ASSOCIATION OF METABOLIC SYNDROME WITH THE DEVELOPMENT OF GALLSTONE DISEASE – A PROSPECTIVE STUDY

Dr. Romi Gaudani
Junior Resident, Dept. of General Surgery, DYPMCH

Dr. Dakshayani Satish Nirhale
Professor, Dept. of General Surgery, DYPMCH

Dr. Pushkar Galam
Assistant Professor, Dept. of General Surgery, DYPMCH

Dr. Vaishnavi Reddy
Junior Resident, Dept. of General Surgery, DYPMCH

Dr. Pragna Puvvada
Junior Resident, Dept. of General Surgery, DYPMCH

Abstract:

Aim: To study the correlation between individual components metabolic syndrome and gall stone disease and to study the rate of gallstone associated complications such as cholecystitis, gallstone pancreatitis, and post cholecystectomy complications in patients with metabolic syndrome.

Materials and Methods: A total of 120 patients visiting the medicine and general surgery OPD fulfilling the inclusion and exclusion criteria and willing to participate were included in the study. Patient were then subjected to a complete workup including Laboratory and Radiological investigations. After completion of data collection, data analysis was achieved using SPSS version 16 software, and the correlations sought after were achieved using the chi-square test of significance.

Results: According to our study findings, among the 120 patients who visited the surgical outpatient department for gallstone disease, 73 were diagnosed with metabolic syndrome, while the remaining patients exhibited derangement in one or two components. Based on our study, metabolic syndrome was associated with a more than two-fold risk of gallstone disease. More the components of metabolic syndrome, higher the prevalence of gall stone disease. Furthermore, our study provides strong evidence that each component may contribute to different degrees of incidental cholelithiasis. Of the 5 components of metabolic syndrome, absolute predictors and the risk factors for gallstone disease and its complications, were Obesity(65.75%), Diabetes Mellitus(60.27%) and hypertriglyceredemia(50.68%). Therefore, the management of metabolic components, especially Obesity, hypertriglyceredemia and diabetes mellitus, may effectively reduce the risk of gallstone formation. Patients who had both metabolic syndrome and gallstone disease experienced few preoperative complications, such as cholecystitis and gallstone-induced

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pancreatitis, but these occurrences did not show statistical significance. In our study, there were very few postoperative complications noted, including wound gape and seroma formation

Categories: Internal Medicine, General Surgery

Keywords: Gallstones, Metabolic syndrome, Obesity, Hypertension, Cholecystectomy

Introduction

Gallstones are increasingly prevalent in India, a trend partly attributed to the widespread adoption of ultrasonography over the past two decades and socioeconomic changes. This condition, which is common in the western world, significantly impacts healthcare costs and can lead to life-threatening complications. Early detection and appropriate treatment are crucial in preventing severe and potentially fatal outcomes (1). In adults, the prevalence of gallstones is 6.12%, with higher rates among women (9.6%) compared to men (3.07%). The prevalence increases with age, peaking in the sixth decade. Additionally, gallstone prevalence is notably higher in women who have had children compared to those who haven't(3).

Over 20% of individuals diagnosed with gallstones experience biliary colic or complications related to gallstones, such as acute pancreatitis, cholangitis, cholecystitis, and stones in the common bile duct. Recent years have seen extensive global research into the relationship between Metabolic Syndrome and gallstones. Studies have identified common risk factors shared by both conditions, such as age, gender, obesity, and abnormalities in lipid and glucose metabolism(2).

Metabolic Syndrome:

Metabolic syndrome, also known as syndrome X or insulin resistance syndrome, encompasses a cluster of metabolic abnormalities that elevate the risk of cardiovascular disease (CVD) and diabetes mellitus.

Clinical definition given by National Cholesterol Education Programme (NCEP) Adult Treatment Plan (ATP III), 2001 metabolic syndrome is

present if any 3 out of the following 5 are present:

a. Abdominal Obesity

b. Diabetes

c. Hypertension

d. Serum Hypertriglyceridemia

e. Decreased Serum High Density Lipoprotein (HDL) Levels

Patients who have gallstones often present with concurrent Non-Alcoholic Fatty Liver Disease (NAFLD), alongside metabolic syndrome. These conditions share common risk factors such as obesity, hypertriglyceridemia, and diabetes mellitus. Factors contributing to the formation of

gallstones include waist circumference, gender, use of contraceptives, raised lipid levels, diabetes mellitus, sedentary lifestyle, multiple pregnancies, alcohol, water with high iron content, metabolic syndrome, and NAFLD. Similar associations have been observed in Western countries(4).

The prevalence of Metabolic Syndrome in the adult population of India is 30%. This burden shows a consistent increase across age groups, ranging from 13% in the 18–29 years age group to 50% in the 50–59 years age group. Urban residents exhibit a higher prevalence compared to those in tribal or rural areas. Among genders, females have a higher prevalence at 26% compared to males(5).

Studies have shown a strong association between gallstone disease and several factors including female sex, older individuals, obesity, race, alcohol use, liver cirrhosis, hyperlipidemia, diabetes mellitus, and metabolic syndrome. Obesity, hyperlipidemia, diabetes mellitus, and metabolic syndrome are particularly recognized as significant cardiometabolic risk factors. Non-alcoholic fatty liver disease is also considered a manifestation of metabolic abnormalities.

Diabetes mellitus and cholelithiasis are often thought to be closely related conditions, suggesting that disturbances in glucose metabolism could raise the risk of gallstone formation in certain individuals. Recent research has focused extensively on understanding the physiological processes involved in gallstone development.

Serum lipid levels play a pivotal role in the onset of cholelithiasis, especially in cases of cholesterol gallstones where lipid profiles reflect characteristics akin to those seen in metabolic syndrome. Studies indicate that metabolic syndrome may pose a potential risk factor for the occurrence of gallstones.

In a study conducted in Western countries, the prevalence of gallstone disease was found to be 12.1%, with rates of 13.1% in men and 10.2% in women. Compared to controls, individuals in the cases group had higher values of waist circumference, blood pressure, fasting blood sugar, and raised serum triglycerides (TG). Conversely, serum high-density lipoprotein levels were lower in the cases group. Men exhibiting a higher number of metabolic disorders showed a statistically significant increase in the prevalence of gallstone disease. Having all five components of Metabolic syndrome was associated with a 3.4-fold increase in the risk of developing gallstones(6).

Gallstone disease is prevalent and a leading cause of hospitalizations for gastrointestinal conditions worldwide. At the same time, Metabolic syndrome is increasingly becoming a global epidemic. However, there is limited information currently available on how gallstones and Metabolic syndrome are related in the Indian population. This study aims to investigate if there is any correlation between Metabolic syndrome and the development of Gallstone diseases among Indians.

MATERIALS AND METHODS

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A Prospective observational study was conducted at a tertiary health centre in the period between 2022-2024, which included 120 patients having cholelithiasis and metabolic syndrome. Ethics clearance committee approval was taken and informed consents were taken from all the patients. All patients of age group 18-60 year old

and with Metabolic Syndrome having gallstone disease were included in this study. Any patients who have undergone Cholecystectomy,with history of Acute Pancreatitis, Pregnancy, Immunocompromised patients, history of any major GI surgeries or Malignancy were excluded from the study.

Socio-demographic data and Clinical information was obtained from patients by detailed history, clinical examination and laboratory (Complete Hemogram, Blood Group, Liver Function Tests, Renal Function Tests, Lipid Profile, Serum Amylase, Serum Lipase, Random Blood Sugar Levels, HbA1C, Serology (HIV, HBsAg, HCV), Prothrombin Time, International Normalized Ratio, (PT-INR), Serum Albumin, Total Protein, Serum Electrolytes, Urine Routine Microscopy, Electrocardiograph (ECG) and radiological investigation [Chest X ray, Ultrasound of abdomen and pelvis, Magnetic Resonance Cholangiopancreaticography (MRCP), Contrast enhanced computed tomography (CECT) (Abdomen + Pelvis)] and recorded.

Appropriate Medical optimization was done for patients with Metabolic Syndrome

Oral hypoglycemic agents or insulin for Diabetes mellitus patients

Oral antihypertensives for Hypertensive patients

Oral statins for Trigyleride control

Proper diet counselling

Exercise and lifestyle modifications

Based on the Investigations, patients fitting into the criteria of Metabolic Syndrome were subjected to Open or Laparoscopic Cholecystectomy after preoperative optimisation.

Appropriate surgical management of open or laparoscopic cholecystectomy was done. Preoperative antibiotics were given. Intraoperative time, complications, amount of blood loss were recorded.

Post operatively, patient will be given appropriate treatment with

Inj. MONOCEF 2g, Inj. METRONIDAZOLE 400mg, Inj. TRAMADOL, Inj. EMESET 4mg, Inj. PANTOPRAZOLE as required.

Check dressings were done on post operative day 3 and suture line were checked. Sutures removal was done as per standard protocol.

Follow up: All the Metabolic Syndrome patients with asymptomatic Gallstone Disease: Blood Pressure, Random Blood Sugar, Fasting Lipid Profile, Waist circumference were monitored at 1 month, 3 months, 6 months and 1 year, recorded and tabulated.

Patient's HbA1C were monitored at 6 months and 1 year. Any variation from the baseline were recorded and tabulated.

Post-operative complications like delayed wound healing, pancreatitis were recorded and tabulated. All the patients with Metabolic Syndrome with Gallstone Disease who were not operated were kept in follow up with lifestyle modifications.

All the data was noted down in a pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed using Chi square test. A p-value <0.5 was taken as the level of significance. Results were graphically represented where deemed necessary. SPSS version 21.0 was used for most analysis and Microsoft Excel 2010 for Graphical representation.

Results:

1. Association of obesity with development of the gallstone disease

N=120	Waist circumference(cm)			
	Male		Female	
Metabolic syndrome	<90cm	≥ 90cm	<80cm	≥80cm
Yes	10(8.33%)	11(9.16%)	15(12.5%)	37(30.83%)
No	14(11.6%)	2(1.66%)	24(20%)	7(5.83%)
Chi square test	141.52			
P value	<0.001			

2. Correlation of Diastolic Blood Pressure of the patients with the gallstone disease

Diastolic Blood Pressure (mmHg)	Metabolic Syndrome Count (%)

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	Yes	No
70-80	36(30%)	46(38.33%)
90-110	37(30.83%)	1(0.83%)
Chi square= 31.0		
P value= <0.001		

3. Association of Fasting blood glucose of the patients with the gallstone disease

N=120	Metabolic Syndrome Count (%)	
Fasting Blood Sugar (mg/dl)	Yes	No
<190	29(24.16%)	47(39.16%)
>191	44(36.66%)	0
Chi square= 43.02		
P value= <0.001		

4. Relation of Triglyceride of the patients with the gallstone disease

N=120	Metabolic Syndrome Count (%)	
Triglyceride	Yes	No
<200	36(30%)	42(355%)
>201	37(30.83%)	5(4.16%)
Chi square= 20.09		

P value= <0.001

5. Correlation of High density Lipoproteins of the patients with the gallstone disease

N=120	Metabolic Syndrome Count (%)	
HDL (mg/dl)	Yes	No
<30	12(10%)	2(1.66%)
>31	61(50.83%)	45(37.5%)
Chi square= 3.76		
P value= <0.05		

6. Comparison of patients with number of preoperative complications in gallstone disease with metabolic syndrome and gallstone disease without metabolic syndrome

Pre-operative Complications	Metabolic Syndrome Count (%)	
	Yes	No
Present	9(75.0%)	3(25.0%)
Absent	64 (59.26%)	44(40.74%)
Total	73(60.83%)	47(39.17%)
Chi square= 1.12		
P value= 0.289		

7. Comparison of patients with number of postoperative complications in gallstone disease with metabolic syndrome and gallstone disease without metabolic syndrome

Post-operative Complications	Metabolic Syndrome Count (%)

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	Yes	No
Present	7(5.83%	1(0.83%)
Absent	66(55%)	46(38.33%)
Chi square= 2.52		
P value= 0.112		

Discussion:

Gallstone disease is prevalent and a major reason for hospital admissions due to gastrointestinal issues in the modern world. Metabolic syndrome is increasingly becoming a global epidemic. This rising trend contributes to increased health issues from heart diseases and diabetes. Early diagnosis and management of metabolic syndrome is essential to prevent its complications. However, there is limited data on the relationship between gallstone disease and metabolic syndrome among Indians. Consequently, this study primarily aims to investigate whether there is a link between the presence of gallstones and metabolic syndrome.

In our study, out of the 120 patients having gallstone disease, 73 patients have Metabolic syndrome. Out of them, 21(56.76%) are males with metabolic syndrome and 52 (62.65%) are females. In the study conducted by Kumar et al [7], the ratio of females to males was 8.2:1 in the group with complicated gallstone disease (CGSD) and 4:1 in the group with uncomplicated gallstone disease (UGSD).

In patients with metabolic syndrome, there are 16 individuals in the 50-60 years age group and 33 individuals in the 40-50 years age group. Similarly, Kumar N et al. [7] found that the average age in the complicated gallstone disease (CGSD) group was 47.2±13.2 years (ranging from 20 to 85 years), while in the uncomplicated gallstone disease (UGSD) group, the average age was 46.7±13.8 years (ranging from 20 to 75 years).

Metabolic syndrome and obesity in male and female are dependent on each other in patients having gallstone disease. In this study, 11(9.16%) males and 37(30.83%) females with metabolic syndrome had waist circumference of more than 90 cm and 80 cm respectively. Hence, 11 males and 37 females with gallstone disease were obese. Qi Zhu et al. [8] found that metabolic syndrome elevates the risk of gallstones, particularly in individuals with abdominal obesity. Managing and treating metabolic syndrome can significantly lower the risk of developing gallstones. A study by Sanchez NM et al. (11) suggested that there is a correlation between patients having gallstone disease and larger waist circumference. Patients having a larger waist circumference have higher risk of development of gallstone disease.

Gallstone disease is not dependent on Hypertension. In this study, 36(30%) patients without metabolic syndrome had a diastolic Blood pressure of 70-80 mmHg, as compared to only 37(30.83%) patients with the metabolic syndrome. A study by Yalan Zhang et al. [9] found that there was no statistically significant link between hypertension and the need for cholecystectomy. This suggests that while hypertension may be associated with gallstones, it is not directly related to symptomatic gallstone disease that necessitates cholecystectomy. In contrast, research by Nakeeb et al. [14] indicated that insulin resistance might be a key factor in gallbladder dysmotility, potentially leading to acalculous cholecystitis or gallstone formation.

Fasting blood sugar and Metabolic syndrome are dependent on each other. A total of 44(36.66%) patients are having Fasting Blood sugar levels of >191 mg/dl.Ata N et al. [10] investigated the connection between complicated gallstone disease (CGSD) and metabolic syndrome or its components. They found that fasting blood sugar levels were significantly higher in the CGSD group compared to the uncomplicated gallstone disease (UGSD) group (47% vs. 24%). Insulin resistance was linked to low serum HDL-cholesterol levels and gallbladder dysmotility, both of which are risk factors for gallstone disease. Similarly, Kumar N et al. [7] reported that hyperglycemia was more frequently observed in the CGSD group compared to the UGSD group.

Gallstone disease and Hypertriglyceredemia are dependent on each other. A total of 42 patients having gallstone disease fall under the group of triglyceride levels of >201 mg/dl, wherein 37(30.83%) patients have metabolic syndrome and the rest 5(4.16%) do not have metabolic syndrome. This finding aligns with the study by Sanchez NM et al. [11], which reported that metabolic syndrome was associated with over a three-fold increased risk of gallstone disease (OR = 3.20; 95% CI, 1.71-6.01; P = 0.0001). Additionally, Kumar N et al. found that while hypertriglyceridemia was more common in the CGSD group, there was no statistically significant difference in its occurence between the CGSD and UGSD groups.

HDL levels and Gallstone disease are independent of each other. In our study, out of the 14 patients having HDL level of <30 mg/dl, 12(10%) patients of gallstone disease had metabolic syndrome. Thus based on this, the conclusion drawn is that Gallstone disease is not dependent on HDL levels. Kumar N et al. [7] investigated the relation between metabolic syndrome and complicated gallstone disease, finding that metabolic syndrome was more frequently observed in the CGSD group compared to the UGSD group.

Similarly, Ching LI et al. [12] found that patients with gallstone disease had a 1.99 times higher incidence of metabolic syndrome (OR = 1.99). Their multivariate logistic regression analysis showed that age (OR = 1.037), abdominal obesity (OR = 1.013), and HDL levels (OR = 0.985) were associated with gallstone disease after adjusting for other variables.

In this study, the majority of the patients experienced no preoperative complications, with gallstone-induced pancreatitis affecting 5 patients. The study concluded that metabolic syndrome and preoperative complications are independent of each other in patients with gallstone disease.

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There are few post-operative complications such as seroma formation, wound gape found in patients having gallstone disease. These findings align with Sunil Kumar Kota et al.'s(13) research, which suggests that metabolic syndrome leading to gallstone induced pancreatitis are relatively uncommon, accounting for only 5%-10% of cases, which is considered insignificant.

CONCLUSION

According to our study findings, among the 120 patients who visited the surgical outpatient department for gallstone disease, 73 were diagnosed with metabolic syndrome, while the remaining patients exhibited derangement in one or two components. Based on our study, metabolic syndrome was associated with a more than two-fold risk of gallstone disease. More the components of metabolic syndrome, higher the prevalence of gall stone disease. Of the 5 components of metabolic syndrome, absolute predictors and the risk factors for gallstone disease and its complications, were Obesity(65.75%), Diabetes Mellitus(60.27%) and hypertriglyceredemia(50.68%). Therefore, appropriate and timely treatment of metabolic components, especially Obesity, hypertriglyceredemia and diabetes mellitus, may effectively decrease the risk of gallstone formation. Patients who had both metabolic syndrome and gallstone disease experienced few preoperative complications, such as cholecystitis and gallstone-induced pancreatitis, but these occurrences did not show statistical significance. In our study, there were very few postoperative complications noted, including wound gape and seroma formation.

Lifestyle modifications such as weight control by good glycemic index, regular exercise (minimum of 150-200 minutes of moderate exercises and 75-150 minutes of intense exercises), controlling blood glucose levels by changing diet habits and initiating statin therapy to control triglyceride levels can potentially reduce the incidence of gallstone disease and its associated complications.

LIMITATIONS

The limitations of this study included the patients were recruited from a single center with small sample size, which may limit the generalizability to the entire population of India, Non-adherence to the modifiable factors as advised, The study's follow-up duration was comparatively short, which constrained its capacity to thoroughly examine the long-term effects of each metabolic component on gallstones formation.

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