

ANALYSIS OF SERUM LIPID PROFILE IN CHOLELITHIASIS PATIENTS

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ABSTRACT: This study was conducted to find the effect of Cholelithiasis on the lipid profile. Seventy blood samples of Cholelithiasis patients were collected from Lahore General Hospital, Mayo Hospital Lahore and Govt. Kot Khawaja Saeed Teaching Hospital, Lahore and thirty blood samples of control subjects were collected from different areas of the Lahore. All samples were tested by Enzymatic Photometric Assay Technique to estimate the levels of plasma cholesterol, triglyceride, HDL, LDL, VLDL and total lipid in the blood. It was found that the level of cholesterol, triglyceride, LDL, VLDL and total lipid were significantly higher as compared to control subjects. While level of HDL was significantly lower as compared to control subjects. Results were discussed in the light of previous reports of different population. These results suggested that the higher level of cholesterol, triglyceride, LDL, VLDL, total lipid and lower level of HDL in Cholelithiasis patients may leads to many heart diseases including atherosclerosis with significant systematic impact.

Key Words: Lipid profile, Cholelithiasis

INTRODUCTION

Cholelithiasis is a common gastrointestinal (GI) disorder characterized by the accumulation of hardened bile constituents, leading to further complications [1]. Cholesterol cholelithiasis is increasing in children and adolescents day by day [2]. Cholelithiasis is becoming highly prevalent in western countries [3]. In American Indians 60-70% cholelithiasis spread epidemically. A decrease had been observed in Hispanics of mixed Indian origin and in developed countries [4]. Increasing age, female gender, obesity and metabolic syndrome have all been associated with an increased risk of cholesterol gallstones [5]. Other risk factor for cholesterol gallstones are the diabetes, estrogen, oral contraceptive pills and family history [6].

In the formation of gallstones, serum lipids play very important role. Especially in the formation of cholesterol gallstones, the serum lipids become altered. Some previous studies showed a significant increase in serum TC, TG, LDL-C, VLDL-C and a significant decrease in serum HDL-C in gallstone patients compared to the apparently healthy controls [7, 8, 9, 10, 11]. These changes in the levels of lipid profile may be used as markers for gallstone formation [12].

However, some other studies showed a significant elevation in serum HDL in cholelithiasis patients when compared with controls unlike in other studies [13,14]. It has also been demonstrated that low serum HDL levels do not seem to affect the occurrence of gallbladder stones. The relationship between cholesterol, LDL, and HDL levels and cholesterol gallstone formation is multifactorial and complex and is also dependent on other individual properties [15].

These different results in the different populations of the world compel us to study the alteration in the normal values of lipid profile in cholelithiasis patients as compare to control subjects in ours local population.

MATERIALS AND METHODS

Clinical facility for the present investigation to diagnose the association between lipid profile and cholelithiasis was available at Lahore General Hospital (LGH), Mayo Hospital Lahore and Govt. Kot Khawaja Saeed Teaching Hospital, Lahore. Cholelithiasis patients with changed lipid profile were admitted in surgical ward of Mayo Hospital and pathology section of Govt. Kot Khawaja Saeed Hospital.

Study was designed as a prospective based clinical trial. Patients with cholelithiasis were already diagnosed by hepatology on the basis of ELISA, PCR, Screening and Biopsy. The clinical history and other details of patients were obtained from the above mentioned hospitals of Lahore. Blood samples of cholelithiasis patients were collected in fasting state from surgical ward of LGH, Mayo hospital and pathology section of Govt. Kot Khawaja Saeed hospital, Lahore. Blood samples of controls subjects were also collected in fasting state from the different areas of the Lahore city.

The study was based on 30 control subjects, 70 patients with Cholelithiasis belonging to different age groups. Blood samples were taken in fasting of each of the control subjects and cholelithiasis patients. The lipid profiles of patients were compared with control subjects to find out the association between lipid profile and gallstone infection.

Blood samples were collected and for 20-25 minutes allow, to clot at room temperature and centrifuge for 2 minutes for the separation of serum. The speed of centrifuge machine was 40 rotations per minute (rpm). The serum was floated on top of the blood clot. A dropper was placed in the tube and the serum was sucked and added to the labeled tubes.

Lipid profile was determined by commercially available kit (Spectrum Egyptian Company for Biotechnology S.A.E) employing the Direct Enzymatic colorimetric, Liquid method. Experimental data were analyzed by student t-test.

RESULTS

Thirty control subjects and seventy cholelithiasis patients were involved in the study. The average age among the different groups was 38.93 ± 2.06 and 45.55 ± 3.63 years for control subjects and cholelithiasis patients respectively (Table 1). Table 1 shows the mean values with the standard error of various lipid fractions of cholelithiasis patients and controls subjects. The mean serum HDL-C level of cholelithiasis patients was lowered as compared to control subjects (53.44 vs 56.37, $P > 0.05$). The mean serum LDL-C level in cholelithiasis patients was higher as compared to control subjects (122.33 vs 83.74, $P < 0.001$). The mean Total Lipids level in cholelithiasis patients was higher as compared to control subjects (817.81 vs 608.96, $P < 0.001$). Mean serum Cholesterol level in cholelithiasis patients was higher as

compared to control subjects (220.74 vs 168.26, $P < 0.001$). Mean serum Triglycerides level in cholelithiasis patients was higher as compared to control subjects (224.04 vs 140.80, $P < 0.001$). The mean serum VLDL-C level in cholelithiasis patients was higher as compared to control subjects (35.94 vs 23.30, $P < 0.001$).

Table 1. Comparison of lipid levels of cholelithiasis patients and control subjects.

Lipids	Cholelithiasis Patients	Control Subjects	P value
HDL-C	53.44 ± 2.99	56.37 ± 2.35	> 0.05
LDL-C	122.33 ± 6.65	83.74 ± 5.34	< 0.001
Total Lipid	817.81 ± 20.99	608.96 ± 19.97	< 0.001
Cholesterol	220.74 ± 6.51	168.26 ± 5.39	< 0.001
Triglyceride	224.04 ± 14.15	140.80 ± 11.24	< 0.001
VLDL-C	35.94 ± 2.25	23.30 ± 1.66	< 0.001

DISCUSSION

The present study was conducted to check the complete lipid profile (HDL-C, LDL-C, Total Lipids, VLDL-C, Triglycerides and Cholesterol) in Cholelithiasis patients and their comparison with control subjects.

Our results showed that serum HDL-C level in Cholelithiasis patients was non-significantly lower as compare to control subjects. These results are comparable with some previous studies. Many researchers in their studies described lower levels of HDL-C in Cholelithiasis patients as compare to control subjects of Iraqi population [9], in Guntur, Andhra Pradesh, Indian population [16], in Sudanese population [17] and in Najaf, Iraqi population [18]. In addition, there was a significant increase in HDL-C ($P=0.001$) in cholelithiasis patients as compared to control subjects in Middle East population [13]. In contrast, some of the researchers have described high levels of HDL-C in Cholelithiasis patients such as 41.78 ± 2.11 mg/dl in Cholelithiasis patients before cholecystectomy, 170.57 ± 9.28 mg/dl in Cholelithiasis patients during cholecystectomy and 47.40 ± 3.17 mg/dl in control subjects in Bangladeshi population. In this respect, their findings of lower HDL-C level in pre-cholecystectomy serum but not significantly higher in post-cholecystectomy serum and significantly very high HDL-C level in during cholecystectomy bile are of considerable interest. Possibly, high levels of HDL-C in post-cholecystectomy serum and during cholecystectomy bile may have protective role in gall bladder against cholelithiasis [19].

Many researchers found that low serum HDL-C levels do not seem to affect the occurrence of gallbladder cholesterol stones (60.0% vs. 58.3%, respectively, $P > 0.05$) or gallbladder stone cholesterol concentrations (50.8% vs. 52.4%, respectively, $P > 0.05$). Also the relationship between HDL-C level and cholesterol gallstone formation is multifactorial and complex and is also dependent on other individual properties [15]. HDL-C was lower in carriers of the common alleles for *ABCG5/ABCG8* than in carriers of the rare alleles [20].

Our results showed that serum LDL-C level in Cholelithiasis patients was significantly higher compared to control

subjects. These results are comparable with some previous studies. Many researchers in their studies described higher levels of LDL-C in cholelithiasis patients as compared to control subjects in Iraqi population [9,12], in Guntur, Andhra Pradesh, Indian population [16], in Bangladeshi patients [19] and in Indian population [10].

Gall Stone Disease (GSD) is associated with abnormal lipid profile [10]. A high serum LDL-C level was described as a marker for increased risk of cholesterol gallstone disease [21]. High serum LDL-C level was associated with high cholesterol stone rates (75.0% vs 48.9%, $P < 0.05$). Similarly, high serum LDL-C level was correlated with high gallbladder stone cholesterol concentrations (62.3% vs 46.0%, $P < 0.001$) [15].

The higher levels seen before cholecystectomy may be due to abnormal secretory function [22] or down-regulation of LDL-ApoB receptors by inhibition of LDL-ApoB receptor gene expression [23] or prolonged high fatty diet [22]. Furthermore, the gradual increase in lipoprotein lipase activity and hepatic lipase activity in gall stone patients may be considered [24].

Patients with the $X^{+/-}$ genotype had a significantly higher concentration of LDL-C and *apo B* in serum than patients with the $X^{-/-}$ genotype. The X^{+} allele of the *apo B* gene is characterized by a higher LDL-C concentration in serum, and it may be a marker for increased risk of cholesterol gallstone disease [25].

Our results showed that Total Lipids level in Cholelithiasis patients was significantly higher in Cholelithiasis patients as compared to control subjects. These results are comparable with previous studies which showed higher level of Total Lipids in Cholelithiasis patients as compared to control subjects in Indian population [26].

It is observed that GSD is associated with abnormal lipid profile [10]. Regulation of lipid metabolism and energy homeostasis is complex and the GB has been considered to have a minor regulatory role in both the intestinal absorption of lipids and metabolic homeostasis of the whole body [27].

Several studies have indicated the hypothesis that insulin plays a significant role in the enterohepatic circulation of lipids. The two more common abnormalities of biliary lipid metabolism that induce CH supersaturated bile in CH GBD are increased biliary CH secretion and decreased BS pool and biliary secretion rate [28,29].

Our results showed that serum total Cholesterol in Cholelithiasis patients was significantly higher as compare to control subjects. These results are comparable with some previous studies. Many researchers in their studies described higher levels of cholesterol in Cholelithiasis patients as compare to control subjects in Iraqi population [9,12], in Bangladeshi population [19], in Indian population [10], Najaf, Iraqi population [18] and in North Indian population [30].

Polymorphisms in *ABCG5/ABCG8* genes might contribute to the genetic variation in plasma lipid levels and in cholesterol saturation of the bile [20].

Changes in the concentration of one of the key promoters of crystallization, mucus glycoprotein, are mediated by mucosal prostaglandins (PGs). Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) prevent microcrystal and gallstone formation by decreasing PG synthesis. Gallbladder motor dysfunction and stasis also contribute to gallstone formation [31].

Previous results showed that free cholesterol increases steroid synthesis, which in turn decreases the production of bile acids, is responsible for the precipitation of cholesterol in bile, which is a prerequisite for gallstone formation [32]. Super saturation of cholesterol is believed to be due to abnormal production of bile from liver. The concept of cholesterol super saturation as a basis for gallstone formation has been emphasized for cholesterol stones, which are composed of mainly cholesterol [33].

The result of our tests revealed that serum Triglyceride level in Cholelithiasis patients was significantly higher as compared to control subjects. These results are in line with some previous studies. Many researchers in their studies described higher levels of triglycerides in Cholelithiasis patients as compared to control subjects in Bangladeshi population [19], in Iraqi population [9,12], in Indian population [10] and in Guntur, Andhra Pradesh, Indian population [16].

The higher concentrations of TG seen before cholecystectomy may be due to abnormal secretory mechanisms [34] or signs of metabolic syndrome [29]. Triglyceride levels were higher in carriers of the common alleles for *ABCG5* Q604E and *ABCG8* D19H sequence variants [20].

Some evidence suggests that high levels of triglycerides may impair the emptying actions of the gallbladder. The mechanisms by which cholesterol stones form is not fully understood, but are likely as the result of a complex alteration in hepatobiliary function [35].

Our results also showed that serum VLDL-C in Cholelithiasis patients was significantly higher as compare to control subjects. These results are comparable with other previous studies. Many researchers in their studies described higher levels of VLDL-C in cholelithiasis patients as compare to control subjects in Iraqi population [9,18], in Indian population [36] and in Meerut, Indian population [37].

The series of studies in humans showing increased serum VLDL-apoB and serum TG concentrations after ablation of the GB, suggest that cholecystectomy and GB disease may impact negatively on the metabolic homeostasis of the whole body [27].

CONCLUSION:

Lipid profile may be helpful in the diagnosis of Cholelithiasis infection and severity of the disease. Therefore it must be analyzed in all Cholelithiasis patients. However, further studies are required to find out the other parameters as well for its diagnosis and severity of the infection.

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