ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

ROLE OF HYPERCHOLESTEROLEMIA IN GALLSTONE FORMATION

Puneet Jain, Narinder Singh, Hardeep Singh Gill , Anantbir Singh Lubana, Gurmanpreet

1. Dr. Puneet Jain, Assistant professor, Department of General Surgery, Dr. Y.S Parmar Government Medical College, Nahan, Himachal Pradesh.
2. Dr. Narinder Singh, Assistant professor, Department of General Surgery MM Institute of Medical Sciences & Research, Mullana University, Ambala, Haryana.
3. Dr. Hardeep Singh Gill, Professor, Department of General Surgery, MM College of Medical Sciences & Research, Sadopur, Ambala, Haryana.
4. Dr. Anantbir Singh Lubana, Post graduate resident, Department of General Surgery, GGS Medical College & Hospital, Faridkot, Punjab, India.
5. Dr. Gurmanpreet, Professor, Department of Biochemistry, MM College of Medical Sciences & Research, Sadopur, Ambala, Haryana.

CORRESPONDING AUTHOR-

Dr. Hardeep Singh Gill, Professor, Department of General Surgery, MM College of Medical Sciences & Research, Sadopur, Ambala, Haryana.

PHONE- 9877983226

E MAIL- hardeepgill77@gmail.com

Abstract: Hypercholesterolemia plays a significant role in the formation of gallstones more important being the cholesterol gallstones. Lipid parameters including total cholesterol, triglycerides, high density lipoproteins and low-density lipoproteins show a significant relation with cholesterol gallstones. Patients with cholesterol type of gallstones have lipid profile parameters towards undesirable ranges as compared to other stones.

Keywords: Hypercholesterolemia, gallstones, triglycerides, lipid, cholesterol

INTRODUCTION

Cholesterol plays an important role in formation of gallstones. Cholesterol gallstone formation involves: Supersaturation of bile with cholesterol as a result of enhanced hepatic cholesterol synthesis. Cholesterol is secreted into bile as cholesterol-phospholipid vesicles. Cholesterol is held in solution by micelles, a conjugated bile salt-phospholipid-cholesterol complex, as well as by the cholesterol-phospholipid vesicles. The presence of vesicles and micelles in the same aqueous compartment allows the movement of lipids between the two. Vesicular maturation occurs when vesicular lipids are incorporated into micelles. Vesicular phospholipids are incorporated into micelles more readily than vesicular cholesterol. Therefore, vesicles may become enriched in cholesterol, become unstable and then nucleate cholesterol crystals. In unsaturated bile, cholesterol enrichment of vesicles is inconsequential. In the supersaturated bile, cholesterol-dense zones develop on the surface of the cholesterol-enriched vesicles, leading to the appearance of cholesterol crystals. About one third of biliary cholesterol is transported in micelles, but the cholesterol-phospholipid vesicles carry the majority of biliary cholesterol [1]. Hypertriglyceridemia is associated with an increased incidence of gallstone formation. Epidemiologic investigations have shown that plasma HDL cholesterol levels are inversely related with the prevalence of cholesterol gallstones. [2]

Impaired lipid homeostasis can give rise to cholesterol hyper secretion from biliary canaliculi and patients with cholesterol gallstones are more likely to have serum lipid parameters towards the undesirable cut off levels of their respective normal ranges [3].

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

It is now widely accepted that the primary event in pathogenesis of cholesterol gallstones is an altered lipid metabolism because of which there is a relative increase in the cholesterol levels compared to other lipids secreted by the liver into the bile and the changes in serum lipid profile are a possible consequence of presence of gallstones within the biliary tract.[4]

MATERIALS AND METHODS

Source of data: Patients admitted to tertiary care hospital with the diagnosis of gallstone disease for open and laparoscopic cholecystectomy from November 2021 to November 2023 were taken for this observational study. 50 cases with calculous cholecystitis or chronic cholelithiasis in age groups 21-60yrs were studied. Patients on lipid lowering drugs were excluded from study. Serum sample of 50 patients of gallstones was sent for analysis of parameters of lipid profile which included total cholesterol, triglycerides, HDL and LDL. These parameters were estimated by enzymatic test assays on fully automated biochemical analyzer in clinical biochemistry lab of the hospital.

Data analysis was performed after dividing the patients into four separate groups on basis of stone type and arranging as per total cholesterol, triglycerides, HDL and LDL values. Results were expressed as Mean ± Standard Error and $p < 0.05$ was taken as significant. Statistical analysis was performed on Statistical Package for the Social Sciences (SPSS) 20.0 software

RESULTS

Table – 1 Comparison of serum lipid profile in cholesterol and pigment gallstone patients

Lipid profile	Type of Gall stone		p-value	Significance
	Cholesterol (n =26)	Pigment (n = 22)		
Total Cholesterol	225.58±6.04	198.23±2.79	0.000	S
Triglycerides	178.69±8.36	139.82±6.03	0.001	S
HDL	47.08±2.89	59.86±2.68	0.002	S
LDL	148.00±6.52	126.00±6.35	0.021	S

$p<0.05$ – Significant(S)

Table – 2 Comparison of serum lipid profile in cholesterol and pigment gallstones in age group 21-40 years

Lipid profile	Type of Gall stone		p- value	Significance
	Cholesterol (n =5)	Pigment (n = 7)		
Total	186.00±10.95	187.43±2.52	0.884	NS

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

Cholesterol				
Triglycerides	151.20±22.88	122.71±12.80	0.270	NS
HDL	55.80±9.77	57.57±4.21	0.856	NS
LDL	116.20±8.60	113.71±6.50	0.819	NS

p<0.05 – Significant(S) NS-Non significant

Table – 3 Comparison of serum lipid profile in cholesterol and pigment gallstones in age group 41-60 years

Lipid profile	Type of Gall stone		p- value	Significance
	Cholesterol (n=21)	Pigment (n=15)		
Total Cholesterol	234.95±4.76	203.27±3.19	0.000	S
Triglycerides	186.90±8.96	147.80±5.73	0.002	S
HDL	45.19±2.61	60.93±3.47	0.001	S
LDL	152.05±6.37	131.73±8.54	0.060	NS

p<0.05 – Significant(S)

NS-Non significant

Table – 4 Comparison of serum lipid profile between age groups 21-40 years And 41-60 years

Lipid profile	Age group (years)		p- value	Significance
	21-40 (n = 12)	41-60 (n = 38)		
Total Cholesterol	186.83±4.50	224.56±4.15	0.000	S
Triglycerides	134.58±12.22	169.64±6.26	0.008	S
HDL	56.83±4.49	51.64±2.48	0.298	NS
LDL	114.75±4.98	145.64±5.64	0.004	S

p<0.05 – Significant(S)

NS-Non significant

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

DISCUSSION

Comparison of serum lipid profile in cholesterol and pigment gallstone patients revealed significant differences in mean values of all serum lipid profile parameters with total cholesterol, triglycerides and LDL values towards higher side in patients with cholesterol gallstone and HDL toward lower side as compared to pigment gallstones **(Table 1).**

Cholesterol plays an important role in formation of gallstones. It is now widely accepted that the primary event in pathogenesis of cholesterol gallstones is an altered lipid metabolism because of which there is a relative increase in the cholesterol levels compared to other lipids secreted by the liver into the bile and the changes in serum lipid profile are a possible consequence of presence of gallstones within the biliary tract. This is in accordance with study of undisputable behaviour of lipid profile in cholelithiatic gallbladder by Nagaraj and Satish Kumar and hence consistent with our study [4].

Detection of significantly high **serum triglycerides** in patients with cholesterol gallstones is supportive evidence to indicate hypertriglyceridemia as a risk factor of cholesterol gallstones. Hypertriglyceridemia is identified as a cause for gallbladder hypomotility as it reduces the gallbladder sensitivity to cholecystokinin, a paracrine hormone that regulates the gallbladder contraction. Gallbladder hypomotility is one of the main causes for cholesterol crystallization. Therefore, the negative effect of serum triglyceride on gallbladder motility can be considered as a cause to develop cholesterol gallstones than pigment gallstones in people with high risk of gallstone disease. High serum triglycerides in patients with gallstones is revealed in case control studies carried out in countries with high prevalence of gallstone disease as well.[3] [5] [6].The findings of these studies were consistent with our present study where we found significantly higher values of serum triglycerides in patients with cholesterol gallstones.

Andreotti et al.[6] in their population based study on serum lipid levels and risk of biliary stones concluded that low levels of **serum HDL** were associated with 4.2 fold risk of biliary stones and Fu et al.[7] identified a positive correlation between a low serum HDL level and cholesterol gallstone development whereas Thijs et al.[5] also revealed a relationship between a low serum HDL level and gallstone disease. These findings were consistent with our present study where serum HDL levels in patients with cholesterol gallstones were on lower side as compared to patients with pigment gallstones and this difference was statistically significant.

A high **serum LDL** level was described as a marker for increased risk of cholesterol gallstone disease by Fu et al. Similarly, Halldestam et al and Han et al. revealed a positive correlation between a high serum LDL level and cholesterol gallstone development [8]. Also Nagaraj et al.[4] study on undisputable behaviour of lipid profile in cholelithiatic gallbladder concluded that serum LDL levels also play an important role in formation of gallstones. The findings of above mentioned studies are consistent with our study where serum LDL levels in patients with cholesterol gallstones were on higher side and showed significant difference as compared to serum LDL levels in patients with pigment gallstones.

Patients with cholesterol and pigment gallstones were divided into two age groups one from 21-40 years and other from 41-60 years. Mean serum lipid profile values of patients with cholesterol and pigment gallstones in age group 21-40 years was compared and no significant differences ($p>0.05$) were observed **(Table 2).** In patients with cholesterol and pigment gallstones in age group 41 to 60 yrs there was significant elevation in mean total cholesterol and triglyceride levels in patients with cholesterol gallstones, whereas significantly lower mean value of HDL in patients with cholesterol gallstones. Mean value of

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 11, 2023

LDL was noted to be higher among patients with cholesterol gallstones but no significant difference were noted when compared to patients with pigment gallstones **(Table 3).**

This shows alteration in serum lipid profile values in higher age group range. Also on comparison of mean serum lipid profile values of patients in two different age groups 21-40 and 41-60 years irrespective of stone type it was observed that lipid profile values significantly alter with increasing age with mean total cholesterol, triglycerides and LDL values towards higher side and showing statistically significant differences and lower mean value of HDL in 41-60 year age group range(but statistically not significant).Majority of cholesterol gallstones(n=21) occurred in higher age group range (41-60 years) and also were associated with mean lipid profile values towards undesirable range **(Table 4).**

Einarsson K. et al.[9]in their study on the influence of age on secretion of cholesterol and synthesis of bile acids by the liver concluded that cholesterol saturation of bile increases with age as a consequence of enhanced hepatic secretion of cholesterol and decreased bile acid synthesis. As per their study age was positively correlated with cholesterol secretion rate and hence consistent with our study.

CONCLUSION

Hypercholesterolemia plays a significant role in the formation of cholesterol gallstones. Investigation of serum lipid profile must always be included as a part of routine workup in the treatment of gallstone disease more importantly in individuals of higher age group as they mostly show lipid profile parameters towards undesirable range and appropriate medical treatment for altered lipid profile parameters must be started along with treatment of gallstone disease.

REFERENCES

1. F. Charles Brunicardi. Gallbladder and the Extrahepatic Biliary System Schwartz principles of surgery.10th ed, page no.1309-1340. Mc Graw Hill Company, New York, 2015.
2. Mark Feldmen, Lawrence S. Friedman, Lawrence J. Brandt. Gallstone Disease. Sleisenger and Fordtran's Gastrointestinal and Liver Disease.10th ed. Page no. 1100-1133 ,Elsevier Company, Philadelphia, 2016
3. Weerakoon HT1, 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.
4. Nagaraj, Kumar SD. Undisputable behavior of lipid profile in cholelithiatic gall bladder. J Biomed Pharma Res. 2014; 3(4):54-57.
5. Thijs C, Knipschild P, Brombacher P. Serum lipids and gallstones: A case-control study. Gastroenterology. 1990; 99(3):843-9.
6. Androtti G, Chen J,Gao YT, Rashid A, Chang SC, Shen MC et al. Serum lipid levels and the risk of biliary stones: A population-based study in China. Int J Cancer. 2008; 122(10):2322-29.
7. Fu X, Gong K, Shao X. The relationship between serum lipids, apolipoproteins level and bile lipids level, chemical type of stone Zhonghua Yi Xue Za Zhi. 1995; 75(11):656-9.
8. 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(1):187-190.
9. Einarsson K, Nilsell K, Leijd B, Angelin B. Influence of age on secretion of cholesterol and synthesis of bile acids by the liver. N Engl J Med. 1985; 313(5):277-82.