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Cholelithiasis and Its Relationship with Serum Lipids in a Tertiary Care Hospital of Rajshahi.

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Abstract

Background:It is now almost accepted that the disturbance of lipid metabolism may help to develop gallstone disease. Therefore, an increased Lipid profile may be a good predictor for developing gall stones, especially cholesterol stones.

Aim of the Study: *To find the association between gallstones and serum lipids.*

Methods*:* All patients diagnosed with gallstone diseases were enrolled by purposive sampling. After that, they were scrutinized according to eligibility criteria, and 150 patients were finalized in the Department of Surgery at Rajshahi Medical College Hospital, Rajshahi, Bangladesh, from September 2018 to August 2019. Besides, 150 medical staff and patients' attendance with age and sex matches were considered a control group. A pre-tested, observation-based, peer-reviewed data collection sheet was prepared before the study. Data regarding clinical, biochemical, and surgical profiles were recorded. Data were compiled, edited, and analyzed.

Results*: The mean age of both groups was 39.7918.16 years and 38.67±7.99 years respectively. The male-to-female ratio in both groups wasthesame 1:2.57 as it was an age and sex-matchedcase-control study. Out of 150 participants in the study group 48%,24%,23% and 5% were suffering from chronic cholecystitis with cholelithiasis, chronic cholecystitis with choledocholithiasis, acute calculus cholecystitis and empyema gallbladder with cholelithiasis respectively. 61% and 39% of patients had cholesterol stone and mixed stone respectively and undesirable lipid parameters in patients with cholesterol gallstone and mixed stone.The mean values of all cholesterols except HDL-C were higher in the participants of the case group than in the controls.*

Conclusion*: This study emphasized that the lipid profile can be a good indicator for gallstone diseases.*

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I. Introduction

Gallstones disease (GD) or Cholelithiasis is one of the most prevalent gastrointestinal diseases, with a substantial burden to health care systems [1]. The prevalence of GD varies widely by region. In Western countries, the prevalence of gallstone disease reportedly ranges from approximately 7.9% in men to 16.6% in women. In Asians, it ranges from approximately 3% to 15%, is nearly non-existent (less than 5%) in Africans, and ranges from 4.21% to 11% in China. With an overall prevalence of 10-20%, GD represents one of the industrialized countries' most frequent and economically relevant health problems [2]. The prevalence of cholesterol gallstones is increased in obese persons. The risk is especially high in those with the highest body mass index, Erlinger S [3]. The incidence of gallstones increases with age, Massarrat S [4]. Gallstones are classified into three types according to their chemical composition cholesterol, pigment, and mixed stones. Most stones originate in the gallbladder and travel distally into the common duct; however, if the common bile duct is partially obstructed, stones can also form there. Most Cholelithiasis comprises cholesterol, calcium carbonate, calcium bilirubin, or a mixture. Gallstones are believed to form when cholesterol concentration exceeds that which can be held in mixed micelles solution with bile acids and phospholipids. Cholesterol gallstones result from bile secretion by the liver supersaturated with cholesterol. This results in cholesterol crystallization and stone growth within the gallbladder, which can be exacerbated by gallbladder stasis. This may be associated

with obesity, high-caloric and cholesterol-rich diets, or drugs [for example. clofibrate) Moreover, it may result from increased activity of hydroxy methyl glutaryl Co-A (HMG COA) reductase, the rate-limiting enzyme of hepatic cholesterol synthesis, and increased hepatic uptake of cholesterol from the blood. In patients with gallstones, dietary cholesterol increases biliary cholesterol secretion. The composition of the bile salt pool may also influence the ability to maintain cholesterol in solution. Patients over age 60 and those with numerous bowel operations [particularly in the region where the small and large bowel meet] are at especially high risk, Al-Saddi et al. [5]. High triglycerides and low HDL have been most consistently associated with gallstones, whereas the associations of total cholesterol and LDL with gallstones are less consistent, Andreotti G et al. [6]. The etiology of the gallstone is probably multifactorial. The implicated factors are metabolic, infection, and bile stasis. Pathogenesis of black and pigment stones is due to hemolytic, e.g., hereditary spherocytosis, sickle cell anemia, thalassemia, and malaria, in which bilirubin production is increased. Systems mainly in the intra or extrahepatic duct. Their pathogenesis may be due to stasis and infection by gram-negative bacteria, D.Conte et al. [7]. The gallstone can be divided into three groups depending upon their colour: pale yellow and Whitish stones as cholesterol, black and blackish brown as pigment calcul and brownish Yellow or greenish with laminated features as mixed calculate; on the whole, the elevation of serum total cholesterol, LDL cholesterol, tri-acyl glycerols and reduction of HDL cholesterol level seem to play a major contributing role in the pathogenesis of gallstones, especially in females, Channa NA et al. [8]. The role of serum lipids in the etiology of gallstones has been assessed in a case-control study. The highest gallstone risk was. found at low high-density cholesterol levels and high triglyceride levels. An additional weakly negative association was found between total cholesterol level and gallstone risk by Thijs C et al. [9].The main aim of this study was to assess the lipid profile status of cholelithiasis patients and the control group. Gallstones are common in the Western world. The prevalence among adults is approximately 10-15% for men and 20% for women in Europe and North America. American Indians and Mexican Americans have a higher prevalence than Afro-Americans, Schemer et al. In Asia, Kapoor et al. analyzed different risk factors associated with gallstones in a survey conducted in Jharkhand, India [10, 11]. The study purported that a cholesterol-rich diet, especially non-vegetarian consumption (68% of patients were non-vegetarian), and age are the major risk factors. The study also revealed that gallstones are found more frequently in women than men. The ratio of male to female gallstone patients was about 13. Furthermore, 72.6% of cases were between the age of 21-50. The study concluded that the incidence of gallstones increases with age, while genetics, diabetes, and smoking are not much related to gallstone formation. A very high and increasing prevalence has been reported in the northern states. Gallbladder diseases commonly manifest as gallstones (Cholelithiasis), polyps, sludge, cholecystitis, choledocholithiasis, cholesterolosis, and gallbladder cancer. Amongst these numerous gallbladder diseases, gallstones appear to be the most prevalent in American Indians (60-70%), but less prevalent in Hispanics of mixed Indian origin and further reduced amongst Black Americans Shaffer A By analysis of their chemical compositions, gallstones can be categorized into three main types: cholesterol, black pigment stones, and brown pigment stones [12]. The black pigment stones are derived from the precipitation of calcium hydrogen bilirubin, where pigment supersaturation and deposition of inorganic salts, phosphate, and calcium bicarbonate accelerate the nucleation, as reported in the study of Conte et al. [13]. Cholesterol gallstones, on the other hand, form by unphysiological biliary supersaturation from hypersecretion of cholesterol, gallbladder hypo motility, and the accumulation of mucin gel. The explanation given by Conte et al. further illustrates that the brown pigment stones are formed in the ducts due to bile stasis, parasites, uncompleted polymerization of calcium hydrogen bilirubin, saturated fatty acids, and bacterial infection with enzymatic hydrolysis of biliary lipids [14]. As the incidence of gallstone disease escalates, there is a concomitant increase in complications like gallstone-related pancreatitis. Previous work in Saudi Arabia shows that cholesterol stones were predominant compared to mixed and pigment stones, while 57% of the gallstones were of cholesterol variety. The result conforms with the studies conducted in Korea, Germany, the United States, and Singapore. It means that cholesterol stones are high in Saudi Arabia, like in western and other developing countries. Factors predisposing to cholesterol hypersecretion are obesity, ageing, diabetes mellitus, and the use of drugs ageing thiazide and oral conceptions. Estrogenic influences, including oral contraception and pregnancy, increase the expression of hepatic lipoprotein receptors and stimulate hydroxyl-methyl glutaryl Coenzyme A (HMGCOA) reductase activity. Thus both cholesterol levels and biosynthesis are increased from the above observations; the increased incidence of cholesterol stones in Saudi Arabia may be due to a high-fat diet. Again the custom of multiple marriages, multiple pregnancies, and the use of oral contraception by females may be responsible for the increased occurrence of gallstones in females three and half times more as compared to males, Abu-Eshy et al. [15]. The study aimed to find out the association between gallstones and serum lipids.

II. Methodology & Materials

The study was carried out in the Department of Surgery at Rajshahi Medical College Hospital, Rajshahi, Bangladesh, from September 2018 to August 2019. All patients who were diagnosed as patients of gallstone diseases were enrolled by purposive sampling. After that, they were scrutinized according to eligibility criteria, and 150 patients were finalized. Besides, 150 medical staff and patients' attendance with age and sex-matched were considered the control group. A pre-tested, observation-based, peer-reviewed data collection sheet was prepared before the study. Data regarding clinical, biochemical, and surgical profiles were recorded. Data were compiled, edited, and analyzed.

Inclusion Criteria:-

- Adult patient who was diagnosed to have gallstone disease in RMCH
- Sex: Both sex.
- Control was a healthy volunteer from the medical staff& patient's relative (matched for age & sex) who gave consent.

Exclusion Criteria:-

- Patients under 18 years
- Patient with gallbladder malignancy diagnosed by ultrasonography and histopathology, liver cirrhosis, cholangitis, pancreatitis
- Patients on current anti-cholesterol medication
- Hemolytic disorders e.g. sickle cell disease, hereditary spherocytosis
- Diabetes Mellitus, pregnancy 6. Cardiac (Myocardial infarction, CHD, Angina pectoris) and renal disease and others with serious illness will be excluded from the study.

Collected data were analyzed upon completion of the study using the computer SPSS (Statistical Package for Social Science) and Microsoft Excel Software (version 21.0 windows). Statistical student's t-test did the statistical analysis. A 95% confidence interval was taken, and a p-value less than 0.05 was considered statistically significant. Data were expressed in the form of tables and charts where feasible. Ethical clearance from the concerned authority, the Institutional Review Board (IRB) of Rajshahi Medical College, was taken to carry out this study after an explanation of the study purpose, and informed consent, both verbal and written, was taken from the patients. The confidentiality of the patient will be maintained.

III. Result

The overall demographic profile of the case and control groups where it was portrayed that the mean age of both the groups were 39.7918.16 years and 38.67±7.99 years, respectively. The male-to-female ratio in both groups was the same 1:2.57 as it was an age and sex-matched case-control study. This study showed a female predominance with 72% female and 28% male, with a ratio of male and female, which was 1:2.57 in Table-I. Figure 1 shows that out of 150 participants in the study group, 48%, 24%, 23%, and 5% were suffering from chronic cholecystitis with cholelithiasis, chronic cholecystitis with choledocholithiasis, acute calculus cholecystitis and Empyema gallbladder with cholelithiasis respectively diagnosed by ultrasonography. Figure 2 shows that out of 150 participants in the study group, 81% (91) had cholesterol stones, and 39% (59) had mixed stones, respectively (NB-Pigment stones were excluded as per exclusion criteria). Table ll shows that out of 150 participants in the study group, 61% (91) had cholesterol stones. Among them, triglyceride, HDL-C, total cholesterol, and LDL-C were 63%, 80%, 45%, and 40%, respectively. Also, 39% (59) had mixed stones. TN glyceride, HDL-C, and total cholesterol LDL-C were 59.32%, 52.84%, 28.81%, and 25.42%, respectively. Table III Shows that the mean BMI of the case was significantly higher than controls, as these values were 25.73+2.10 and 22.38±1.82, respectively. ($p<0.001$). Table IV shows that the serum TC, LDL-C, and TG were all statistically higher in the case group than in the control group. HDL-C was statistically lower in the case of the study group than in the control. In this study, case group TC (191.78 +/-15.66), TG (146.59 +/-11.97), LDL-C (128.13 +/-10.48), and HDL C (35.46 +/-2.89). The serum TC and TG LDL-C were all statistically significantly higher in the case group than the control group [$p =<0.031$, $p<0.036$, $p<0.001$), respectively. HDL-C was statistically significantly lower in the case group than in the control group. [$pe<0.049$). Figure 3 shows that out of 150 participants in the case group, 148 (98.66%) had non-malignant, and 2 (1.33%) had malignant, respectively.

Table 1: Distribution of patients according to demographic variables (n=300)

Demographic variables	Case (N=150)	Control (N=150)	P-value
Mean age (Years) (Mean±SD)	39.79±8 16		0.43
Sex Distribution			
Gender	12.57	12.57	-
Male	42 (28%)	42 (28%)	-

Female	108 (72%)	108 (72%)	-

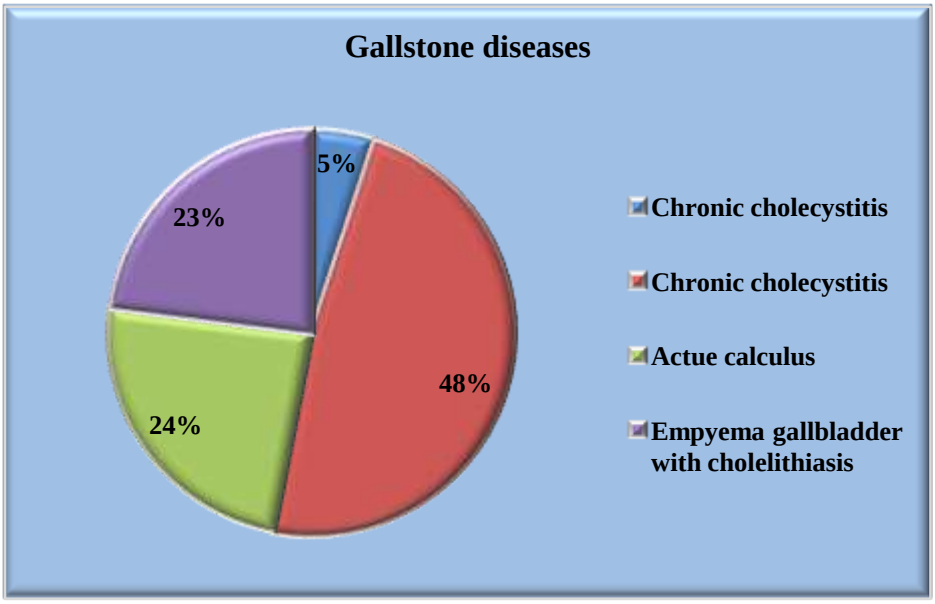

Figure 1: Distribution of cases according to gallstone diseases (n=150)

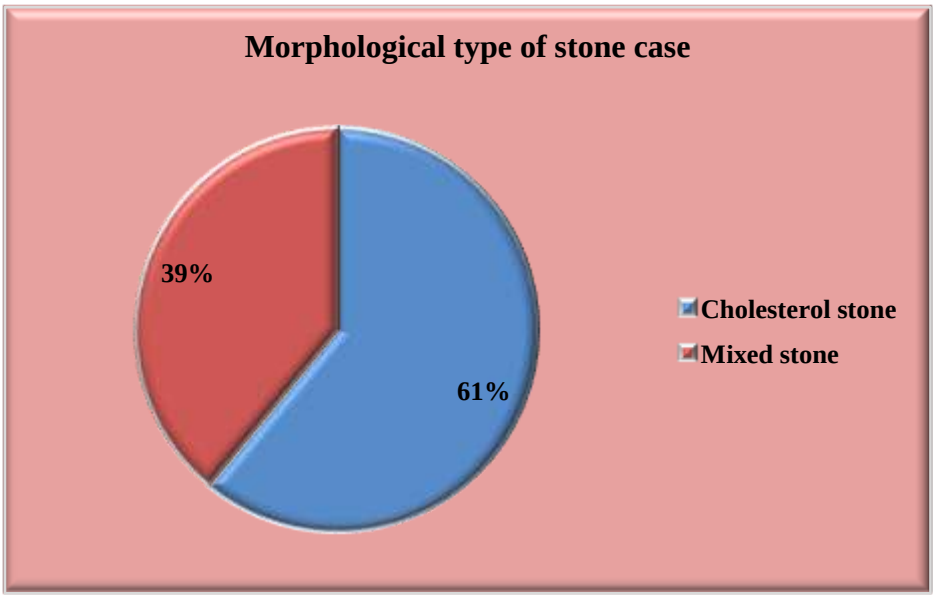

Figure 2: Distribution of Morphological type of stone in case (n=150).

Table ll: Dyslipidemia in cases with cholesterol gallstone and mixed gallstone (n=150)

Serum lipid parameter	Cholesterol stone 91 (61%)		Mixed stone 59 (39%)	
	N	%	N	%
TG	57	62.64	35	59.32
HDL-C	55	60.44	31	52.54
TC	32	35.16	17	28.81
LDL-C	29	31.87	15	25.42

Table III: Distribution of participants according to BMI (n-300)

BMI Category	Case(N=150)		Control(N=150)	
	N	%	N	%
Underweight (<18.5)	0	0.00	0	0
Normal weight(18.5-24.9)	48	32.00	141	94
Overweight (25.0-29.9)	67	44.67	9	6
Obese (>30)	35	23.33	0	0
Mean BMI ± SD	25.73±2.10		22.38±1.82	

Table IV: Distribution of participants according to mean lipid Lipid profile Distribution (n=300)

Lipid profile (Mean ± SD)	Case(N=150)	Control(N=150)	p-value
TC (mg/dl)	191.78±15.66	123±10.04	<0.031[s]
HDL-C (mg/dL	191.78±15.67	123±10.05	<0.049[s]
LDL-C (mg/dL)	191.78±15.68	123±10.06	<0.0015[s]
TG (mg/dL)	191.78±15.69	123±10.07	<0.036[s]

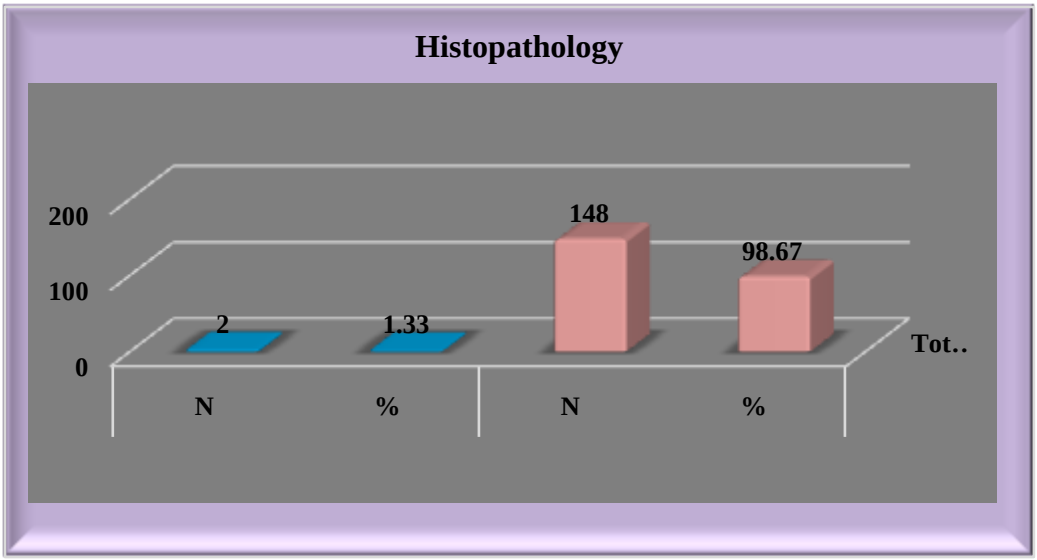

Figure 3: After cholecystectomy, Histopathological examination of gallbladder specimen:

IV. Discussion

Galatones are the most common biliary pathology Formation of gallstone are multifactorial and complex such as metabolic, infection, and stasis. Biliary cholesterol supersaturation is identified as the main prerequisite for forming cholesterol gallstones, and elevated unconjugated bilirubin in bile is considered the primary cause of the pigment gallstone. Thus gall stones are formed due to impaired metabolic regulation of the human body Serum high TG and low HDL-C have shown a significant association with gallstone disease, H Thilanka et al. Gallstones are formed in the gall bladder and Billary tract [16]. There are three types of gallstones usually observed among cholelithiasis patients. Among them, cholesterol stone is the commonest form. Unfortunately, our country does not routinely examine gallstones to determine the types. Adult patients and both sex groups are included in the study. The mean age of the presentation groups in the case was 39.79, and in control, 38.86 years, respectively. The bulk of the disease presented in the age group of 35-45 years Le 40% of the total cases. This study showed a female preponderance, with 72% female and 28% male, with a ratio of male to female, which was 12.57. Our study correlated with the studies conducted by Nagaraj SK et al. [17]. In this study, Cholelithiasis had a peak incidence in the age group of 35-45 years. Nevertheless, Nagaraj SK et al. show that the peak incidence age group is 40-50 years, and male to female ratio is 1.2:57. Schirmer et al. show that the peak incidence age reproductive years and the male-to-female ratio is 1:4. Gallstone disease or Cholelithiasis was diagnosed by ultrasonography[18]. One hundred fifty participants in the study group 48% 24%, 23%, and 5% were /suffering from chronic cholecystitis with Cholelithiasis, chronic cholecystitis with choledocholithiasis, acute calculus cholecystitis and Empyema gallbladder with Cholelithiasis respectively. Stone was analyzed morphologically. Then only cholesterol stones and mixed stones were included in this study. One hundred fifty cases are selected to have cholesterol stones (61%) and mixed stones (39%), respectively. Out of 150 participants in the study group, 91(61%) had cholesterol stones; Triglyceride, HDL-C total cholesterol, and LDL-C were 63%, 61%, 35%, and 31%, respectively. Also, 39% (59) had composite stones. Among them triglyceride HDL-C, and total cholesterol LDL-C were 59%, 53. %, 29%, and 25%, respectively. Nevertheless, H.Thilanka et al. study show that out of 73 participants, 37(51%) cholesterol stones, including Triglyceride, total cholesterol, LDL-C, HDL-C, were 19%, 14%, 19%, and 0% Obesity is a significant risk for gastone[19]. A larger body size (BM) was suggested to be associated with a higher risk of stone formation. My study shows that out of 150 participants, 32%, 44.00%, and 23.33%, 0% were average, overweight, obese, and underweight, respectively. In our study, we observed that the mean BMI of the case group than the control group was higher (25.73+/-2 ten vs. 22.38+/-1.82) and statistically significant ($p<0.001$) v Bhandar et al. study shows that The mean BMI was statistically higher in the case group than the control group

(27.5+/-0.71 vet 2431+/-0.32 and p<0.001. All the patients were subjected to the determination of the serum lipid profile like total cholesterol, HDL cholesterol, LDL cholesterol, and Triglyceride. The results were compared with the lipid profile of healthy persons taken as control. The result of serum total cholesterol, triglycerides, and LDL cholesterol show a significant increase, whereas serum HDL cholesterol shows a significant decrease compared to the control subject. The serum lipid parameters were compared to that of different studies conducted by different authors, which were similar to their findings. The serum TC, LDL-C, and TG were all statistically higher in the case group than in the control group. HDL-C was statistically lower in the case of the study group than control In my study case group TC (191.78 +/-15.66), TG (146 59 +/-11.97), LDL-C (128 13 +/-10.48), and HDL-C (35.46 +/ 2.89) The serum TC, TO LDL-C were all statistically significantly higher in case of the group than the control group (p<0.031, p<0.036, p<0.001) respectively HDL-C was statistically significantly lower in the case group than the control group (p<0.049) V Bhandari et al., study shows that TC(186.78+/- 49 13)[20].TG (142.54 +/-58.52) LDL-C (126.06 +/-45.82) HDL C (39.46 +/-27.97). TC, TG, and LDL-C are statistically significantly higher in the case group than the control group, [p (<0.001) and HDL-C was lower, but that are not statistically significant [p 0179) S Hayat et al. [21], study shows that TC (154.50), TG (1982) HDL-C (29.54) and LDL-C (118.40) [p<0.625 p<0.013, p<0.000 and p<0.544] respectively. TC level was higher than the control group but not statistically significant, TG level was higher than the control group and statistically significant, HDL-C level was lower in the case group, and statistically significant. The patient's LDL-C level was low compared to the control group, but the result was not statistically significant. Chana NA et al. [22]. Study shows that TC (199.3+/-5.4), TG (191.4 +/-10.0), HDL-C (23.9+/-0.28). LDL-C (118.7+/-3.8) and TC [p=0.275 LTG [p=0.437], HDL-C [p-0.085] and LDL-C [p=0.315] Serum lipid profile between case and control showed no significant variation except TG. Gall bladder malignancies diagnosed by ultrasonography were excluded as per exclusion criteria. However, histopathological examination of gallbladder specimen after cholecystectomy, incidental gall bladder malignancy were found 2 (1.33%) and non-malignancy 148 (98.60%) in my study Tadeusz et al. [23] study shows that gall bladder malignancy after histopathology 0.87% and Faisal G Siddiqui et al., study shows that gallbladder malignancy after histopathology 2.8%, So it is a highly justifiable histopathological examination of all gallbladder specimen after cholecystectomy[24]. My study reveals that high lipids levels, especially TG, TC, LDL-C, and low HDL-C, contribute to Cholelithiasis. However, it is not conclusive as it is a case-control study. The sample size was small, the stones were not analyzed chemically, and the duration was short. Further study, especially RCT, should be conducted about this topic in this region.

Limitations of the study:It was a case-control study, *conducted in a single hospital with a small sample size in a short duration. So, the results may not represent the whole community***.**

V. Conclusion And Recommendations

This study emphasized that the increased lipid profile can be a good indicator for gallstone diseases, and females are more susceptible to forming gallstones with high cholesterol levels. Obesity is a risk factor for gallstones, so people should maintain an ideal body weight. Gallstones are a predisposing factor for malignancy, so all gallbladder specimens should be investigated histopathologically after cholecystectomy. A multicentered study in Bangladesh's divisional/tertiary hospitals can reveal an accurate picture. The study period should be the long andMulti-disciplinary approach to research work can make a study more precise and authentic in this regard.

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Ethical approval: *The study was approved by the Institutional Ethics Committee.*

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