ORIGINAL ARTICLE

The Association of Dyslipidemias with Cholelithiasis: A Case-Control Study Conducted at Pakistan Institute of Medical Sciences, Islamabad

Ayesha Siddiqa[1], Sara Khan[2*], Maryam Rafiq[3], Farah Hanif[1], Muhammad Shahzad Anwer[2], Asma Khattak[1]

ABSTRACT

Objective: To find the association of lipid profile with cholelithiasis.

Study Design: A case-control study.

Place and Duration of Study: The study was carried out at the Department of Pathology, Pakistan Institute of Medical Sciences (PIMS) Hospital, Islamabad from April 2022 to April 2023.

Methods: This study recruited 100 known cases of cholelithiasis aged 20 to 70 years, having gall stones diagnosed through ultrasonography presenting to the hospital. These cases were compared with 100 controls who had past records of their laboratory reports from this hospital, in this case-control study. The past data of their laboratory reports of lipid profile including serum concentrations of Total Cholesterol, Triglycerides, HDL cholesterol, and LDL cholesterol levels and other tests such as fasting blood glucose (FBG), total bilirubin (T-bil), alanine transaminase (ALT), serum creatinine (Cr), uric acid (UA), and urea nitrogen (UN) were compared.

Results: The mean ages of the cases and controls were 51.71±13.48 and 42.00±13.14 years, respectively. There was no variance in the BMI of both groups. The logistic regression analysis presented data where significant differences within lipid profile values of cases and controls could be seen having higher values reported in cases than controls. The multivariant analysis of the lipid profile analyzed values presented a significant variance in the odds ratio of high-density lipoprotein, HDL cholesterol levels, and Triglycerides of the cases and controls.

Conclusion: Low levels of high-density lipoprotein (HDL) cholesterol and high levels of Triglycerides are associated with a high risk of gall bladder stone formation.

Keywords: *Cholelithiasis, High Density Lipoprotein Cholesterol (HDL), Triglycerides.*

How to cite this: *Siddiqa A, Khan S, Rafique M, Hanif F, Anwer MS, Khattak A. The Association of Dyslipidemias with Cholelithiasis: A Case-Control Study Conducted at Pakistan Institute of Medical Sciences (PIMS), Islamabad. Life and Science. 2024; 5(2): 166-171. doi: http://doi.org/10.37185/LnS.1.1.428*

[1]*Department of Pathology*
Pakistan Institute of Medical Sciences (PIMS) Hospital,
Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan
[2]*Department of Pathology*
CMH Institute of Medical Sciences, Bahawalpur, Pakistan
[3]*Department of Pathology*
Sahiwal Medical College, Sahiwal, Pakistan
Correspondence:
Dr. Sara Khan
Assistant Professor, Pathology
CMH Institute of Medical Sciences, Bahawalpur, Pakistan
E-mail: sarakhan105@gmail.com

Funding Source: NIL; Conflict of Interest: NIL
Received: June 14, 2023; Revised: Sep 01, 2023
Accepted: Oct 11, 2023

Introduction

Gall bladder stones is the common condition of biliary tree which affects 10-20 percent of population in west while 5-8% of Eastern Asian population.[1,2] It is among the hepatobiliary diseases associated with the highest socioeconomic costs.[3] Around 20% of the cases have no biliary symptoms or complications related to gallstones.[4] There is a wide number of surgical interventions performed for the removal of gall stones. This not only cause patients a high cost but also provides lifetime of health compromises.[5]

Gallstones are the risk factor for gall bladder carcinomas, colorectal cancers as well as cardiovascular diseases.[6] The mortality event is also

high in asymptomatic cases of cholelithiasis.[7] This highlights the significance of preempting the disease and reducing the risk of complications. The majority of the gallstone composition is based on cholesterol, leading to the enhanced role of cholesterol metabolism in gall stone production.[8] There are several researches focusing on the association of cholelithiasis with dyslipidemia. Unfortunately, there is a considerable discrepancy within the findings of various studies in terms of sample size, ethnicity, dyslipidemias, and the subjects enrolled.[9,10] The present study is distinctive as it evaluates the association of dyslipidemias with cholelithiasis in the patients presenting to PIMS Islamabad, the busiest government tertiary care hospital of the federal capital of Pakistan. The results of this study assist in understanding and controlling dyslipidemias for reducing the risk of complex cholecystectomies and can also identify lipid profiling as an early sign of gall stone formation to help reduce the risk of complications and mortality.

Methods

A case-control study was conducted in the Department of Pathology, Pakistan Institute of Medical Sciences (PIMS) Islamabad, Pakistan from April 2022 to April 2023. All 100 cases were adults male and female aged 20 to 70 years, who were patients of symptomatic cholelithiasis, diagnosed by clinical symptoms and confirmed on ultrasonography. A convenient consecutive sampling was used. The 100 controls were all adults of the same age group admitted to PIMS hospitals for complaints other than cholelithiasis and with normal abdominal ultrasound done for any other reason. The sample size was generated by using the WHO sample size calculator. The power of the test was taken as 80% and a confidence interval of 95%. The study was performed after approval was granted by the Ethics Committee of PIMS Hospital vide letter No.F.3-1/2023(ERRB), held on 15th March 2022, and informed consent was obtained from all participants. Each participant selected for the study was personally interviewed in the inpatient department. Patients were interviewed regarding their demographic details, clinical profile and their past laboratory reports were retrieved. Data from laboratory reports with values of Lipid profile including serum concentrations of Total cholesterol, HDL cholesterol, Triglycerides, and LDL cholesterol levels and other tests such as fasting blood glucose (FBG), total bilirubin (T-bil), alanine transaminase (ALT), serum creatinine (Cr), uric acid (UA), and urea nitrogen (UN) were taken. These laboratory reports including the lipid profiles of both groups were compared. All related clinical history was documented on a well-structured proforma. The patient's age, gender, BMI, waist circumference, blood glucose, systolic and diastolic blood pressure, and indicators for liver and kidney functions were also recorded. Data were statistically analyzed using Chi-square and odds ratio from SPSS version 26.0. *P* value <0.001 was taken as significant.

Results

The mean ages of the cases and controls were 51.71±13.48 and 42.00±13.14 years, respectively. There was no variance in the BMI of both groups. However, the systolic blood pressure of the controls was lower than that of the cases. There was a significant difference in the total cholesterol, triglycerides, and low-density lipoproteins levels (p<0.001) between cases and controls with much higher values reported in the cases. There were 49% and 45% females in cases and controls respectively. Figure.1 and Table-1.

The incidence of kidney stones was higher in the cases than in controls while hypertension was more commonly reported in 36% of the cases in comparison to the 19% of the controls. Of all the cases, there were 51% who underwent cholecystectomy. Figure.2.

The multivariant analysis of the lipid profile analyzed values presented a significant variance in the odds ratio of high-density lipoprotein cholesterol levels and triglycerides of cases and controls. The logistic regression analysis presented a data where significant difference within lipid profile values of cases and controls could be seen having high values reported in cases than controls. However, total cholesterol and low density lipoproteins association with gall stones formation was not as remarkable as that of total cholesterol. (Table-2).

Table-1: Baseline features of cases and controls

Characteristics	Cases (n= 100)	Control (n= 100)	*P*-value
Age (year)	51.71 ± 13.48	42.00 ± 13.14	0.561
BMI (kg/m ^{2})	24.55 ± 3.40	23.24 ± 3.43	0.613
WC (cm)	84.45 ± 13.12	81.44 ± 27.63	0.655
DBP (mmHg)	78.17 ± 12.18	74.52 ± 11.45	0.894
SBP (mmHg)	129.96 ± 19.48	122.80 ± 17.17	0.382
FBG (mmol/L)	5.82 ± 1.58	5.40 ± 1.11	0.563
ALT (U/L)	27.94 ± 25.22	26.64 ± 25.67	0.564
T-bil (umol/L)	13.90 ± 5.68	13.68 ± 5.40	0.659
Cr (umol/L)	141.21 ± 944.42	102.30 ± 651.11	0.051
UA (umol/L)	347.66 ± 92.65	345.17 ± 96.22	0.441
UN (mmol/L)	5.29 ± 1.46	5.18 ± 1.30	0.622
TC (mmol/L)	5.12 ± 1.00	4.68 ± 0.94	0.001
TG (mmol/L)	1.91 ± 1.85	1.59 ± 1.43	<0.001
LDL-C (mmol/L)	3.14 ± 0.85	2.93 ± 0.81	<0.001
HDL-C (mmol/L)	1.36 ± 0.35	1.41 ± 0.36	0.02

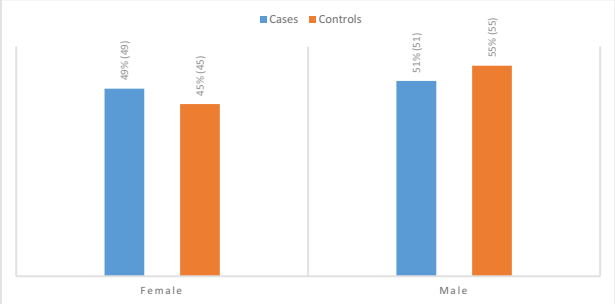

Fig. 1: Gender Distribution of cases and controls

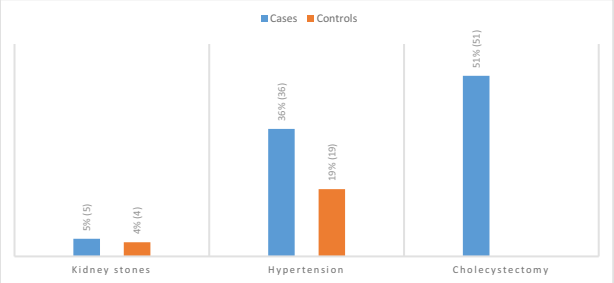

Fig. 2: Percentage comparison of complications realted to cholecystitis

Table-2: Multivariate analysis by logistic regression of cases and controls lipid profile values

mmol/L	Cases OR (95%CI)	*P-value*	Control OR (95%CI)	*P-value*
Total Cholesterol				
Normal	0.715(0.600, 0.853)	< 0.001	0.858(0.689, 1.067)	0.171
High	0.673(0.557, 0.817)	< 0.001	0.770(0.609, 0.965)	0.024
Triglycerides				
Normal	0.761(0.525, 1.088)	0.133	1.089(0.476, 2.493)	0.852
High	0.898(0.623, 1.296)	0.563	1.273(0.555, 2.916)	0.571
Low Density Lipoproteins-cholesterol				
Normal	0.934(0.868, 1.003)	0.056	0.903(0.850, 0.959)	0.001
High	0.883(0.820, 0.955)	0.002	0.906(0.832, 0.991)	0.022
High Density Lipoproteins-cholesterol				
Normal	0.906(0.824, 0.996)	0.042	0.920(0.822, 1.020)	0.107
High	0.698(0.605, 0.804)	< 0.001	0.725(0.624, 0.85)	< 0.001

Total cholesterol: 3.1-5.7, High >5.7, TG:0.4–1.7, High >1.7, LDL cholesterol: 2.07-3.1, High >3.1, HDL cholesterol: 0.9-2.0

Discussion

The current study elaborated the association between dyslipidemias and cholelithiasis through comparative analysis of cases versus controls. The combined analysis presented results with triglycerides to be positively related with the risk of gall stones. This has also been detailed in another research by Hayat et al. in Lahore which concluded that serum triglyceride levels and serum HDL levels in gallstone patients had a positive correlation between these parameters and gallstone disease.[11] Atamanalp et al. in Turkey also had similar findings.[12] However, a Mendelian randomization (MR) study suggested a null association between plasma LDL-C and symptomatic gallstone disease.[13] The relationship between blood lipids and cholelithiasis has, therefore, been unsettled for years, especially for total cholesterol and LDL-C, as mentioned in the introduction.[11-14]

In the current study, the mean age of most of the cases was in the early 50s. Rahman et al. elaborated in their research that most of the patients having cholelithiasis are > 35 years of age.[15] In another study by Teekaraman et al. the highest incidence of cholelithiasis was observed in the age group 40-50 years wherein the male-to-female ratio was presented as 1:2.57.[16]

The cholesterol stone formation mechanism is related to the cholesterol bile crystals with a high association with increasing bile saturation of cholesterol. However, there is a negative association of later with bile salts.[15] Previously reported research on High-density lipoproteins have found similar data where the negative association of HDL was found with gallstone formation.2,8,11,16 Hepatic bile acids have been reported to be facilitated in their synthesis through HDL blood levels in addition to the reduction in cholesterol-saturation and bile solubility.[17-19]High density lipoproteins also assist in the transportation of cholesterol to the bile.[20]

The morphological evidence suggests that within the various calculi composition identified from gall stones, the highest incidence is of cholesterol-based stones (61%). Mostly the stones that have been identified in research as Triglyceride based (59-63%) followed by high-density lipoprotein cholesterol (53-61%). Thilanka et al. also reported the cholesterol composition of gall stones followed by LDL-C and HDL-C.[21] Similar results are presented in the current research.

Triglycerides' positive association with increasing risk of gall bladder stone formation was consistent to the research conducted in a Korean cohort as well.[22] Although the actual mechanism linked with the increased triglycerides production with susceptibility of gallstone formation is unclear.[21,23] However, this study design being single-center, with a small sample size and retrospective may limit generalizability and comprehensive data collection. Addressing these limitations in future studies could contribute to a more comprehensive understanding of the relationship between dyslipidemia and cholelithiasis, thereby refining preventive strategies and early interventions for individuals at risk.

Conclusion

High levels of triglycerides and low levels of HDL cholesterol are associated with the risk of gall bladder stones formation. This study provides a basis for identifying the population at high risk for Cholelithiasis and also a possible way for the prevent and control of Gallstone disease, that is, implementing preventive intervention for patients with high and low concentrations of triglyceride and HDL cholesterol, respectively. Further preventive intervention trials are needed to verify the effects of triglyceride and HDL cholesterol on Gallstone disease.

REFERENCES

1. Wang J, Shen S, Wang B, Ni X, Liu H, Ni X, et al. Serum lipid levels are the risk factors of gallbladder stones: a population-based study in China. Lipids Health Disease. 2020; 19: 50. doi: 10.1186/s12944-019-1184-3
2. Zhang X, Guan L, Tian H, Li Y. Prevalence and risk factors of gallbladder stones and polyps in liaoning, China. Front Medicine. 2022; 9: 865458. doi: 10.3389/fmed.2022.865458
3. Lammert F, Gurusamy K, Ko CW, Miquel JF, Méndez-Sánchez N, Portincasa P, et al. Gallstones. Nature Reviews Disease Primers. 2016; 2: 16024. doi: 10.1038/nrdp.2016.24
4. Gross AR, Bacaj PJ, Williams HJ. Educational Case: Gallstones, Cholelithiasis, and Cholecystitis. Academic Pathology. 2020; 7: 2374289520951902. doi: 10.1177/2374289520951902

5. Ponce CB, Scherer D, Brinster R, Boekstegers F, Marcelain K, Garate-Calderon V, et al. Gallstones, body mass index, C-reactive protein, and gallbladder Cancer: Mendelian randomization analysis of Chilean and European genotype data. Hepatology. 2021; 73: 1783-96. doi: 10.1002/hep.31537
6. Ward HA, Murphy N, Weiderpass E, Leitzmann MF, Aglago E, Gunter MJ, et al. Gallstones and incident colorectal cancer in a large Pan-European cohort study. International Journal Cancer. 2019; 145: 1510-16. doi: 10.1002/ijc.32090
7. Fairfield CJ, Wigmore SJ, Harrison EM. Gallstone disease and the risk of cardiovascular disease. Scientific Reports. 2019; 9: 5830. doi: 10.1038/s41598-019-42327-2
8. Konyn P, Alshuwaykh O, Dennis BB, Cholankeril G, Ahmed A, Kim D. Gallstone disease and its association with nonalcoholic fatty liver disease, all-cause and cause-specific mortality. Clinical Gastroenterology Hepatology. 2023; 4: 940-48. doi: 10.1016/j.cgh.2022.04.043
9. Zhang M, Mao M, Zhang C, Hu F, Cui P, Li G, et al. Blood lipid metabolism and the risk of gallstone disease: a multi-center study and meta-analysis. Lipids Health Disease. 2022; 21: 26-9. doi: 10.1186/s12944-022-01635-9
10. Aghazadeh-Attari J, Mobaraki K, Ahmadzadeh J, Mansorian B, Mohebbi I. Quality of observational studies in prestigious journals of occupational medicine and health based on Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: a cross-sectional study. BMC Research Notes. 2018; 11: 266. doi: 10.1186/s13104-018-3367-9
11. 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. Annals of Medicine and Surgery. 2019; 42: 11-3. doi: 10.1016/j.amsu.2019.04.003
12. Atamanalp SS, Keles MS, Atamanalp RS, Acemoglu H, Laloglu E. The effects of serum cholesterol, LDL, and HDL levels on gallstone cholesterol concentration. Pakistan Journal of Medical Sciences. 2013; 29: 187-90. doi: 10.12669/pjms.291.2798
13. Stender S, Frikke-Schmidt R, Benn M, Nordestgaard BG, Tybjærg-Hansen A. Low-density lipoprotein cholesterol and risk of gallstone disease: A Mendelian randomization study and meta-analyses. Journal of Hepatology. 2013; 58: 126-33. doi: 10.1016/j.jhep.2012.08.013
14. Shabanzadeh DM, Sørensen LT, Jørgensen T. Determinants for gallstone formation—a new data cohort study and a systematic review with meta-analysis. Scandinavian Journal of Gastroenterology. 2016; 51: 1239-48. doi: 10.1080/00365521.2016.1182583
15. Rahman F, Iqbal K, Khan MS, Mal L, Sadiq MA, Rehman K. Incidence of various types of gallstones in association with age. Pakistan Journal of Medical & Health Sciences. 2022; 16: 947-8. doi: 10.53350/pjmhs22162947
16. Lin H, Zhou X, Zhang Z. The Diagnostic Value of GGT-Based Biochemical Indicators for Choledocholithiasis with Negative Imaging Results of Magnetic Resonance Cholangiopancreatography. Contrast Media & Molecular Imaging. 2022; 2022: 7737610. doi: 10.1155/2022/7737610
17. Portincasa P, Moschetta A, Palasciano G. Cholesterol gallstone disease. Lancet. 2006; 368: 230-39. doi: 10.1016/S0140-6736(06)69044-2
18. Kim YK, Kwon OS, Her KH. The grade of nonalcoholic fatty liver disease is an independent risk factor for gallstone disease: an observational study. Medicine. 2019; 98: e16018. doi: 10.1097/MD.0000000000016018
19. Janowitz P, Wechsler JG, Kuhn K, Kratzer W, Tudyka J, Swobodnik W, et al. The relationship between serum lipids, nucleation time, and biliary lipids in patients with gallstones. Clinical Investigation. 1992; 70: 430-6. doi: 10.1007/BF00235527
20. Thornton JR, Heaton KW, Macfarlane DG. A relation between high-density-lipoprotein cholesterol and bile cholesterol saturation. British Medical Journal. 1981; 283: 1352–4. doi: 10.1136/bmj.283.6303.1352
21. Thilanka H, Weerakoon W, Ranasinghe S, Navaratne A, Galketiya KB, Rasario S. Serum lipid concentration in patients with cholesterol and pigment gallstone. British Medical College Research Notes. 2014; 7: 548. doi: 10.1186/1756-0500-7-548
22. 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. 2017; 96: e6477. doi: 10.1097/MD.0000000000006477
23. Chang CM, Chiu THT, Chang CC, Lin MN, Lin CL. Plant-based diet, cholesterol, and risk of gallstone disease: A prospective study. Nutrients. 2019; 11: 335. doi: 10.3390/nu11020335

Authors Contribution

AS: Idea conception, study designing, data collection, data analysis, results and interpretation, manuscript writing, and proofreading

SK: Idea conception, study designing, data analysis, results and interpretation, manuscript writing, and proofreading

MR: Idea conception, study designing, data analysis, results and interpretation, manuscript writing, and proofreading

FH: Idea conception, study designing, data collection

MSA: Study designing, data analysis, results and interpretation, manuscript writing, and proofreading

AK: Idea conception, study designing, data collection