

Study on Lipid Profile of Blood and Bile in Patients with Gall Stone Disease

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Article Received:10-07-2015

Article Accepted:12-10-2025

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ABSTRACT

Background Cholelithiasis is the commonest disease affecting the gall bladder, which is a major cause of upper abdominal emergencies. The aim of our study is to determine the levels of various lipids in serum and bile viz. cholesterol, triglycerides, HDL-cholesterol, Low Density Lipoprotein (LDL)-cholesterol, and phospholipids in patients of cholelithiasis and in control subjects and to critically analyze these estimations and to make observations as to their role in the etiopathogenesis of gallstones. **material and methods** The present randomized prospective observational study was conducted on a total of hundred cases which included half in the study group and the other half in the control group. **results** The serum cholesterol levels in study group had a mean value of 161.54mg% while the control group had 156.78mg% which was statistically not significant. Serum phospholipids levels in study group had a mean value of 166.59mg% while it was found to be 121.06mg% in control group. **Conclusion** the plasma triglyceride value may possibly be a biological marker of susceptibility to gallstone disease. Among those prone to stone formation, increased exposure to a causal factor such as diet or oral contraceptive, may result in a raised plasma triglyceride concentration together with formation of gallstones early in life.

Keywords: Lipid Profile, Gallstone Disease, Blood and Bile

INTRODUCTION

Cholelithiasis is the commonest disease affecting the gall bladder, which is a major cause of upper abdominal emergencies^{1,2}. Various constituents of gall stones include cholesterol, bilirubin, calcium, triglycerides, fatty acids, phospholipids and proteins^{3,4}. These stones may be classified as cholesterol, pigment and mixed stones⁵ of which mixed stones constitute the majority and pure cholesterol stones being a rarity⁶. Researchers have tried to understand the pathogenesis of stone formation. Super saturation and concentration of bile, crystal nucleation and gall bladder dysmotility have been implicated as aetiological factors⁷. Supersaturation of bile with cholesterol is found to be the most significant factor for formation of cholesterol stones^{8,9}.

Hyperlipidemia may lead to cholesterol hypersecretion in biliary canaliculi. Relatively higher levels of cholesterol and reduced phospholipids as well as bile acids leads to nucleation of cholesterol crystals causing cholesterol stone formation¹⁰. However, high unconjugated bilirubin levels in bile is a pre-requisite for pigment stone formation¹¹.

Altered lipid metabolism with more secretion of cholesterol into bile by liver generally is considered as the pathological cause for cholesterol stones¹². Various situations like female gender, oestrogen therapy, hypertriglyceridemia, obesity, diabetes, excess fat diet and genetic causes have found to be having close relation with cholesterol stone formation^{12,13,14}. Moreover, high levels of triglycerides (TGs) and low levels of high density lipoproteins (HDL) have been found to be consistently associated with gall stones¹⁵.

Thus, the aim of our study is to determine the levels of various lipids in serum and bile viz. cholesterol, triglycerides, HDL-cholesterol, Low Density Lipoprotein (LDL)-cholesterol, and phospholipids in patients of cholelithiasis and in control subjects and to critically analyze these estimations and to make observations as to their role in the etiopathogenesis of gallstones.

MATERIAL AND METHODS

The present randomized prospective observational study was conducted on a total of hundred cases which included half in the study group and the other half in the control group. The sample size was calculated in consultation with the statistician to keep power of the study more than 85%.

The study group comprised of 50 adult patients of acute and/or chronic cholecystitis and cholelithiasis diagnosed on the basis of clinical picture supported by ultrasonography study. These patients were undertaken for cholecystectomy. The

control group comprised of 50 adult patients who underwent laparotomy for diseases other than hepatobiliary disorders. These patients were included in the control group after gall stones were ruled out clinically and on ultrasound examination.

In all the cases detailed clinical history was taken and physical examination was recorded on a proforma specially prepared for this study.

Patients with obesity due to excessive intake of fats, diabetes mellitus, excessive alcohol consumption and women using oral contraceptive pills were excluded from the study as these factors alter lipid metabolism.

Serum Lipidogram consisted of the following:

S. Cholesterol

S. Phospholipids

S. HDL Cholesterol

S. LDL Cholesterol

S. Triglycerides

Biliary Lipidogram comprised of the following evaluation

Biliary Cholesterol Biliary Phospholipids Biliary HDL

Biliary LDL

Biliary Triglycerides

These biochemical estimations were done using Bayer Technicon RA-XT autoanalyser in the Biochemistry laboratory. The observations were recorded in the proforma and results were statistically analysed using SPSS 22.0 software keeping a p value of < 0.05 to be significant.

Observations and Results Table 1 Serum Lipid Levels

Serum Lipids	Study group	Control group	p- value
S. Cholesterol	161.54+ 47.5	156+-179.36	>0.10 (NS)
Phospholipids	166.59+71.17	121.06+36.72	<0.01(S)
HDL	40.18+12.85	31.5+13.5	>0.01(NS)
LDL	100.80+38.29	66.13+68.67	<0.001(S)
TGs	134.98+65.68	96.64+68.29	<0.01(S)

Table 2 Biliary Lipid Levels

Biliary lipid levels	Study group	Control group	p-value
Cholesterol	349.42+174.60	178.16+136.94	<0.01 (S)
Phospholipids	1819.15+1040.10	1753.84+1427.55	>0.10(S)
HDL	182.80+111.15	43.06+15.25	<0.01(S)
LDL	129.58+103.68	63.46+103.68	<0.01(S)
TGs	179.40+142.22	327.20+295.55	<0.01(S)

Table 3 Serum and Biliary Lipids in Study Group

Lipid values	Serum	Bile	p-value
Cholesterol	161.54+47.51	349.42+174.60	<0.01(S)
Phospholipids	166.59+71.17	1819.15+1040.10	<0.001(S)
HDL	40.18+12.85	182.80+111.15	<0.001(S)
LDL	100.80+38.29	129.58+103.68	>0.10(NS)
TGs	134.98+65.68	179.40+141.42	<0.10(S)

Table 4: Serum and Biliary Lipids in Control Group

Lipid values	Serum	Bile	p-value
Cholesterol	156.78+179.36	178.16+136.44	>0.10(NS)
Phospholipids	121.06+36.72	1753.84+1427.55	=0.001(S)
HDL	31.5+13.51	43.06+15.25	>0.10(NS)
LDL	66.13+68.67	63.46+64.67	>0.01(NS)
TGs	96.64+68.29	327.20+295.55	<0.01(S)

The demographic profile in our study in both the groups (study as well as control) were similar and no statistical significance was found in the two groups in terms of age and sex distribution. The study included patients with ages

ranging from 26-72 years of age. In the study group, 23 patients (46%) were in the age range of 25-44 years, 21 patients (42%) were in the age range of 45-64 years, only 6 patients (12%) were 65 years and above. A large majority of patients 26 out of 50 (52%) in the control group were in the age range of 25-44 years, 18 patients (36%) fell in the age range of 45-65 years and 5 patients (10%) were 65 years and above. Majority of patients in the study group as well as the control group comprised of females, 34 patients (68%) in study group and 35 patients (71.4%) in the control group respectively. On recording the serum lipid values in the two groups, the serum cholesterol was found to be comparable and no statistical difference was found between the two groups. (p-value>0.01). The serum phospholipids were found to be significantly higher in the study group as compared with the control group (p-value< 0.01). However, the HDL levels in the serum were found to be comparable and had no statistical difference in the study and the control group. (p-value >0.01). On recording the serum LDL and TGs levels, the result values were found to be significantly higher in the study group. (p values

<0.001 and <0.01 respectively).(Table 1)

The biliary lipid profile was noted and the levels of biliary cholesterol, phospholipids, HDL, LDL were recorded and statistically analysed. The levels of biliary cholesterol, phospholipids, HDL, LDL and TGs were found to be significantly higher in the study group in comparison to the control group with no hepatobiliary disease. (p- values<0.01). However, the levels of phospholipids in the bile were found to be comparable in both the groups. (p-value>0.01). (Table 2)

On comparing the serum lipidogram with the biliary lipid levels the values were found to be statistically significant for phospholipids levels and triglyceride levels in the sera and bile. The remaining parameters were found to be comparable on statistical analysis.

DISCUSSION

This study describes the levels of serum and biliary lipids in patients having acute or chronic cholecystectomy as compared to those who underwent the abdominal surgeries due to causes other than hepatobiliary.

The age of the patients ranged from 26 to 75 years, with 23 patients in study group (46%) having ages ranging from 25 to 44 years. The control group had 52% patients in comparable age range (26 patients). In 45-64 age group, 21 patients (42%) belonged to study group. Only 6 patients (12%) in study group were beyond 65 years of age. This is in concordance with study by Ahi et al in April 2017 who have found this disease to be having maximum incidence between 31- 40 years⁶.

Majority of the patients in the study as well as control groups comprised of females (68% and 71.4% respectively). The preponderance of gall stone disease in female gender has been well documented in literature. Role of estrogens in formation of gall stones has been experimentally proved by Scragget al¹⁶ (ref from thesis).

Progesterone too appears to promote production of saturated bile by causing smooth muscle relaxation and impaired gall bladder emptying. Singletary et al have demonstrated presence of estrogen and progesterone receptors in human gall bladder (ref from thesis). Studies by Pradhan et al , Jindal et al and Gaharwar et al also echo similar results as in our study with respect to sex distribution^{17,18,19}.

The serum cholesterol levels in study group had a mean value of 161.54mg% while the control group had 156.78mg% which was statistically not significant. However, difference in levels of biliary cholesterol between the two groups showed statistically significant favour toward the study group, with levels of 349.42mg% as compared to 178.16mg% in control group. Alkatean MAG et al and Nilsell et al have reported high levels of blood

as well as biliary cholesterol in cases of gall stones^{20,21}. Channe N.A. et al²², Jindal et al¹⁸ and Pettite BD et al²³ (20 of B) also found high total serum cholesterol levels in cholelithiasis cases. Channe N.A. et al, in their research showed that there is increase in steroid synthesis due to free cholesterol, which leads to low production of bile acids and is responsible for supersaturation of bile with cholesterol. Jaraari et al and Shiina et al also showed significant rise in serum cholesterol levels in gall stone patients. On the contrary, Perrson et al(thesis), found decreased levels of serum cholesterol in women with cholelithiasis^{24,25,26}.

In our study, biliary cholesterol was found to be significantly higher than serum cholesterol. These finding coincide with findings of Rubin et al , who concluded that high biliary cholesterol causes lithogenic changes in bile composition, thus leading to sludge formation and cholelithiasis²⁷. Similarly, Cooper et al, Janowitz et al, Helpean et al, Kern et al and Gustafsson et al concluded that high biliary levels lead to shorter nucleation time, presence of crystals in bile and increased gall stone formation.^{28,29,30,31,32}.

Serum phospholipids levels in study group had a mean value of 166.59mg% while it was found to be 121.06mg% in control group. This difference was found to be statistically significant. However, differences in biliary phospholipid levels in both groups was not found to be statistically significant.

Tandon et al in their study found high serum phospholipid levels in gall stone patients⁹. Studies by Harpern et al as well as Jungst et al (2001) also echoed similar results. Jungst et al emphasized the role of phospholipids in viscosity of gall bladder bile^{33,34}.

Mean serum HDL cholesterol levels in our study group was 40.18mg% and 31.5mg% in control group. This difference was statistically non significant. Biliary HDL levels in study group and control group was found to be 182.80mg% and

43.06mg% respectively (statistically significant). Petitti et al pointed at the relation between low HDL levels and gall stones disease²³ (thesis ref).

Thornton et al stated that HDL levels are inversely proportional to bile cholesterol saturation³⁵. Scragg et al studied that HDL may be inhibiting liver cholesterol synthesis¹⁶ (THESIS REF). Scrobry et al concluded in their study that high serum HDL levels leads to enhanced cholesterol delivery to liver(thesis ref)³⁶. Janowitz et al reported a positive correlation between total bile acids and serum HDL levels in patients with rapid nucleation time²⁹. Recently some authors like Rasheed et al (2014) have reported low HDL levels in the patients with gall stones³⁷. On the contrary, Rao et al in 2012, have reported high serum HDL levels to be associated with gall stones¹².

Statistically significant serum HDL levels were observed in our study group mean value 100.80 mg% and 66.13% in the control group. Similarly, the mean biliary LDL levels were also significantly higher in the study group (129.5 mg%) as compared to the control group (63.46%). Pettiti et al have linked high LDL cholesterol levels with gall stone disease (thesis ref)²³. Halpern et al and kern et al also found similar results^{30,31}.

Shiina et al (2011) reveal significant rise in cholesterol, LDL and triglyceride levels in patients with cardiac disease who developed gall stones after cardiac surgery. Ahi et al (2017) also found similar results with respect to LDL cholesterol(ref B)^{6,25}

Biliary LDL levels did not show statistically significant correlation with serum LDL levels in both study and control groups in our study. Cooper et al, Rubin et al and Gustaffson et al found higher biliary LDL levels in patients having cholelithiasis, which are in concordance with our study results^{27,28,32}.

Mean triglycerides levels in serum in our study group was 134.98mg% in comparison to 96.64in control group. Similarly, biliary triglyceride levels in study group averaged at 179.40mg% and in control group were 327.20mg%. These values were found to be statistically significant. These findings are in concordance with existing

literature which reveals that high plasma triglycerides are associated with gall stone formation independent of obesity. Scragg et al, Petit et al and Harper et al echo observations similar to those in our study^{16,23,33}. Weerakoon et al showed high serum triglyceride levels in every young patient with cholesterol gall stone as compared to pigment gall stones³⁷. Swelt et al also showed similar results¹³.

High serum triglyceride levels are also revealed by other case control studies^{37,38,39}. Hypertriglyceridemia has been found to cause hypomotility of gall bladder by lowering its sensitivity to cytokines. This may lead to cholesterol crystallization, thus forming cholesterol stones.However, author like Olokoba et al have found no association of serum triglyceride with gall stones

CONCLUSION

According to our opinion, the plasma triglyceride value may possibly be a biological marker of susceptibility to gallstone disease. Among those prone to stone formation, increased exposure to a causal factor such as diet or oral contraceptive, may result in a raised plasma triglyceride concentration together with formation of gallstones early in life.

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