

**The Association between Gallstone Disease & Metabolic Syndrome – A Prospective Observational Study**Raj Kumar Paliwal<sup>1</sup>, M.M. Mangal<sup>2</sup><sup>1</sup>Assistant Professor, Department of Surgery, Pacific Medical College and Hospital (PMCH), Udaipur<sup>2</sup>Senior Professor, Department of Surgery and Principal & Dean, Pacific Medical College and Hospital (PMCH), Udaipur

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Conflict of interest: Nil

**Abstract**

**Background** – Gall stone disease a common clinical condition ,mostly affecting the females. Its incidence is increasing in the recent times , owing to various risk factors.Previous literature have reported metabolic syndrome to be present in patients diagnosed with gall stone disease.

**Aims & Objectives-** To assess the association between the presence of gallstone disease and metabolic Syndrome.

**Material & Methods-** This prospective, observational study recruited patients (n=60, age range 20-65 yrs) having cholelithiasis who were admitted in the Department of Surgery , of our tertiary care Hospital from January 2023 to September 2023. Normal healthy persons (n=60, age range 20-65 yrs) with no evidence of cholelithiasis on ultrasonography were taken as controls.CBC, fasting blood sugar, serum lipid profile,ultrasonography was conducted. Metabolic syndrome was defined by adult treatment panel III (ATP III) criteria.<sup>6</sup>

**Results** - Both the groups were comparable with respect to age and gender & with no statistically significant difference. In the Case group, 24 (40%), while in control group 11(17% ) of the study participants fulfilled the criteria for metabolic syndrome which showed statistically significant difference (p<0.05). Waist circumference , diabetes mellitus , low serum high density lipoprotein were statistically significantly higher in Case group as compared to control group . Hypertension & serum triglycerides levels were also elevated in case group with no statistically significant difference. A positive association was found between waist circumference , DM & low serum high density lipoprotein & gall stone disease which was statistically significant(p<0.05).

**Conclusion** – Metabolic syndrome was statistically significantly associated with gall stone disease & can be used to predict the risk . Increased waist circumference , diabetes & low serum high density lipoprotein are the noted findings in Gall stone disease & should be management to prevent any complications.

**Key words** – Metabolic syndrome ,Gall stone disease, dyslipidemia, insulin resistance ,diabetes mellitus

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**Introduction**

Gallstone formation disease(GSD) is a common occurrence in the western population<sup>1-6</sup>, with a prevalence of 5.9–21.9% & 3.2% to 15.6% in Asian population. [1] In recent times, Indian population has shown an increased incidence of GSD attributed to changes in diet , lifestyle, other socioeconomic factors. The incidence increases with age , with highest incidence in fifth to sixth decade. GSD is a chronic disorder marking a huge impact on the health of the patients with its severe complications .There occurs a great impact on the quality of life of patients with associated risks of cholecystitis, pancreatitis, biliary tract obstruction and gall bladder cancer. [2,3] In India , the overall prevalence of gallstone disease is around 4.15%;with a female predilection. [4] If diagnosed promptly , the potential complications can be prevented. Thus

,efforts should be made to identify the risk factors & preventive measures should be taken. GSD may be asymptomatic but some people may experience severe pain in the back or upper right abdomen , indigestion, nausea & vomiting. [5]

Metabolic syndrome(Met Syn) includes the presence of multiple risk factors for cardiovascular disease (CVD). Met Syn as defined by National Cholesterol Education Programme (NCEP) Adult Treatment Plan (ATP III), 2001 is diagnosed to be present if any of the three of the following five criteria are met :include six componenets i.e. abdominal obesity, raised blood pressure, insulin resistance, glucose intolerance, serum hypertriglyceridemia , decreased serum high density lipoprotein (HDL) levels. [6] Met Syn is a known risk factor for atherosclerotic cardiovascular

disease. It is also related to various gastrointestinal tract diseases, such as fatty liver, nonalcoholic steatohepatitis, and unexplained liver cirrhosis. [2]

Gallbladder has physiological role of concentration of bile, thus incidence of stone formation is high as compared to other organs. [7] Although supersaturation of bile is required for the gallstones to develop, but not all people with supersaturated bile form gallstones. [8] It is Studies have reported DM and cholelithiasis to be closely linked diseases, thus, altered glucose metabolism might be responsible for development of cholelithiasis. [9] Risk factors for GSD include sex, age, body mass index (BMI), hyperlipidemia, usage of oral contraceptives, alcohol consumption, diabetes mellitus (DM), and race. [10]

The diagnostic features of Met Syn overlap with the risk factors for the development of GSD. Lin et al study, concluded Met Syn to be associated with GSD. Waist circumference and HDL-C were found to be associated with GSD. [5] Thus, the present prospective, observational study was aimed to assess the relationship between metabolic syndrome and gall stone disease.

#### Material & Methods

This prospective, observational study recruited patients (n=60, age range 20-65 yrs) having cholelithiasis who were admitted in the Department of Surgery, of our tertiary care Hospital from January 2023 to September 2023. Patients with acute cholecystitis, liver diseases renal failure, nephritic syndrome, malignancies, cardiovascular disease, on statins or fibrates and pregnant women were excluded. Normal healthy persons (n=60, age range 20-65 yrs) with no evidence of cholelithiasis on ultrasonography (USG) were taken as controls. The study was approved by the institutional ethical committee and prior written informed consent taken from the study participants.

A complete history recording, sociodemographic details & clinical examination was undertaken. Venous blood was drawn & sent to laboratory for CBC, fasting blood sugar, serum lipid profile (Triglyceride (TG) & HDL-C). All the patients underwent USG whole abdomen for confirming the diagnosis of gall bladder stone disease.

Waist circumference was measured at the level of umbilicus with the patient standing position. Metabolic syndrome was defined by adult treatment

panel III (ATP III) criteria.<sup>6</sup> All patients underwent laparoscopic cholecystectomy.

Study participants were defined as having the metabolic syndrome if they fulfilled three or more of the following criteria [11]: 1. Waist circumference greater than 102 cm for men, greater than 88 cm for women;

2. Diagnosed with hypertension or receiving antihypertensive medication, or mean of two blood pressure measurements exceeding 130/85 mmHg

3. Diagnosed with diabetes mellitus or receiving antidiabetic treatment, or a fasting blood glucose level

of greater than 110mg/dL

4. Serum HDL level lower than 40 mg/dL for men, lower than 50mg/dL for women

5. Serum TG levels above 150mg/dL.

#### Statistical Analysis-

The collected data was tabulated in excel spreadsheet & put to statistical analysis. The data was expressed as mean and standard deviation & percentage. Association between the various metabolic parameters & GSD was analysed using Chi-square test. P value <0.05 was considered statistically significant.

#### Results -

Both the groups were comparable with respect to age and gender & with no statistically significant difference. In the case group, 40 patients were females & in control group 44 were females.

In the Case group, 24 (40%), while in control group 11(17%) of the study participants fulfilled the criteria for metabolic syndrome which showed statistically significant difference (p<0.05). The comparison of prevalence of Met Syn between the two groups as per the gender is shown in Table 1. The comparison for the components of metabolic syndrome as per the gender was done between the cases & controls and is shown in Table 2. Waist circumference, DM, low serum HDL were statistically significantly higher in Case group as compared to controls. Hypertension & serum TG levels were also elevated in case group with no statistically significant difference. A positive association was found between waist circumference, DM & low serum HDL & GSD which was statistically significant (p<0.05). Also, a positive association was found between hypertension, serum TG & GSD which was not statistically significant (p>0.05).

**Table 1: Comparison of prevalence of Metabolic syndrome between the two groups as per the gender**

Criteria fulfilled for metabolic syndrome	Cases (n=60)		Controls (n=60)	
	Males (n=20)	Females (n=40)	Males (n=18)	Females (n=42)
Yes	8	16	4	7
No	12	24	14	35

**Table 2: Comparison between the two groups for five components of Metabolic syndrome**

S.No.	Component Criteria	Cases (n=60)			Controls (n=60)			P value
		Males	Females	Total	Males	Females	Total	
1.	Waist circumference: Criteria fulfilled >102cm for men; > 88cm for women	16	33	49	7	15	22	<0.05
2.	Known diabetic/ On medications/ FBS >110mg/dl	10	19	29	7	14	21	<0.05
3.	Known Hypertensive/ On medications/ BP >130/85 mmHg	10	19	29	8	16	24	>0.05
4.	Serum Triglycerides >150mg/dl	9	13	22	6	9	15	>0.05
5.	Serum HDL -C - males < 40 mg/dl; females < 50mg/dl	4	7	11	2	4	6	<0.05

### Discussion

GSD is one of the common reasons for hospital admissions for gastro-intestinal problems in the recent times. Met syn was first described by Archard and Thiers in 1921, in association with polycystic ovary syndrome. [12] Met Syn is becoming an epidemic affecting the population worldwide. Gall stone development is a multifactorial disease with a female predilection, increasing age, hereditary traits. Other factors due to lifestyle changes are obesity, dyslipidemia, diabetes hypertriglyceridemia. [13]

In the present study, prevalence of Met Syn in case group was 40% as compared to 17% in control group. Similarly Peshwani et al study observed prevalence of Met Syn in case group & control group to be 36% & 16% resp. [11] Kumar N et al study found Met Syn to be present in 58.2% patient in complicated GSD group & 21.8% patients of uncomplicated GSD, which was statistically significant. [13]

In the present study, waist circumference was statistically significantly higher in the Case group than control group. With higher difference in the females. (p value < 0.05). Accordingly, studies by Peshwani et al noted that only the waist circumference criteria among all the criteria of Met Syn, was found to be statistically significant. Similar conclusions were drawn by Méndez-Sánchez N et al study which concluded abdominal obesity to be an important risk factor for GSD, higher in women than for men. [14] Among all the components of Met Syn, abdominal obesity is the becomes the foremost factor significantly associated with the risk of developing gallstones. Female population with higher obesity are at a greater risk of developing gallstones than obese men. [15]

In adiposity, fatty acids are accumulated inside the body tissues, which act as precursors for the cholesterol synthesis. Higher cholesterol production, leads to secretion of cholesterol in the bile which exceed the solubility capacity of the bile

acids and phospholipids. This high ratio of cholesterol to solubilizing lipids (bile acids and phospholipid) which leads to higher crystallization of cholesterol and gallstone formation. The bile of females is more lithogenic than males, as males secrete more bile acids and phospholipids into bile. [16]

In the present study, DM was found to be higher in Case group as compared to control group (p value <0.05). Similarly Peshwani et al study, observed DM to be present in 44% of the cases as compared to 42% in controls. Diabetic population is at a higher risk of development of GSD, which may progress at a higher rate with associated complications. [11] Sanchez NM et al noted total metabolic syndrome to be associated with more than three-fold risk of GSD. The risk of development of GSD was 7.89 fold with the presence of higher waist circumference, DM & lower HDL. [17] Ata N et al studied the relationship between complicated gall stone disease & Met Syn & concluded FBS to be statistically significant more in complicated GSD than uncomplicated GSD. [18]

Similarly, Ching LI et al reported a 1.99 times increased risk of GSD in patients having Met Syn. The increased age, waist circumference, low HDL were found to be associated with GSD after adjusting for the other factors. [19]

In the present study, no significant difference in serum triglyceride levels in Case & control group was observed. Also, no correlation observed between serum triglyceride levels & GSD.

Insulin resistance is associated with a low serum HDL Cholesterol concentration and gallbladder dysmotility, which is a risk factor for gall stone disease. [20] Peshwani et al study reported hyperglycemia & lower serum HDL-C level to be more in complicated GSD. A study by Nagraj et al. [21] in population of Karnataka, India observed 64% of the cholelithiasis patients to have altered lipid profile which was much higher than in our study.

In diabetes, increased insulin resistance & compensatory hyperinsulinemia leads to overproduction of very low density lipoprotein cholesterol (VLDL). Resulting in high serum TG levels, high LDL & low serum HDL. A relative deficiency of lipoprotein lipase (insulin sensitive enzyme) may in part be responsible for reduced clearance of TGs & decreased formation of HDL. [18] The result is the increased levels of cholesterol ester rich fasting & postprandial triglycerides which is the central lipoprotein abnormality of the Met Syn. [19] This may also act as a risk factor for coronary artery disease & GSD. [22] Increased insulin level, increase the activity of methylglutaryl-coenzyme A reductase, which is the rate limiting step in the cholesterol synthesis, increasing hepatic uptake of LDL cholesterol, increased nucleation of cholesterol crystals & GSD. [17] Changes in the diet, exercising & improving dyslipidemia through medications lowers the risk of GSD [23]

### Conclusion

The present study concludes Metabolic syndrome to be a potential risk factor for the development of gall stone disease. Waist circumference, hyperglycemia & low serum HDL cholesterol were found to be statistically significantly associated with gall stone disease. Metabolic syndrome plays an important role in pathogenesis of cardiovascular disease & diabetes. Adequate measures should be taken to monitor & manage dyslipidemia & insulin resistance to avoid the risk of gall stone disease & its complications.

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