

To Compare Serum Lipid Profiles in Patients with and Without GallstoneVaidehi¹, Akhilesh Kumar^{2*}, Yogesh Krishna Sahay³, Usha Kumari⁴, Lalan Kumar⁵¹Tutor, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.²Ex-Senior Resident, Department of Surgery, Patna Medical College Hospital, Patna, Bihar, India.³Professor and Head of Department, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.⁴Professor, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India.⁵Assistant Professor, Department of Surgery, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar.

Received: 30-04-2024 / Revised: 10-05-2024 / Accepted: 18-05-2024

Corresponding Author: Dr. Akhilesh Kumar

Conflict of interest: Nil

Abstract:**Background:** The pathogenesis of Gallstone is multifactorial. Serum lipids are among the most important risk factor involved in the pathogenesis of gallstone disease. Impaired lipid metabolism causes hypersecretion of hepatic cholesterol, which leads to supersaturation of bile and development of solid cholesterol crystals which contribute in gallstone synthesis.**Objective:** The main motive of this study was to determine the significance of serum lipid abnormalities in the etiology of gallstone disease and to identify the confounding effects of gender, age and body mass index on gallstone disease.**Material and Methods:** A comparative cross sectional study was conducted on 50 ultrasonically confirmed gallstone patients and 50 gender and age matched healthy individuals as controls. This study was conducted in the Department of Biochemistry in collaboration with the Department of Surgery, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, from October 2023 to March 2024. The serum parameters were estimated using the enzymatic colorimetric method.**Results:** The mean serum levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) were significantly higher in gallstone patients as compared to healthy individuals with p value < 0.001. The HDL-C level was observed to be lower in gallstone patients compared to healthy individuals and the difference in the mean levels of HDL-C was significant in two groups with p-value < 0.05.**Conclusion:** It concludes that deranged lipid profile as high levels of TC, TG, LDL-C and low levels of HDL-C is an important risk factors which significantly contributes to the development of gallstones in this area.**Keywords:** Gallstone disease, Serum lipid profile, Total cholesterol, Triglyceride, Low-density lipoprotein, High-density lipoprotein.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Gallstone disease is one of the most common disorder of the gastrointestinal tract, having a prevalence of 10%-15% in developed countries [1]. Gallstone disease prevalence varies in different communities of India. Its highest frequency rate has been reported in adult population (7.4%) of North Indians [2]. The pathogenesis of Gallstone is multifactorial. Multiple risk factors which are responsible for Gallstone formation are female sex, increasing age, dietary factors (high fat, high cholesterol, high calorie intake, high refined carbohydrate and low fibre intake), hypertriglyceridemia, pregnancy, parity, physical inactivity, overweight and obesity [3], metabolic syndrome (obesity, diabetes mellitus, dyslipidemia

and hyperinsulinemia) [4-7]. Serum lipids are among the most important risk factor involved in the pathogenesis of gallstone disease [1,8-9]. Impaired lipid metabolism causes hypersecretion of hepatic cholesterol, which leads to supersaturation of bile and development of solid cholesterol crystals [10-12], bile stasis also plays an additional role [13]. Gallstones are classified into cholesterol, black pigment and brown pigment stones. Cholesterol stones are most common types and it contain 51-99% pure cholesterol. Black pigment stones are mainly composed of mixture of insoluble bilirubin pigment polymer with calcium phosphate and carbonate. Brown pigment stones are composed of calcium bilirubinate, calcium

palmitate, calcium stearate and cholesterol [14]. The risk factors contributing to the development of gallstones need to be identified, so that appropriate preventive measures can be undertaken. Some of the previous studies show a positive correlation between altered lipid profile and formation of gallstone [1,15]. This study aims to find out the association of serum lipid profile with gallstone in our geographical area.

Aim and Objective

The objective of this study is to compare serum lipid profile of gallstone patients with the controls to determine the significance of serum lipids in the etiology of gallstone disease. and to identify the confounding effects of gender, age and body mass index on gallstone disease.

Material and Methods

Study design: Comparative cross sectional study

Study Place and period of study: This study will be carried out in the Department of Biochemistry in collaboration with the Department of Surgery, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar. Where data were collected from October 2023 to March 2024.

Study subjects: A total of 50 clinical cases of gallstone diagnosed through ultrasound as mobile echoes in the gallbladder with acoustic shadow will be included in the study. 50 inpatients with no history of gallstone will be recruited as control group. Control group comprised of age matched and sex matched normal, healthy individuals from the same hospital with the ultrasonic exclusion of gallstone. Patients with acalculous gallbladder disease on ultrasound, terminal ileal resection, haemolytic diseases (Sickle cell anemia, hereditary spherocytosis on history and CBC film), liver

cirrhosis (on USG) and patients on antihyperlipidemic drugs will be excluded from the study. The work was carried out after due clearance and approval from institutional ethical committee. Informed written consent was taken from all the study subjects after explaining them the objective of the study.

Sample collection and analysis of sample: With all aseptic and antiseptic precautions approximately 5ml of venous blood was collected from patients and controls after 10-12 hours of fasting in red capped clot activator collecting tube and properly labelled. Blood sample was allowed to clot by placing in a rack at room temperature for at least 30 minutes. Then it was centrifuged at 2000 rpm for 10 minutes. Biochemical analysis of serum cholesterol, serum triglyceride, serum LDL and serum HDL will be done by enzymatic colorimetric method using Fully Auto Biochemistry Analyzer Selectra Pro M Lite. All the reagents were supplied by ELITech Group.

Statistical Analysis: The results obtained were further analysed for mean, standard deviation and p-value. Student t-test was employed to compare the data between the cases and the control groups, p-value < 0.05 will be considered statistically significant.

Results

The study done was a comparative cross sectional study conducted on 50 clinical cases of gallstone diagnosed through ultrasound as cases and 50 age matched and sex matched normal, healthy individuals from the same hospital with the ultrasonic exclusion of gallstone as control group. The comparison of serum lipid profile was done to find out the association between dyslipidemia and gallstone disease (Table III)

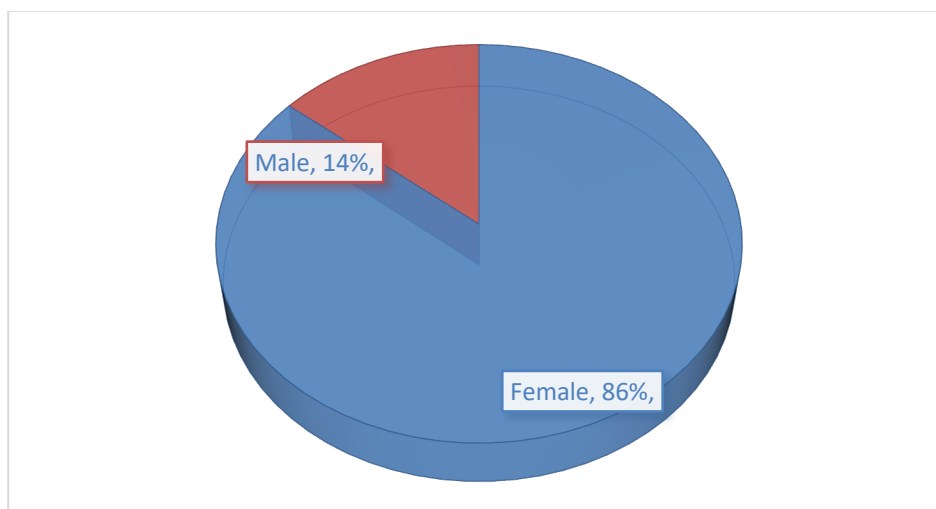


Figure I: Showing Gender distribution in Gallstone patients.

This figure shows that the maximum prevalence of gallstone (86%) was in female patients.

Table 1: Showing age (years) distribution in gallstone patients (case) and healthy individuals (control)

Group	Range	Mean	SD
Gallstone patients	18 - 78	46.18	13.8
Healthy individual	17 - 75	40.12	11.4
p-value < 0.05		Significant*	

This table shows mean age \pm SD for gallstone patients was 46.18 ± 13.8 and for healthy individuals was 40.12 ± 11.4 . The difference in age was significant with $p < 0.05$ (significant at 5% level *).

Table 2: Showing distribution of cases according to BMI in gallstone patients and healthy individual

BMI	Gallstone patients n (%)	Healthy individual n (%)
Obese	31 (62%)	20 (40%)
Non-obese	19 (38%)	30 (60%)

This table shows that the maximum prevalence of gallstone (62%) was in obese patients.

Table 3: Showing comparison of the serum lipids profile between Gallstone patients and healthy individuals

Serum lipid parameters (mg/dl)	Gallstone patients (n =50)		Healthy individuals (n =50)		p - value	Sig.
	Mean	SD	Mean	SD		
TC	187.42	37.18	148.79	23.43	<0.001	***
TG	146.50	27.23	116.21	18.56	<0.001	***
HDL-C	39.08	4.65	41.34	5.91	<0.05	*
LDL-C	117.52	16.68	86.12	15.01	<0.001	***

This table shows the comparative study of lipid profile between gallstone patients and healthy individuals and the analysis revealed that the levels of serum TC, TG, LDL-C were significantly higher in gallstone patients as compared to healthy individuals with p- value < 0.001 (significant at

0.1% level***).The HDL-C level was observed to be lower in gallstone patients compared to healthy individuals and the difference in the mean levels of HDL-C was significant in two groups with p-value < 0.05 (significant at 5% level*)

Table 4: Showing comparison of serum lipids between female gallstone patients and healthy females \geq 40 years of age

Serum lipid parameters(mg/dl)	Age \geq 40 years		P value	Sig.
	Mean \pm SD			
	Female gallstone patients (n=25)	Healthy females(n=24)		
TC	190.48 \pm 28.74	162.04 \pm 19.84	<0.001	***
TG	180.68 \pm 25.12	134.56 \pm 16.80	<0.001	***
HDL	35.68 \pm 3.86	42.87 \pm 4.98	<0.001	***
LDL	118.40 \pm 14.01	90.25 \pm 13.01	<0.001	***

This table shows the effect of lipid profile on gallstone patients in relation to age (by categorizing the females of gallstone patients and healthy females into two age groups with \geq 40 years and < 40 years) in the age group \geq 40 years. The analysis revealed that the levels of serum TC, TG, LDL-C were significantly higher in female gallstone patients as compared to healthy females with p-

value < 0.001 (significant at 0.1% level***).The HDL-C level was observed to be lower in female gallstone patients compared to healthy females and the difference in the mean levels of HDL-C was significant in two groups with p-value < 0.001 (significant at 0.1 % level***)

Table 5: Showing comparison of serum lipids between female gallstone patients and healthy females < 40 years of age

Serum lipid parameters(mg/dl)	Age < 40 years		P value	Sig.
	Mean ± SD			
	Female gallstone patients (18)	Healthy females(17)		
TC	170.57 ± 19.43	137.56 ± 16.41	<0.001	***
TG	162.68 ± 17.58	110.27 ± 19.27	<0.001	***
HDL	32.67 ± 3.04	35.86 ± 4.81	<0.05	*
LDL	106.68 ± 12.54	78.56 ± 6.8	<0.001	***

This table shows the effect of lipid profile on gallstone patients in relation to age (by categorizing the females of gallstone patients and healthy females into two age groups with ≥ 40 years and < 40 years) in the age group < 40 years. The analysis revealed that the levels of serum TC, TG, LDL-C were significantly higher in female gallstone

patients as compared to healthy females with p-value < 0.001 (significant at 0.1% level***). The HDL-C level was observed to be lower in female gallstone patients compared to healthy females and the difference in the mean levels of HDL-C was significant in two groups with p-value < 0.05 (significant at 5 % level*).

Table 6: Showing comparison of serum lipids between female gallstone patients and healthy females according to BMI

Serum lipid parameters(mg/dl)	Mean ± SD		P value	Sig.
	Obese gallstone patients	Obese healthy individuals		
TC	205.12 ± 30.15	170.46 ± 27.20	<0.001	***
TG	201.87 ± 32.58	160.55 ± 20.55	<0.001	***
HDL	40.52 ± 4.67	44.14 ± 3.57	<0.01	**
LDL	121.27 ± 15.63	99.34 ± 8.2	<0.001	***

This table shows the effect of lipid profile on gallstone patients in relation to BMI (by categorizing the gallstone patients and healthy individuals into two groups obese and non obese). The analysis revealed that the levels of serum TC, TG, LDL-C were significantly higher in obese gallstone patients as compared to obese healthy individuals with p-value < 0.001 (significant at 0.1% level***). The HDL-C level was observed to be lower in obese gallstone patients compared to obese healthy individuals and the difference in the mean levels of HDL-C was significant in two groups with p-value < 0.01 (significant at 1 % level**)

Discussion

Gallstone is a chronic gastrointestinal disorder. The etiopathogenesis of Gallstone is multifactorial which involves the interaction of environmental and genetic factors. Serum lipids are among the most important risk factors involved in the pathogenesis of gallstone disease [1,8-9]. Gallstone is a metabolic problem in which lipid abnormalities, obesity and diabetes are found to be very common [16]. The incidence of gall stone increases with age [17]. In present study mean age of the patients was 46.18±13.8 years which are comparable with the study of Nayal et al [18] who reported mean age of patients with gallstone as 48.6 ± 11.5 years.

The findings of present study justified the hypothesis of our study in which comparative cross sectional study of serum lipids profile suggested that abnormal lipid levels especially elevated TC, TG, LDL-C and decreased HDL-C were responsible for the formation of gallstone. There are many other studies which clearly indicated the association between serum lipids and gallstone disease. One such study which was conducted by Dwivedi et al. the association of serum lipids with gallstone disease revealed the increased levels of TC, TG, LDL-C, VLDL-C and decreased level of HDL-C in gallstone patients as compared to healthy controls [19]. Similarly, Batazoo et al. did the study in which the serum TC, LDL-C and TG levels were higher in female patients of age group ≥ 40 years in comparison to controls, of these parameters, only LDL-C level was found to be statistically significant. Findings similar to the current study has been observed in the study conducted by Naseem et al. who did the quantitative analysis of serum lipids in gallstone patients and controls, in which the serum TC, TG, LDL-C were higher and HDL-C was diminished in female gallstone patients of age group ≥ 40 years in comparison to controls [20].

Many studies considered increased age as a responsible factor in the gallstone formation. Some studies also reported that the possibility of gallstone disease in females increases with age

(≥ 40 years) as compared to males with the rise in its symptoms and complications such as abnormal lipid profile [16,20]. In the present study comparative analysis of females ≥ 40 years age group revealed high serum TC, TG, LDL-C and reduced HDL-C in the gallstone patients. Female hormone estrogen can increase cholesterol levels in bile and is responsible for sluggish gallbladder movement

Obesity is also a contributing factor for the development of gallstone. Present study revealed that the maximum prevalence of gallstone was in obese patients. Similarly, Corrina et al. also showed the strongest association between obesity and gallstone disease [21]. Study conducted by Eun et al. showed the association between gallstone disease and dyslipidemia with increased TG and diminished HDL-C levels in obese female patients [22].

Conclusion

It is concluded from this study that significantly high levels of TC, TG, LDL-C and significantly low levels of HDL-C were found in the serum lipid profile of gallstone patients as compared to healthy individuals. It reflects that deranged lipid profile is an important risk factors which contributes to the development of gallstones in this area. Results of this study also revealed that increased age in females with the rising epidemic of obesity is certain to elevate the frequency of gallstone synthesis. These findings have medical implications, highlighting the importance of comprehensive monitoring and control of serum lipid profile in gallstone patients to avoid future cardiovascular disease.

Acknowledgement

We are thankful to the patients; without them the study could not have been done. We are thankful to the supporting staffs of hospital who were involved in patient care of the study population.

List of abbreviations: TC: Total cholesterol, TG: Triglyceride, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, USG = Ultrasonography, BMI: Body mass index, SD: Standard deviation, n: Number

Source of funding: No funding received.

Bibliography

- Batajoo H., Hazara N. K. Analysis of serum lipid profile in cholelithiasis patients. J. Nepal Health Res. Counc. 2013; 11:53-55.
- Sachdeva S, Khan Z, Ansari MA, et al. Lifestyle and gallstone disease: Scope for primary prevention. Indian J Community Med 2011;36:263-7.
- Attili AF, Carulli N, Roda E, et al. Epidemiology of gallstone disease in Italy: prevalence data of the Multicenter Italian Study on Cholelithiasis(MI COL.). American Journal of epidemiology. 1995 Jan 15; 141(2):158-65.
- Mendez-Sanchez N, Chavez-Tapia NC, Motola-Kuba D, et al. Metabolic syndrome as a risk factor for gallstone disease. World J Gastroenterol 2005;11:1653-7.
- Ata N, Kucukazman M, Yavuz B, et al. The metabolic syndrome is associated with complicated gallstone disease. Can J Gastroenterol 20 11;25:274-6
- Cuevas A, Miquel JF, Reyes MS, et al. Diet as a risk factor for cholesterol gallstone disease. J Am Coll Nutr 2004;23:187-96.
- Shaffer EA. Epidemiology and risk factors for gallstone disease: Has the paradigm changed in the 21st century? Curr Gastroenterol Rep 2005; 7:132-40.
- Celika S, Doganb S, Arslanc H. Is the presence of single or multiple gallstones a matter of chance? What is the relationship between the number of stones and lipid profile, age gender, and stone type? J Univ Surg 2015;3:13
- Lambou-Gianoukos S, Heller SJ. Lithogenesis and bile metabolism. Surg Clin North Am 2008;88:1175-94,vii.
- Di Ciaula A, Wang DQ, Bonfrate L, Portincasa. Current views on genetics and epigenetics of cholesterol gallstone disease. Cholesterol 2013;2013:298421.
- Abdullah UY, Jassim HM, Baig AA, et al. Gallstones in patients with inherited haemolytic diseases. Int J Pharm Sci 2015;7:9-15.
- 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.
- Wang DQ, Cohen DE, Carey MC, Biliary lipids and stone disease. J Lipid Res. 2005;50 (Suppl);406-411.
- R.C. G. Russel. The gall bladder and bile ducts, In: R.C.G. Russel, Norman S. William (Eds).
- Bailey and Love's Short Practice of Surgery. 24th edition. London, UK: ARNOLD;2004. 1103.
- Dr. Mohammad Shaha Alam, Dr. A.K.M. Harun-Ar-Rashid, et al. The Association of the serum lipid abnormalities in cholelithiasis patients. Scholars Journal of Applied Medical Sciences; 2021; doi:10.36347/sjams.2021.vo9i01.022.
- Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: Cholelithiasis and cancer. Gut Liver 2012;6:172-87.

18. Il'ChenkoAA. On the problem of classification of cholelithiasis. *Eksp. Klin. Gastroenterol.* 2004;8:12-14.
19. Nayal B, Devaki R. Correlation of serum lipids and glucose tolerance test in cholelithiasis. *Int J Pharma. Bio. Sci.* 2011;2(1):224-28.
20. Dwivedi S, Singh S, Singh D, Tiwari S. Association of non clinical characteristics and lipid profile with gall bladder stone patients; a case control study. *Panacea J Med Sci.* 2014;4:62-4.
21. Channa NA, Khand F, Ghangro AB, et al. Quantitative analysis of serum lipid profile in gallstone patients and controls. *Pak J Anal Environ Chem* 2010;11:59-65.
22. Koebnick C, Smith N, Black MH, et al. Pediatric obesity and gallstone disease: Results from a cross-sectional study of over 510,000 youth. *Pediatr Gastroenterol Nutr* 2012; 55: 328-33.
23. Yoo EH, Lee SY. The prevalence and risk factors for gallstone disease. *Clin Chem Lab Med* 2009; 47:795-807.