Original Research Article

Evaluation of the abnormalities of lipid profile in patients with cholelithiasis

ABSTARCT

Objective: Cholelithiasis is a chronic recurrent illness that affects the hepatobiliary system. Gall stone formation is caused by the impaired metabolism of cholesterol, bile acids and bilirubin. Hence, the aim of this study was to compare the serum lipid parameters of gallstone patients with the control group.

Methodology: This was a Case control study conducted in surgical department of Sindh Government Hospital Korangi 5by using convenient sampling technique. The duration of the study was about 06 months. A total of 54 patients aged above 15 years of both the genders wherein 28 patients diagnosed with Gallstone disease were considered as case group and 29 patients with no history of gallstones as controls were included in the study. Demographic characteristics such as age, gender and Continuous variables such as lipid parameters (HDL, VDL, VLDL, Triglycerides, Cholestrol) were documented as frequencies and percentages. Student's t-test was used to compare the data between the cases and the control groups.

Results: The study results showed that out of 54 patients, 44(81.5%) were female and 10(18.5%) were male. Lipid profile of the cases and controls revealed that serum low density lipoprotein was significantly higher (p=0.014) in control group 17(31.5%) as compared to cases 8(14.8%). most of the patients of case group 26(48.1%) had serum HDL levels between 35-45 mg/dl as compared to the controls 8(14.8%) with a statistically significant difference between them (p=0.001). Moreover, higher serum triglyceride levels > 200 mg/dl observed in 1(1.9%) patients in case group and 7 (13.0%) in controls with statistically significant difference between them (p=0.006)

Conclusion: This study concluded that serum low levels of high density lipoprotein were statistically significant in the cases as compared to the control group. Furthermore, triglyceride levels and low density lipoprotein levels were significantly raised in the control group as compared to cases.

INTRODUCTION

Gallstone disease (GSD)is a frequently observed disease of the gastrointestinal tract with10%–15% occurrencerate and a frequency of 1.4% annually in the adult populace of developed nations [1,2].Gallstones are categorized into three major types: pigment, cholesterol, and mixed gallstones. Cholesterol gallstones are composed of 51%–99% of pure cholesterol. Mixed gallstones contain cholesterol in addition to bile acids, calcium salts, phospholipids and bile pigments. Approximately 70–80% cases have mixed gallstones [3]. In addition to, about 75%–80% of cases in Western countries contain cholesterol gallstones [4].

It is evidently stated that multiple risk factors are involved in the development of GSD [5] that are aging, gender, nutritional status, low fiber ingestion, high calorie intake, highly refined carbohydrates, raised level of triglycerides in blood, physical immobility, pregnancy, parity, heaviness and obesity [6,7].Additionally, it was predicted by one research that in generalincidence of gallstone in patients was about 2.4%. The possibility of gallstone formation was 2.60 folds greater in 45 years and above 45 years of age people [8]. It is stated that females indicated highincidence of asymptomatic cholelithiasis in age < 40 years as compared to males (2.7% against 1.9%)[9]. A mnemonic for remembering the risk factors related to gallstones is female, fat, fertile and forty. Furthermore, those femalesare more prone to develop gallstones that intake oral contraceptive pills, multiparous women having 3 or more children or experienced full term pregnancies.[10]

The process ofgall stone formation involves complex mechanism. Most important factors that direct the stone formation includes concentration of secreted bile within the gall bladder, Nucleation of triglyceride crystals, and incompleteemptying of gall bladder [11].Most fundamental factor in the formation of gallstone is increase concentration of cholesterol in the bile which is insoluble in water and secreted from the canalicular membrane in unilamellar phospholipid vesicle. Bile salts and phospholipids, mainly phosphatidylcholine in the bile are

essential for the cholesterol solubility.[12] Excessive cholesterol or decreasedphospholipids and/or bile acid leads to form multi lamellar vesicles resulting a nucleation of the cholesterol crystals that causes stone formation. The secretion of cholesterol supersaturated bile promoting a formation of stone by reducingphospholipids, gallbladder immobility, deferredtransit times of large intestine that supports the re-absorption of deoxy-cholic acid and the ileum resection (lessen the acid pool), have all been connected in the gallstone formation [13].

Generally, hyperlipidemia is recognized by high serum total cholesterol, triglycerides, low density lipoproteins (LDL), and low high-density lipoprotein (HDL) levels. It is thought to be controversial that lipid abnormalities are related to cholelithiasis. Few researches revealed a existence of significant association between hyperlipidemias and gallstones particularlyin an increased LDL and triglyceride levels[14,15] whereassome studies reported an insignificant association between hyperlipidemias and cholelithiasis [1,16,17].

It is believed that conflicting data exists regarding association of cholesterol serum levels, triglycerides, being overweight, serum glucose levels and nutritional status with gallstone. One research demonstrated that raised TG levels, duration of obesity, reduce physical exercise can cause gallstone diseases [18]. Similarly, one research demonstrated that vegetables and fruits consumption reduce the probability of formation of gallstone on the other hand, ingestion of fried and spicy foods significantly enhance the chances of gallstone formation [5]. In contrast to some studies, a non-vegetarian or vegetarian diet, fruit consumption, lack of physical activity, HDL cholesterol, triglyceride levels and body mass index were not recognized as a remarkable cause for the occurrence of gallstone formation [19].Multiple factors are involved in between formation of gallstone and blood cholesterol levels. Despite the fact that thefunction of blood cholesterol levels in the progression of symptomatic GSD is still not well recognized. It was evidently proved by meta-analysis studies and systemic review that vegetarian diets efficiently lowers the concentration of total cholesterol (TCH), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol in blood [20-22].

There is a scarcity of literature in Pakistan regarding incidence of gallstones and its association with blood cholesterol level. Since the evaluation of risk factors can assist in directing remedial and preventive approaches.Therefore, the aim of this study was to compare the lipid abnormalities in the patients presenting with gallstones with the controls.

METHODOLOGY

This was a Case control study conducted in surgical department of Sindh Government Hospital Korangi 5after taking approval from Ethical review committeeof Hospital, by using convenient sampling technique. The duration of the study was about 06 months.A total of 54 patients aged above 15 years of both the genders wherein 28 patients diagnosed with Gallstone disease were considered as case group and 29 patients with no history of gallstones were recruited as control group admitted through surgical OPD, Emergency or referred from other OPDs were included in the study whereas patients with terminal ileal resection, known severe coronary artery disease, hemolytic diseases (hereditary spherocytosis, sickle cell anemia on history and CBC film), liver cirrhosis (on abdominal ultrasound) and patients on antihyperlipidemic or hypolipidemic drugs were excluded from the study.

Every patient gave written consent in order to participate in this study. Blood samples drawn from the cases and controls that were analyzed for serum triglycerides, cholesterol, LDL and HDL levels. Gallstone was identified on Trans-abdominal ultrasound 3.5mHz in a fasting status. Proforma is used to record all the findings. Fasting lipid profile was measured following all night fasting in hospital laboratory by using CHOP PAP for cholesterol and Triglyceride along with lipid clearing factor for HDL,VDL and VLDL by same technologist.

Data was entered and statistically analyzed by using SPSS software, version 20. Ages of cases and controls were expressed as mean with standard deviation. Demographic characteristics such as age, gender and Continuous variables such as lipid parameters (HDL, VDL, VLDL, Triglycerides, Cholestrol) were documented as frequencies and percentages. Student's t-test was used to compare the data between the cases and the control groups. P value less than 0.05 was considered as statistically significant.

RESULTS

A total of 54 patients were recruited in the study, out of which 28 were cases and 27 were controls. The mean age of the patients was 35.49 years and that of controls was 34.56 years. In the study, 44(81.5%) were females and 10(18.5%) were males. Most of the patients 23(42.6%) were had aged 25-35 years and 19(35.2%) were had aged 35-45 years, as shown in Table I.

Lipid profile of the cases and controls revealed that serum low density lipoprotein was significantly higher (p=0.014) in control group 17(31.5%) as compared to cases 8(14.8%). The study evinced that the most of the patients of case group 26(48.1%) had serum HDL levels between 35-45 mg/dl as compared to the controls 8(14.8%) with a statistically significant difference between them (p=0.001). Furthermore, it was observed that serum Very Low density lipoprotein levels were high in the case group 21(38.9%) as compared to the controls 17(31.5%) but the comparison was not statistically significant (p=0.186). Additionally, serum cholesterol levels were high in 12(22.2%) patients in case group and 18(33.3%) in controls but with a statistically insignificant comparison (p=0.085). Moreover, higher serum triglyceride levels > 200 mg/dl observed in 1(1.9%) patients in case group and 7 (13.0%) in controls with statistically significant difference between them (p=0.006), as shown in Table II.

Table I: Demographic characteristics of patients. (n=54)

Variables		Frequency (n)	(%)
Gender	**Male**	44	(81.5%)
	Female	10	(18.5%)
Age (years)	**15-25**	4	(7.4%)
	25-35	23	(42.6%)
	35-45	19	(35.2%)
	45-55	6	(11.1%)
	55-65	2	(3.7%)

Mean age	Controls	34.56
	Cases	35.49

Table II: Association of lipid parameters with cases and controls.

Variables		Total n (%)=54	cases n (%)	controls n (%)	p-value
Low density lipoprotein (LDL)	< 145	29(53.7%)	19(35.2%)	10(18.5%)	0.014
	> 145	25(46.3%)	8(14.8%)	17(31.5%)	
High density lipoprotein (HDL)	<35	12(22.2%)	0(0%)	12(22.2%)	0.001
	35-45	34(63.0%)	26(48.1%)	8(14.8%)	
	45-65	7(13.0%)	1(1.9%)	6(11.1%)	
	>65	1(1.9%)	0(0%)	1(1.9%)	
Very Low density lipoprotein (VLDL)	< 45	16(29.6%)	6(11.1%)	10(18.5%)	0.186
	> 45	38(70.4%)	21(38.9%)	17(31.5%)	
Cholesterol	< 200	24(44.4%)	15(27.8%)	9(16.7%)	0.085
	> 200	30(55.6%)	12(22.2%)	18(33.3%)	
Triglycerides	< 150	29(53.7%)	20(37%)	9(16.7%)	0.006
	150-200	17(31.5%)	6(11.1%)	11(20.4%)	
	>200	8(14.8%)	1(1.9%)	7 (13.0%)	

DISCUSSION

Gallstone diseases is a chronic recurrent disease that affects the hepatobiliary system characterized by the impaired cholesterol, bilirubin and bile acids metabolism resulting a gallstones formation in the hepatic bile duct, common bile duct, or within the gallbladder.[23] This study demonstrated the lipid abnormalities caused by the presence of gall stones.

One cross-sectional prospective analysis compared the abnormalities in gall stone patients with controls. In their study, the reported mean age of the patients was 40.90 years and that of controls was 34.74 years. Out of them, 46 females included in cases and 44 females werein controls. There was statistically insignificant difference was observed in higher serum cholesterol levels between cases and controls. On the other hand, higher serum triglyceride levels were observed in the patients than the controls with a statistically significant difference between them. Furthermore, lower levels of serum HDL and LDL were found in cases as compared to the controls with a statistically significant association between them.[24] The present study was in accordance with the above mentioned research and revealed that the mean age of cases was reported 35.49 years and that of control was 34.56 years. Mostly patients were females 44(81.5%) while males were only 10(18.5%). Concerning lipid abnormalities associated with gall stone disease, it was revealed that serum cholesterol levels were statistically insignificant in the gallstones patients as compared to the control group. (p=0.085). Triglycerides levels were significantly raised in controls as compared to the case group. (p=0.006). Furthermore, serum HDL levels were significantly low in the case group as compared to the control group.(p=0.001). On the other hand, LDL level was significantly higher in controls than cases but with statistically insignificant (p=0.014).

One of the studies, compared the effects of gall stones on lipid parameters wherein the mean age of the patients was reported 40.90 ± 12.65 years. Most of the patients around 92% were female. [24] Comparablefindings were observed in the researches performed by Weerakoon HT et al. [17] and Gul H et al.[25] with the reported mean ages of 44.6 ± 10.4 years and 43.18 ± 13.970 years,correspondingly. Furthermore, researches conducted by Weerakoon HT et al. [17], Gul H et al. [25] and Halgaonkar P et al. [26] also indicated that the mostly patients were female revealing role of hormone in disease process of gallstones formation. The present study was not in accordance with the above reported studies and revealed that the study subjects had mean age

35.49 years in cases and 34.56 years in controls but most of the patients were belonged to female gender.

Similarly, one research by Al-Saadi N et al. [27] demonstrated that significant elevation of serum cholesterol levels observed in the gallstones patients than the control group. Even though, the super-saturation of bile with cholesterol has distinct role in disease process of gallstones but their relationship of gallstones with higher level of serum cholesterol in patients is debatable in literature that can be broadly elucidated by many factors like genetics, geological, social and nutritionalstatus in causing different kind of gallstones.[27] In contrast to the above findings, the present study revealed that serum cholesterol levels were not statistically significant in the gallstones patients as compared to the control group. (p=0.085)

Another retrospective study compared the serum lipid abnormalities in 133 females who have gall stones with control group. Their study showed that serum LDL level was statistically significant in females over 40 years of age (p<0.05), while they did not show statistically significant association with other parameters.[1] The present study endorsed the above cited research as LDL level was significantly raised in controls than cases. On the other hand, our study showed inconsistency in a manner as statistically significant difference observed in triglycerides levels (p=0.006) and HDL levels (p=0.001) of cases and controls.

Furthermore, one more research targeted to broadlyassess the association between lipid profile (such as serum total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides) and probable factors of GSD.[28]This meta-analysis revealed that triglyceride was positively associated with GSD vulnerability. These findings showed similarity with another cohort trail. [29] Our study was consistent with the above cited study and proved that there was statistically significant difference observed between triglycerides levels of cases and controls (p=0.006).

Similarly, one more research focused to elaborate the preponderance of gall stones in females. They observed that out of 526 patients, 384 were female and 142 were male showing females predilection over males.This is due to the presence of sex hormone like estrogen that is the principal sex hormone in female. This hormone regulates both health and disease process by binding to numerous receptor.[30] It was also evidently supported that high frequency of GD was seen in females as compared to the males, particularlyin the pre-menopausal stage due to

hormonal changes.[30] Similarly findings were shown by previous Pakistani study.[31] Our study was in agreement with the above researches and revealed that out of 54, 44 patients were female indicating females predilection over males

Therefore, it can be assessed that physical inactivity, female sex, older age and marital status has a significant role in pathogenesis of GSD. However, additional prospective researches must be performed in order to recognize the cause of disease. Furthermore, more investigations and researches must be conducted to demonstrate the recentrecognized demographic and biochemical factors responsible for GD prevalence that can help to find out proper remedialalternativesrather than surgical management.

CONCLUSION

This study concluded that serum low levels of high density lipoprotein were statistically significant in the gallstone patients as compared to the control group. Furthermore, triglyceride levels and low density lipoprotein levels were significantly raised in the control group as compared to the gallstone patients. Therefore, it was depicted from the study that lipid abnormalities are significantly associated with the gall stone diseases.

REFERENCES

1. Batajoo H, Hazra NK. Analysis of serum lipid profile in cholelithiasis patients. J Nepal Health Res Counc. 2013 Jan;11(23):53-5.

2. Halldestam I, Kullma NE, Borch K. Incidence of and potential risk factors for gallstone disease in a general population sample. Br. J. Surg. 2009;96(11):1315–1322.

3. Van Erpecum KJ. Pathogenesis of cholesterol and pigment gallstones: an update. Clin Res Hepatol Gastroenterol. 2011;35(4):281–287.

4. Di Ciaula A, Wang DQ, Portincasa P. An update on the pathogenesis of cholesterol gallstone disease. Curr. Opin. Gastroenterol. 2018 Mar; 34(2):71-80.doi: 10.1097/MOG.0000000000000423.

5. Shabanzadeh DM, Sørensen LT, Jørgensen T. Determinants for gallstone formation - a new data cohort study and a systematic review with meta-analysis. Scand J Gastroenterol. 2016 Oct;51(10):1239-48. doi: 10.1080/00365521.2016.1182583.

6. Chandran AP, Sivarajan R, Srinivasan V, Srinivas M, Jayanthi V. Risk profile for gallstone disease in southern Indian population: Is there anything new? Indian J Gastroenterol.2014;33(3):254-257. http://dx.doi.org/10.1007/s12664-014-0453-3

7. Cariati A. Gallstone Classification in Western Countries.Indian J Surg. 2015 Dec; 77(Suppl 2):376-80.

8. Ansari-Moghaddam A, Khorram A, Miri-Bonjar M, Mohammadi M, Ansari H. The Prevalence and Risk Factors of Gallstone Among Adults in South-East of Iran: A Population-Based Study. Glob J Health Sci. 2015 Jul 30;8(4):60-7. doi: 10.5539/gjhs.v8n4p60.

9. Kim SB, Kim KH, Kim TN, Heo J, Jung MK, Cho CM, et al. Sex differences in prevalence and risk factors of asymptomatic cholelithiasis in Korean health screening examinee: A retrospective analysis of a multicenter study. Medicine (Baltimore). 2017 Mar;96(13):e6477. doi: 10.1097/MD.0000000000006477.

10. Henao-Morán S, Denova-Gutiérrez E, Morán S, Duque X, Gallegos-Carrillo K, Macías N, Salmerón J. Recreational physical activity is inversely associated with asymptomatic gallstones in adult Mexican women. Ann Hepatol. 2014 Nov-Dec;13(6):810-8.

11. Njeze GE. Gallstones. Niger J Surg. 2013 Jul;19(2):49-55. doi: 10.4103/1117-6806.119236.

12. Rudling M, Laskar A, Straniero S. Gallbladder bile supersaturated with cholesterol in gallstone patients preferentially develops from shortage of bile acids. J Lipid Res. 2019 Mar;60(3):498-505. doi: 10.1194/jlr.S091199.

13. Reshetnyak VI. Concept of the pathogenesis and treatment of cholelithiasis. World J Hepatol. 2012 Feb 27;4(2):18-34. doi: 10.4254/wjh.v4.i2.18.

14. Channa NA, Ghanghro AB, Soomro AM. Quantitative analysis of serum lipid profile in gallstone patients and controls. Pakistan J. Anal. Environ. Chem. 2010;11(1):59–65.

15. Rao PJ, Jarari A, El-Awami H, Patil TN, El-Saiety SO. Lipid profile in bile and serum of cholelithiasis patients-A comparative study. J. Basic Med. Allied Sci. 2012;1:27–39.

16. Sheng B, Zhao Q, Ma M, Zhang J. An inverse association of weight and the occurrence of asymptomatic gallbladder stone disease in hypercholesterolemia patients: a case-control study. Lipids Health Dis. 2020 Oct 23;19(1):228. doi: 10.1186/s12944-020-01402-8.

17. Weerakoon HT, Ranasinghe S, Navaratne A, Sivakanesan R, Galketiya KB, Rosairo S. Serum lipid concentrations in patients with cholesterol and pigment gallstones. BMC Res. Notes. 2014;7:548.DOIhttps://doi.org/10.1186/1756-0500-7-548.

18. Wang J, Shen S, Wang B, Ni X, Liu H, Ni X, Yu R, Suo T, Liu H. Serum lipid levels are the risk factors of gallbladder stones: a population-based study in China. Lipids Health Dis. 2020 Mar 19;19(1):50. doi: 10.1186/s12944-019-1184-3.

19. Chang CM, Chiu THT, Chang CC, Lin MN, Lin CL. Plant-Based Diet, Cholesterol, and Risk of Gallstone Disease: A Prospective Study. Nutrients. 2019 Feb 4;11(2):335. doi: 10.3390/nu11020335.

20. Wang F, Zheng J, Yang B, Jiang J, Fu Y, Li D. Effects of Vegetarian Diets on Blood Lipids: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.J Am Heart Assoc. 2015 Oct 27; 4(10):e002408.

21. Chiu YF, Hsu CC, Chiu TH, Lee CY, Liu TT, Tsao CK, et al. Cross-sectional and longitudinal comparisons of metabolic profiles between vegetarian and non-vegetarian subjects: a matched cohort study.Br J Nutr. 2015 Oct 28; 114(8):1313-20.

22. Yokoyama Y, Levin SM, Barnard ND. Association between plant-based diets and plasma lipids: a systematic review and meta-analysis. Nutr Rev. 2017 Sep 1;75(9):683-698. doi: 10.1093/nutrit/nux030.

23. Bansal A, Akhtar M, Bansal AK.A clinical study: prevalence and management of cholelithiasis. Int Surg J. 2014;1(3):134-9. DOI: 10.5455/2349-2902.isj20141105

24. Hayat S, Hassan Z, Changazi SH, Zahra A, Noman M, Zain Ul Abdin M, et al. Comparative analysis of serum lipid profiles in patients with and without gallstones: A prospective cross-sectional study. Ann Med Surg (Lond). 2019 Apr 24;42:11-13. doi: 10.1016/j.amsu.2019.04.003.

25. Gul H, Ayub M, Akhtar A. Mean serum calcium and lipid profile in patients with gallstone disease in southern Punjab. Pak. J. Med. Health Sci. 2016 January;10(2):548–551.

26. Halgaonkar P., Verma R., Bhadre R., Unadkat P., Vaja C., Unadkat P. Study to establish the clinical correlation between chemical constituents of gallstones and serum biochemical parameters. Int. J. Sci. Study. 2016 June;4(3):97–102.

27. Al-Saadi N, Al-Ardhi S. Biochemical and demographical study of lipid profile in sera of patients with gallstone. Iraqi J. Sci. 2018 May;53(2):2012.

28. Zhang M, Mao M, Zhang C, HuF. Blood lipid metabolism and the risk of gallstone disease: a multi-center study and meta-analysis. Lipids Health Dis.2022 March; 21(1):26. https://doi.org/10.1186/s12944-022-01635-9.

29. Banim PJ, Luben RN, Bulluck H, Sharp SJ, Wareham NJ, Khaw KT, et al. The aetiology of symptomatic gallstones quantification of the effects of obesity, alcohol and serum lipids on risk. Epidemiological and biomarker data from a UK prospective cohort study (EPIC-Norfolk). Eur J Gastroenterol Hepatol. 2011;23(8):733–40. https://doi.org/10.1097/MEG.0b013e3283477cc9

30. Sharma R, Sachanl SG, Sharma SR. Preponderance of Gallstone in Female. World Journal of Pharmacy and Pharmaceutical Sciences.2013;2(6):5871-5877. Retrieved from http://www.wjpps.com/wjpps _controller/abstract_id/615.

31. Aslam HM, Saleem S, Edhi MM, Shaikh HA, Khan JD, Hafiz M, et al. Assessment of gallstone predictor: comparative analysis of ultrasonographic and biochemical parameters. Int Arch Med. 2013 Apr 24;6:17. doi: 10.1186/1755-7682-6-17.