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Serum Lipid Profile in Patients with Gallstone Disease – Analysis in a Tertiary Care Hospital in North East India

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ABSTRACT

Background: Gallstone disease (GSD) is the most common disorder affecting the biliary system and is also the most common gastro-intestinal disorder requiring hospitalisation. Gallstones in patients without biliary symptoms are commonly diagnosed incidentally on ultrasonography, CT scans, and abdominal radiography. But, there is lack of evidence regarding relation of cholelithiasis and lipid profile. In this study the association of serum lipids to cholelithiasis has been tried to been elucidated. **Methods:** A Cross sectional study was conducted at Jawaharlal Nehru Institute of Medical sciences, Imphal from 1st September 2017 to 31st August 2019. All patients with GSD coming to the general surgery OPD above 18years were included in the study with few exclusion criteria. The diagnoses of gallstones were confirmed by ultrasound (USG) and venous blood sample was used to estimate lipid profile. All data were entered on a personal computer in Microsoft Excel and analysed using SPSS version 20 software. Descriptive data is given in frequency and percentage. Chi-square was used to find the association between different variables. **Results:** In our study of 312 patients, mean difference of the lipid profile had a statistically significantly association with the weight of the stone. All biochemical parameters like T.Cholestrol, TGL, HDL, LDL and VLDL were compared and showed a p-value of less than 0.005. Serum SGOT, SGPT & TGL had a statistical significant association with average weight of stone. (p=0.050). **Conclusion:** Biochemical parameters like SGOT, SGPT, and ALP influenced the type and weight of stone significantly. Similarly, while comparing the weight of the stone with lipid profile, a significant association was observed.

Keywords: Cholelithiasis, Gallstones, Lipid profile.

INTRODUCTION

Gallstone disease (GSD) represents a significant burden for health-care systems worldwide and is one of the most common disorders among patients attending as emergency in hospital with abdominal discomfort.[1] The incidence of gallbladder diseases (GBD) has a specific geographic and ethnic variation. The risk factors of GSD are obesity, multiparity and chronic infection. It is mentioned that GSD play a major role in Gall bladder Carcinoma (GBC) development.[2] Gallstones, or cholelithiasis, are solid masses produced from bile precipitates. These "stones" may occur in the gallbladder or the biliary tract. There are two types of gallstones: cholesterol and pigment stones. Both types have their own unique epidemiology and risk factors. Pigment stoens are of two types viz. black and brown pigment stones. Black pigment stones are more likely to remain in the gallbladder. Brown pigment stones are composed of calcium salts of unconjugated bilirubin with small amounts of cholesterol and protein. These stones are often located in bile ducts causing obstruction and are usually found in conditions where there is infected bile. Brown pigment stones are prevalent in Asian countries.[3]

Most people with gallstones do not have symptoms; however those who do have symptoms are much more likely to develop complications. Often these complications are due to inflammation, infection, or ductal obstruction causing acute cholecystitis, choledocholithiasis, cholangitis, pancreatitis, emphysematous cholecystitis, cholecysto-enteric fistulae, Mirizzi's syndrome, and porcelain gallbladder. Biliary colic is the most common symptom characterized by episodic pain with moderate to severe intensity in the right upper quadrant occasionally in the epigastrium also. The interval between "attacks" is unpredictable and may range from days to months or years. Supersaturation of bile in cholesterol, enhanced nucleation of cholesterol crystals, impaired gallbladder emptying with stasis and intestinal hypomotility are the pathogenetic mechanisms responsible for cholesterol gallstone formation.[4]

There is a paucity of information on association of abnormal lipid profile parameters with gallstone

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disease (GSD) in Western India as earlier studies were carried out in other parts of the country.[5] Therefore, this study was undertaken to compare serum lipid parameters including total cholesterol (TC), triglycerides (TG), HDL-c, low density lipoprotein cholesterol (LDL-c), very low density lipoproteins (VLDL) levels in patients with GSD. 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.[6] Gallstones in patients without biliary symptoms are commonly diagnosed incidentally on ultrasonography, CT scans, abdominal radiography, or at laparotomy. But, there is lack of evidence regarding relation of cholelithiasis and lipid profile. In this study the association of serum lipids to cholelithiasis has been tried to been elucidated.

MATERIALS AND METHODS

This is a cross-sectional study conducted in the department of general surgery, Jawaharlal Nehru Institute of Medical Sciences from 1st September 2017 to 31st august 2019.Patients with intra-hepatic calculi, patients on anti-lipidemic drugs and patients who didn't undergo either open or laparoscopic cholecystectomy were excluded. A total of 312 patients coming with complaints related to GSD were enrolled in the study. The diagnoses of gallstones were confirmed by ultrasound (USG) and venous blood sample was used to estimate lipid profile. Based on the severity of the clinical signs and symptoms and the USG report, the treatment modality was decided. Patients who presented with acute pain abdomen, guarding, rigidity and obstructive symptoms with cholelithiasis were managed with nil by mouth, intravenous fluids, intravenous antibiotics, analgesics and Ryle's tube aspiration if necessary. The study was approved by Institutional ethics committee. Informed consent was taken from all the patients. The gall stones were sent for biochemical analysis and the gall bladder specimens were sent for histopathological examination.

Data on clinical, laboratory results including serum lipid profile was analysed. Additionally data related to Hospital course, Complication, and Outcome were also analysed. All data were entered on a personal computer in Microsoft Excel/SPSS software. The data were analysed using SPSS version 20 software. During analysis of data, Descriptive data is given in frequency and percentage. Chi-square was used to find the association between different variables. Other statistical methods were utilised wherever appropriate. The p value of less than 0.05 was considered as statistically significant.

RESULTS

Females (N=279) population had a majority in the present study as against their male counterparts (N=33).Majority of the study population belonged to the age group of 41-50 years and the least number of gall stones were seen among the age group of 18-20 yrs. Gender distribution had a statistically significant association with gall bladder disease. The mean height of the study participants were 156.24 cms and the mean weight were 58.14 kgs. Mean BMI estimated among the study participants was 24.2. Majority of the study participants had no significant medical history (81.4%). The common surgical procedure they encountered was LSCS which was seen in 36.22% of the study participants. Abdominal pain was the commonest presentation in about 39% of the cases followed by dyspepsia in about 28% cases. None of the patients reported features of cholangitis. 14% of the cases had incidence of thickened gall bladder wall however majority of the participants had normal thickness of gall bladder. Presence of multiple stones happened in 73% of the cases whereas 27% had single gall stones. Pure cholesterol stone was the commonest type of stone in both male (17) and female (173) than other types of stone and the association of type of stones seen among gender distribution was statistically significant.56.8% of the patients with gall stone disease had pure cholesterol stone, 24.9% had mixed stone, Dolomite and Calcium bilirubinate were 8.1% and 10.2% respectively.

Table 1: Association of Lipid profile and weight of the stone.

Variables	T.cholesterol	TGL	HDL	LDL	VLDL
Mean	178.85	119.30	46.35	109.70	26.32
Std. Error of Mean	2.391	3.876	.762	2.379	.883
Median	174.00	96.00	45.00	108.00	22.00
Std. Deviation	42.164	68.362	13.444	41.961	15.569
Minimum	120	22	26	34	6
Maximum	438	415	96	347	116
p-value	0.000	0.000	0.000	0.002	0.000

Table 2: Serum TGL compared with type of stone

TGL (mg/dl)	Type of stone				Total	p-value
	Pure Cholesterol	Mixed	Dolomite	Calcium Bilirubinate		
<50	15	8	0	0	23	
51-60	91	26	13	10	140	

61-70	46	21	7	0	74	0.009
71-80	24	15	0	0	39	
>80	22	5	4	4	35	
Total	198	75	24	14	311	

Table 3: Association of size of the stone and biochemical parameters

Variables	SGOT	SGPT	ALP	Total protein	Serum albumin
Mean mg/dl	35.12	40.66	113.16	7.463	4.109
Std. Error of Mean	1.101	1.501	3.110	.0372	.0245
Median	30.00	35.00	101.00	7.500	4.200
Std. Deviation	19.415	26.472	54.851	.6557	.4314
Minimum	16	11	38	5.5	2.4
Maximum	108	175	438	8.9	4.9
p-value	0.050	0.050	0.050	0.001	0.001

There was a statistical significant mean difference between the biochemical parameters like SGOT, SGPT, ALP, T.Protein and Serum albumin among the study population with cholelithiasis. (P-value 0.050). Mean difference of the lipid profile had a statistically significantly association with the weight of the stone All biochemical parameters such as T.Cholesterol, TGL, HDL, LDL and VLDL were compared and showed a p-value of less than 0.005. Serum SGOT, SGPT & TGL had a statistical significant association with average weight of stone.(p=0.050)

The most frequent post-operative complication observed was upper abdominal pain (68.26%) followed Nausea and Vomiting (25.64%). Maximum number of days stayed post operatively was 4 days. Majority of the cases had a maximum stay of 2 days after surgery (74%). The most common histopathological finding was chronic cholecystitis (66.1%) and the least common finding was acute cholecystitis (2.3%)

Mean difference of the lipid profile was statistically significant based on the weight of the stone. All parameters such as T.Cholestrol, TGL, HDL, LDL, VLDL were compared and showed a p-value of less than 0.005. [Table 1]

Serum TGL had a statistical significant association with the type of the stone as shown above (p=0.009). [Table 2]

There was a statistically significant mean difference between the biochemical parameters like SGOT, SGPT, ALP, Total protein and Serum albumin among the group as shown above. [Table 3]

DISCUSSION

Gallstones (GS) are formed as a result of impaired metabolic regulation in the human body. Abnormal lipid metabolism is partly responsible for the pathogenesis of Gall stones which is mainly rich in cholesterol. Literature review on previous Indian studies showed that the incidence of gall stones was more in northern India as compared to that in southern India. The present study describes the pattern of serum lipid concentrations in patients with Gall Stones from North-east India. The prevalence of GS may vary according to gender. Females have a higher incidence of gall stones when compared with their male counterparts, from this study and the same were also observed in studies done by Shaffer et al.[7,8] Multiple reasons have been evaluated in the identification of gender difference as a cause for gall stone disease. The preponderance of gall stone disease in female gender has been well documented in literature. Role of estrogens in formation of gall stones has been experimentally proved. Progesterone too appears to promote production of saturated bile by causing smooth muscle relaxation and impaired gall bladder emptying. Singletary et al have demonstrated presence of estrogen and progesterone receptors in human gall bladder.[9] Studies by Pradhan et al, Jindal et al and Gaharwar.A also echo similar results as in our study with respect to sex distribution.[10-12] However a possible effect of serum lipids causing high incidence of GS among females was identified in this study. Many studies supported to this findings.[13] This is in concordance with study by Ahi et al in April 2017 who have found the maximum prevalence of this disease between 31- 40 years.[14] Mean height of the participants was 58 cm and BMI was 24. However BMI does not play any role in this study. Only few participants had hypertension, hypothyroidism, diabetes and tuberculosis but none of them was significantly associated with gall stones. We found that the proportion of GSD was increasing with increasing age, and this has been corroborated by several other authors.[15,16] Spontaneous changes in BMI over a decade had no association with incidence of gallstone disease in the present study. We have also analysed the association of different biochemical parameters in the development of GSD.

We found that level of plasma triglycerides, total cholesterol, and LDL cholesterol were found not to be significantly associated with the development of GSD. Similar to this, low level of plasma HDL cholesterol was found to be a risk factor for the development of GSD but not statistically significant; similar findings were seen in some other studies whereas some showed that hyperlipidaemia, plasma HDL cholesterol,[17-19] and plasma triglycerides were not significantly associated with GSD.[16] Liver enzymes (AST and ALT) and total bilirubin were not significantly associated with

gallstone formation, consistent with the findings of many studies. In this study liver enzymes had a significant association with weight of the gall stones. Interestingly female patients in the study group had high serum HDL-C than that of male patients. The favourable effects of female reproductive hormones on serum lipids can be considered as a possible reason for such observation.

Thickness of the gall bladder was increased in gall stone patients in certain studies; however majority of the study participants in the present study had normal thickness of gall bladder wall. In this study 73% of study population had multiple stone. Different types of stones were identified in this study, of which pure cholesterol stones were highly prevalent. Also other types of stone were also high among female patients.

The serum cholesterol levels in this study group had a mean value of 178.85mg, mean TGL was 119mg/dl, mean HDL was 46mg/dl, mean LDL was 109mg/dl, mean VLDL was 26mg/dl. Hence in this study, findings showed that lipid profile does not play any significant role in cholelithiasis. Even though the cholesterol level is expected to be high in cases of cholelithiasis, our study did not show a very significant increase, indicating that there might be other pathways to gallstone formation and this needs further study. Roda E et al evaluated that the lowering of cholesterol in post cholescystectomy period due to a more rapid circulation of the bile acid pool in fasting cholecystectomised patients was leading to improved solubility of cholesterol in bile.[20] The existence of relationship between gall stones and serum lipids is an old assumption based on fact that the majority of the gallstones contain cholesterol as one of the constituents. None of the patients in the study group had serum total lipid above the upper limit of 900 mg%. Therefore, biochemical hyperlipidaemia is an uncommon finding in the patients of cholelithiasis.

The colour of the pigment stones could be attributed to colour of bilirubin which forms salt with calcium to form calcium bilirubinate. Brown pigment stones are found in the bile ducts and believed to be caused by biliary stasis and cholangitis due to anaerobic and aerobic bacterial infection, parasitic infestations, or bile seeking worms.[21-25] They contain more cholesterol and fatty acids than black pigment stones.[22,23] Biochemical parameters such as SGOT, SGPT, Total Protein and ALP were compared with stone size. It was observed that there was a statistically significant association as p-value less than 0.01. Cholecystectomy causes redistribution of bile acid pool in the entero-hepatic circulation and increases the frequency of cycling. This exert negative feedback on bile acid synthesis and cause reduction in pool size and hence exerts effect on lipid profile decreasing total cholesterol and LDL cholesterol levels. But, in previous researches also there is no conclusive evidence linking serum cholesterol, elevated serum cholesterol and gall stones.

CONCLUSION

An interesting finding in this study is that the majority of the stones were pure cholesterol stones. Majority of the study participants had normal BMI. Most of them had multiple stones irrespective of gall bladder wall thickness. High percentage of pure cholesterol stones were observed in the study participants when compared with other types of stones. Biochemical parameters such as SGOT, SGPT, and ALP influenced the type and weight of stone in a significant manner. Similarly, while comparing the weight of the stone with lipid profile, there was a significant association observed. This finding is attributed to high percentage of patients with high risk factors such as dyslipidaemia. However, this observation needs further randomized studies to confirm it. Cholesterol stone was the most common type of stones among the participants and cholesterol seem to be the major component of all types of stones, and hence it is regarded as a major key in controlling cholelithiasis.

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