LDL-C, TG were all statistically higher in case group than control group which was statistically significant. HDL-C was statistically lower in case of study group than control that was also statistically significant.

Discussion:

Gallstones are the most common biliary pathology. Formation of gallstone are multifactorial and complex. Biliary cholesterol supersaturation is identified as a main prerequisite for the formation of cholesterol gall stone. In our study, mean age in case group is 39.79±8.16 and in control 38.67±7.99 years respectively. The commonest (40%) age in case group is 35-45 years with female preponderance (72%) and male to female ratio was 1:2.57. Our study correlated with the studies conducted by Nagaraj SK et al. 2012, where the peak incidence age group 40-50 years and male to female ratio 1:2.57.[9] Schirmer et al. 2005, shown that peak incidence age was reproductive years and male to female ratio 1:4.[10]

Cholelithiasis was commonly diagnosed by ultrasonography. We found that out of 150 participant in case group 48%, 24%, 23% and 5.3% were suffering from chronic calculus cholecystitis, chronic cholecystitis with choledocholithiasis, acute calculus cholecystitis and Empyema gallbladder with cholelithiasis respectively. During morphological study of stone in study case group, 61% (91) had cholesterol stone; among them TG, HDL-C, TC, LDL-C were 63%,61%,35% and 31% respectively. Also 39% (59) had mixed stone; among them TG, HDL-C, TC, LDL-C were 59%, 53%, 29% and 25% respectively. Thilanka H et al. 2014, study shown that 51% participant had cholesterol stone among them triglyceride, total cholesterol, LDL-C, HDL-C were 19%, 14%,19% and 0% respectively[11].

Overweight is one of the major risk factor for cholelithiasis. In our study we found that 45% participant were overweight and 32% participant were normal weight having cholelithiasis. The mean BMI of case group than control group were higher (25.73+/-2.10 vs 22.38+/-1.82) and statistically significant (p-<0.001). Bhandari V et al (2013) study shown that mean BMI was statistically higher in case group than control group (27.5+/-0.71 vs 24.31+/-0.32 and p <0.001).[12]

In our study serum TC, TG, LDL-C were all statistically significantly higher in case group that

control group. [p =<0.031, p=,<0.036, p=<0.001] respectively. HDL-C was statistically significantly lower in case group that control group. [p=<0.049]. Bhandari V et al. 2013, study shown that TC, TG, LDL-C are statistically significantly higher in case group than control group, [p (<0.001)] and HDL-C was lower but that are not statistically significant [p -0.179][12]. Hayat S et al (2019) study shown that TC level [p=<0.625] were higher but not statistically significant, TG level [p=<0.013] were higher and statistically significant, HDL-C level [p=<0.000] were lower and statistically significant and LDL-C level [p=<0.544] in the patient was low but result were not statistically significant in comparison to control group respectively.[13] Incidental gall bladder malignancy were found in 2 (1.33%) cases. Siddiqui et al. 2013, study shown that gallbladder malignancy after histopathology 2.8%.[14]

Limitation of the study:

It was a case control study. Study was done in a single center with small sample size and short study duration.

Conclusion:

The increased lipid profile can be good indicators for gall stone diseases and female are more susceptible to form gallstone who have high cholesterol level. Obesity is a risk factor for gallstone so people should maintain an ideal body weight. Gallstones are predisposing factor for malignancy. So all specimen of gallbladder after cholecystectomy should be investigated histopatho-logically.

References:

1. Reshetnyak VI. Concept of the pathogenesis and treatment of cholelithiasis. World journal of hepatology.2012; feb 27;4(2), 18-34.

2. Sun H, Tang H, Jiang S, Zeng L, Chen E, Zhou T, Wang Y, et al. Gender and metabolic differences of gallstone diseases. World journal of gastroenterology: WJG.2009; 15: 1886.

3. Erlinger S. Gallstones in obesity and weight loss. Eur J Gastroenterol Hepatol. 2000 Dec; 12(12):1347-52.

4. Massarrat S. Prevalence of gallstone disease in Iran. J Gastroenterol Hepatol.2001;16:564-567.

5. Narjis, Hadi, Al-Saadi., Sabah, Abaas, Al-Ardhi.. Biochemical and demographical study of lipid profile in sera of patients with gallstone. Iraqi Journal of Science. 2012; 53(2), 760-768.

6. Andreotti G, Chen J, Gao YT, Rashid A, Chang SC, Shen MC, et al. Serum lipid levels and the risk of biliary tract cancers and biliary stones: A population-based study in China. Int J Cancer. 2008 May 15;122(10): 2322-9.

7. Conte D, Fraquelli M, Giuta M, & Conti C. Gallstones and liver disease: an Overview. Journal of Gastro intestine-Liver Diseases, 2011;20(1): 9-11.

8. Channa NA, Khand F, Ghanghro AB, Soomro AM. Quantitative analysis of Serum Lipid Profile in Gallstone Patients and Controls. Pak. J. Anal. Environ. Chem. 2010; 11(1):59-65.

9. Nagaraj SK, Paul P, Kumar MK, Muninarayanappa S, Anantharamaiah H. Risk Factors and the Biochemical Evaluation of Biliary Calculi in Rural Kolar District, Karnataka. Journal of Clinical and Diagnostic Research. 2012 May (Suppl-1), Vol-6(3):364-368.

10. Schirmer BD, Winters KL, Edlich RF. Cholelithiasis and cholecystitis. Journal of Long Term Effects of Medical Implants, 2005;15:329-38.

11. Thilanka H, Weerakoon W, Ranasinghe S, Navaratne A, Galketiya KB, Rasario S. Serum lipid concentration in patients with cholesterol and pigment gallstone, BMC research notes2014 7:548; doi:10.1186/1756-0500-70548.

12. Bhandari V, Gora S P, Vyas H G, Kaur C, Roy N. Evaluate the relationship of serum lipid profile, Apo-lipoprotiens, BMI, Waist-hip ratio in occurrence of cholelithiasis. IJSSS 2013; Vol1, No.2.

13. Hayat S, Hasan Z, Changaji SH, Zahra A, Noman M, Javed H, Ans AH, Abdin MZU. Comparative analysis of serum lipid profile in patients with and without gallstones. 2019.

14. Siddiqui FG, Memon AA, Abro AH, Sasoli NA, Ahmad L, Routine histopathology of gallbladder after elective cholecystectomy for gallstones. 2013.