DETERMINING RELATION BETWEEN GALLSTONE AND LIPID PROFILE

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ABSTRACT

Introduction

Cholelithiasis is presence of stone in gallbladder. Female sex, obesity, pregnancy, fatty foods, all are associated with an increased risk of developing gallstones. There is paucity of information regarding relation of cholelithiasis and lipid profile. In this study the association of serum lipids to cholelithiasis has been tried to been elucidated.

Objectives

The general objective was to determine the relation of Serum lipid in cholelithiasis. The specific objectives were to compare the relation between serum cholesterol, serum triglyceride, serum HDL and serum LDL in patients with and without gallstones.

Methodology

A prospective, observational, hospital based study was conducted at Koshi Zonal Hospital from March 2017 to Feburary 2018. Fifty four patients having gallstone (Group A) were compared with equal number of patients without gallstone (Group B). Data was entered into SPSS/MS Excel. Statistical Analysis was done by using Chi-square test. A 95% confidence interval was taken, and P value less than 0.05 was considered as statistically significant.

Results

In Group A, 61%(33) patients were of age less than 45 years and 91%(49) were female. In group A, 3.7 %(2) and in group B, 7.4%(4) had raised serum cholesterol. Greater number of patient in group A had raised serum triglyclyceride and LDL as compared to group B. 18.5%(10) of group A had low serum HDL, and 9.3% (5) of group B had low serum HDL. Except for finding of gallstone more common in female, other findings had no statistical significance.

Conclusion

There exists an inverse correlation between Serum Cholesterol and serum HDL with gallstone and positive association between serum Triglyceride and serum LDL with cholelithiasis. However the association could not reach the statistical significance.

KEY WORDS

Cholelithiasis, gallstone, serum lipid

INTRODUCTION

Cholelithiasis is presence of stone in gallbladder. Gallstone disease (GSD) is one of the most common gastrointestinal diseases seen in clinical practice. Female sex, obesity, pregnancy, fatty foods, Crohn's disease, terminal ileal resection, gastric surgery, hereditary spherocytosis, sickle cell disease, and thalassemia are all associated with an increased risk for developing gallstones.[2] However, only first-degree relatives of patients with gallstones and obesity (body mass index >30 kg/m^{2}) have been identified as strong risk factors for development of symptomatic gallstone disease.[3] Prevalence has been found to 11% to 36% in autopsy.[4]

Gallstones are among the most common gastrointestinal illness requiring hospitalization. Approximately 1–2% of asymptomatic patients will develop symptoms requiring cholecystectomy per year, making cholecystectomy one of the most common operations performed by general surgeons.[5] Gallstones in patients without biliary symptoms are commonly diagnosed incidentally on ultrasonography, CT scans, abdominal radiography, or at laparotomy.

There are three types of gallstones, Cholesterol, Pigment and mixed. By definition cholesterol gallstones contain more than 70% cholesterol whereas pigment stones contain <20% cholesterol. Whereas those containing intermediate amounts of cholesterol are labeled as mixed stones. Whether it be cholesterol or mixed stones, the common primary event in the formation of gallstones is supersaturation of bile with cholesterol. Therefore, high bile cholesterol levels and cholesterol gallstones are considered as one disease.

METHODOLOGY

This was a prospective, observational and hospital based study conducted at Koshi Zonal Hospital. study period was one year from March 2017 to Feburary 2018. Using LDL cholesterol values from the study Correlation of Serum Lipids and Glucose Tolerance Test in Cholithiasis,– Standard deviation (SD) for control is 10.2 and for cases is 23.8, with power of 80% and level of significance of 0.05, true difference of population means assumed to be 10, sample size for each group was 54 (Russ length power and sample size). Over a period of study, first 54 patients admitted to the hospital with the diagnosis of cholelithaisis for cholecystectomy formed 1st group whereas 2nd group was constituted by admitted 54 patients with diagnosis other than cholelithiasis. The diagnosis of cholelithaisis and absence of cholelitaisis was based on Ultrasonography finding. Group A: Patients with gallstone and Group B: Patient without gallstone were include in the study. Children <15 yrs, pancreatitis, cholangitis, diabetes, cardiac disease(Myocardial infarction, CHD, Angina pectoris), renal disease and others with serious illness (Perforation peritonitis, Strangulated Hernia) were excluded from the study. Data of the study conducted was obtained from history and physical examination as well as the completed pro forma mainly by the principal investigator after meeting all the criteria mentioned. Upon receiving a case fulfilling the inclusion criteria, the participants were explained about the study in detail. He or she was assured of full confidentiality and a written informed consent taken subsequently. On admission Fasting venous blood samples was collected under strict aseptic precautions with informed consent. Serum total cholesterol, HDL cholesterol, triglycerides, levels were estimated by ERBA fully automated biochemistry analyzer. LDL calculated with following formula LDL=Total cholesterol –(triglyceride/5+HDL). Interim analysis of data was performed upon completion of the study. These data were entered into the computer using SPSS and Microsoft Excel Software. Statistical Analysis were done by using Chi-square test and Fisher's exact test. Data were expressed in the form of tables and charts where feasible. A 95% confidence interval were taken, and P value less than 0.05 was termed as statistically significant. Ethical clearance was obtained from the concerned authority.

RESULTS

Fifty-four cases (Group A) and equal number of controls (Group B) were included in the study. In group A 61%(33) patients were of less than 45 years of age whereas 39%(21) patients were of more than 45 years .Similarly in Group B, 52% (28) were of less than 45 years and 48%(26) were of more than 45 years.

In group A, 91%(49) were female and 9%(5) were male. In group B 70%(38) were female and 30% (16)were male.

Table 1: Odds ratios (with 95% confidence interval)			
Age	**OR**	**95% CI**	
		Lower	**Upper**
<45 yrs	1.459	0.679	3.134
>45 yrs	Ref		
Sex			
Female	4.132	1.386	12.345
Male	Ref		

Probability of having gallstone in those who are less than 45 yrs is 1.459 (0.679-3.134) times higher than those who are more than 45 yrs of age. Probability of having gallstone in female is 4.132 (1.386-12.345) times higher than male.
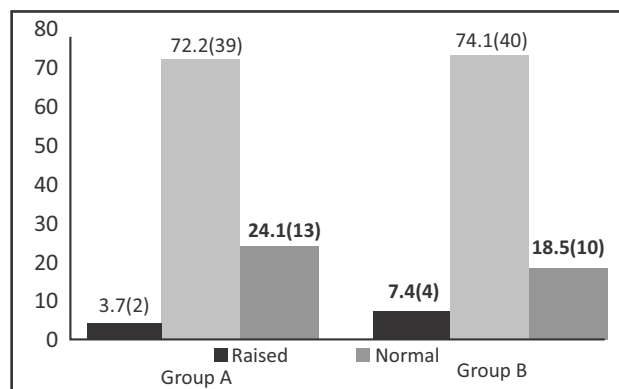

Figure : Distribution of Serum Cholesterol in group A and group B.

In group A, 72% (39) cases had cholesterol level in normal range whereas 4%(2) had increased serum cholesterol and 24% (13) had lower serum cholesterol. Among non gallstone group B 74% (40) had normal serum cholesterol whereas 7%(4) had raised level and 19%(10) had lowered serum cholesterol.
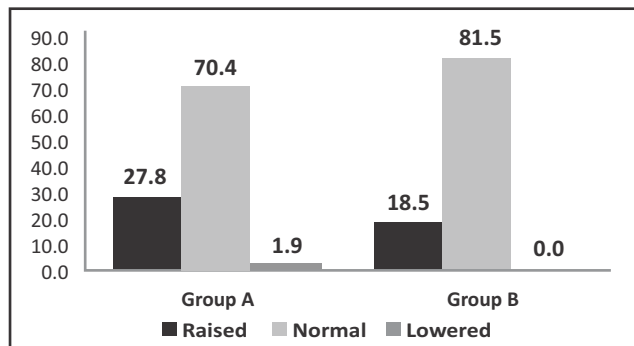

Figure 4 : Distribution of Serum Triglyceride in group A and group B

In Gallstone group, 28%(15) had raised serum triglyceride where as 70% (38) had normal and 2 % (1) had low serum triglyceride. In Group B 19 %(10) had raised serum triglyceride whereas 81% (44) had had normal serum triglyceride.
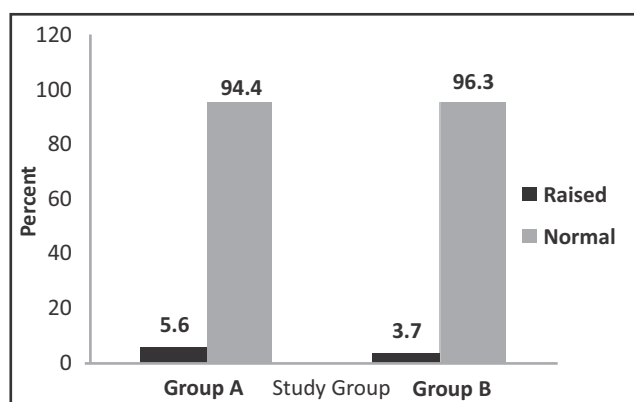

Figure 5 : Distribution of Serum LDL in group A and group B

Among Group A patient 6% (3) had raised serum LDL and 94% (51) had normal serum LDL. In group B 4 % (2) had raised where as 96% (52)had normal serum LDL level.
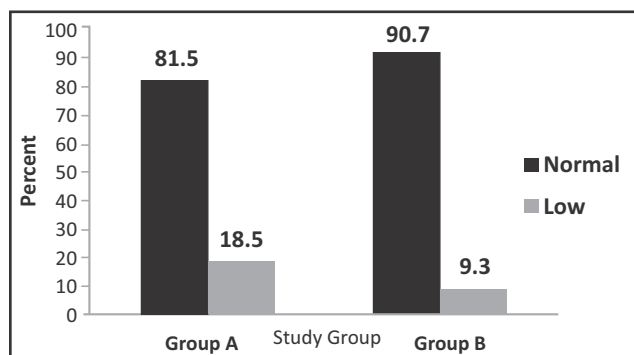

Figure 6 : Distribution of Serum HDL in group A and group B

In Gallstone group 82% (44) had normal where as 18% (10) had low Serum HDL. Similarly in Group B 91% (49) had normal Serum HDL where as 9% (5) had low values.

Table 2 : Comparison of raised serum cholesterol in Group A and Group B.

Serum Cholesterol	Group A		Group B		Total	
	N	%	N	%	N	%
raised	2	**3.7**	4	**7.4**	6	5.6
not raised	52	96.3	50	92.6	102	94.4
Total	54	100.0	54	100.0	108	100.0

p-value: 0.678

Lesser number of patients 3.7% (2) in group A had raised serum cholesterol than group B 7.4%, (4),giving an Odds ratio of 0.481 (0.084-2.742.

Further analysis was done by combining normal and low values of serum triglyceride and was termed as not raised. This was compared with the raised value to obtain odd ratio.

Table 3: Comparison of raised serum triglyceride in Group A and Group B.

Serum triglyceride	Group A		Group B		Total	
	N	%	N	%	N	%
raised	15	27.8	10	18.5	25	23.1
not raised	39	72.2	44	81.5	83	76.9
Total	54	100.0	54	100.0	108	100.0

27.8% (15)of group A has raised serum triglyclyceride and only 18.5 % (10) of group B have raised serum triglyclyceride giving an Odds ratio of 1.692 (0.682-4.199). (p-value: 0.254)

Further analysis was done by comparing normal values of serum LDL and was termed as not raised. This was compared with the raised value to obtain odd ratio.

Table 4 : Comparison of raised serum LDL in Group A and Group B

Serum LDL	Gall stone				Total	
	Group A		Group B			
	N	%	N	%	N	%
Raised	3	5.6	2	3.7	5	4.6
not raised	51	94.4	52	96.3	103	95.4
Total	54	100.0	54	100.0	108	100.0

In only 5.6% (3) of group A showed raised serum LDL where as 3.7 % (2) of group B had increased serum LDL giving an Odds ratio of 1.529 (0.245-9.538). (P-value: 1.000)

Further analysis was done by comparing Lower values of serum HDL and was termed as not raised. This was compared with the raised value to obtain odd ratio.

Table 5 : Comparasion of raised serum HDL in Group A and Group B

Serum LDL	Group A		Group B		Total	
	N	%	N	%	N	%
Normal	44	81.5	49	90.7	93	86.1
Low	10	18.5	5	9.3	15	13.9
Total	54	100.0	54	100.0	108	100.0

Though 18.5% (10) of group A had low serum HDL only 9.3 (5) of group B had low serum HDL giving an Odds ratio of 2.22 (0.706-7.04). (p-value: 0.164)

Table 6 : Mean and Standard deviation of Lipid profile in Group A and Group B

Lipid Profile	Group A		Group B		Total		p-value*
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation	
Serum Cholesterol	168.06	35.215	178.44	43.212	173.25	39.578	0.174
Serum Triglyceride	133.28	69.616	121.98	49.367	127.63	60.332	0.333
Serum LDL	96.52	29.297	90.87	27.330	93.69	28.340	0.303
Serum HDL	42.19	10.146	45.89	11.856	44.04	11.139	0.084

*independent sample t-test

Table 6 gives the average values of Lipids in the forms of means and their Standard deviation. The table shows higher values of Serum Cholesterol and Serum HDL in group B. while Serum Triglyceride and Serum LDL are found to be more in group A.

DISCUSSION

Gall stone disease is one of the common problems attending in surgical outpatient department. The chief constituents of gallstones are cholesterol, bilirubin and calcium.1 Other constutientsmay include fatty acids, triglycerides, protein and polysaccharides. In the great majority of stones encountered in the Western world, the principal constituent is cholesterol, which usually comprises 70 to 98 per cent of the dried substance of the stone.Lipids, such as cholesterol and triglyceride are insoluble in plasma. They are made soluble by attachment to circulating lipoproteins that transport lipids to various tissues for energy utilization, lipid deposition, steroid hormone production, and bile acid formation. A standard serum lipid profile measures the concentration of total and HDL-cholesterol (HDL-C) as well as the triglycerides. In our study we have studied on different variables like age, sex, and serum lipids including serum cholesterol, serum triglyceride, serum low density lipoprotein and serum high density lipoprotein.

Age is a major risk factor for the gallstones. Gallstones are exceedingly rare in children except in the presence of hemolytic states; in addition, less than 5 percent of all cholecystectomies are performed in children. Age 40 appears to represent the cut-off between relatively low and high rates of cholecystectomies. This observation was validated in the Sirmione study in which the incidence between the ages of 40 and 69 years was four times higher than that in younger subjects.[7] In our study we found that 61% of patients belonged to < 45 years and 39% belonged to > 45 years.

Sex is also one of the risk associated with gall stone. A higher prevalence of gallstones has been observed in women in all age groups.[8] In our study also 61% of the patient were < 45 years of age and females predominated in those age group as prevalence cholelithiasis is common in fatty fertile Female of forty. In our study we found probability of having gallstone in those who are less than 45 years was

1.46 times higher than those who are more than 45 yrs of age. As well as probability of having gallstone in female is 4.132 times higher than males The higher rates in young women is almost certainly a result of pregnancy and sex steroids but the actual cause is yet to be delineated and we have not considered these factors in our study.

There are various studies which have shown variability in the association between gallstone and serum lipids. Gallstones appear to be positively associated with apolipoprotein E4 phenotype and elevated serum triglycerides.[9-11] In contrast, a negative association exists between gallstones and high density lipoprotein. There is no conclusive evidence linking elevated serum cholesterol and gallstones.[12]In the study performed by Naseem et al Serum lipid profile were determined in 109 gallstone patients and 100 controls revealed no significant variation except for the triacylglycerols and total lipids, which were differed significantly between females of up to 45 and above 45 years age.[13] We found that 24 % of the cholelithiasis patient had low serum cholesterol, where as only 4 % of them had increase cholesterol level And in 7.4 % of those who did not have gall stone had raised serum cholesterol and 18.5 % had low serum cholesterol level. In a prospective study performed by Kumari et al in a population of Guntur city and compared 82 patients of cholelithiasis cases 117 control subjects of healthy males. Their result showed gall stone was associated with low serum cholesterol and HDL and high serum Triglyceride level which was comparable to our study.[14] This inverse relationship between serum cholesterol level and gallstone disease was also shown by Maria Ximena et al who concluded that an increment in the catabolic pool of cholesterol, reflected in lower levels of plasma cholesterol in subjects with gallstone disease.[15]

In our study 27.8% of cholelithiasis patient had raised serum triglyceride and only 18.5% of control subjects showed raised serum triglyceride level with odds ration of 1.69, though this result was not statistically significant. In Sivakumaran et al increased level of triglyceride level was seen in gallstone patient in both sexes of all age group.[16] They have also shown raised level of cholesterol in patient with gall stones which was just the opposite to our study. Devesa et al have reported a positive association between gallstone and serum triglyceride in Spanish men.[17]

In our study 5.6% of cholelithiasis patient had raised serum Low Density Lipoprotein as compared to only 3.7% of control group showed serum LDL. Similar association between LDL and Chlelithiasis has been shown by various other studies. Chapma et al found a positive association between gallstone disease and serum triglyceride, serum LDL cholesterol and decreased HDL cholesterol all of which were comparable to our results.[18]

In our study serum HDL was low in 18.5% of gallstone patient whereas it was low only in 9.3% of control subjects.

Most of the studies have shown similar association between HDL and gallstone. Chen et al. also found a positive association between gallstone disease and decreased HDL cholesterol level.[18] Similar results as shown by Kumari et al who compared 82 patients of cholelithiasis cases 117 control subjects showed gall stone was associated with low serum cholesterol and HDL and high serum Triglyceride level which was comparable to our study.[14]

Different study showed a positive association between gallstone disease and increased level of serum triglyceride and LDL cholesterol and decreased HDL cholesterol.[18-19] Our study also showed the similar association which could not reach statistical significance.

CONCLUSION

There exist an inverse correlation between serum Cholesterol and serum HDL with gallstone and positive association between serum triglyceride and serum LDL with cholelithiasis. However the association could not reach the statistical significance

RECOMMENDATION

The main objective behind this research is to determine the relationship between serum lipid and gallstone. Based on this study dietary risk factors associated with gallstone disease can be formulated that will help in prevention and management of gallstone disease.

CONFLICT OF INTEREST

We declare no conflict of interest.

FINANCIAL DISCLOSURE

None

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