

Association of gall stone with metabolic syndrome- are we dealing with a new high-risk group?

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Abstract

Background: Gallstone disease (GSD) is a common gastrointestinal disorder with rising prevalence in India, coinciding with an increasing burden of metabolic disorders. Metabolic syndrome, comprising obesity, dyslipidemia, hypertension, and hyperglycemia, has been suggested as a potential risk factor for gallstone formation and complications. This study aimed to assess the association between metabolic syndrome and gallstone disease, with a focus on complicated versus uncomplicated cases.

Methods: A prospective observational study was conducted over two years at the Department of Surgery, Heritage Institute of Medical Sciences, Varanasi. Adult patients (≥ 18 years) with ultrasonographically confirmed gallstones were enrolled. Patients were categorized into complicated gallstone disease (CGSD) and uncomplicated gallstone disease (UGSD). Metabolic syndrome was defined using NCEP ATP III criteria. Clinical, biochemical, and ultrasonographic data were collected and analyzed using SPSS 26.0.

Results: A total of 100 patients were included, with a mean age of 33.5 ± 17.99 years; females predominated (male:female = 0.3:1). Metabolic syndrome was significantly associated with complicated gallstone disease (OR 3.986; 95% CI: 2.142–6.872; $p < 0.001$). Among the components of metabolic syndrome, fasting hyperglycemia and low HDL showed significant correlations with complications ($p < 0.001$ and $p < 0.05$, respectively). ROC analysis indicated a limited predictive value of individual components (AUC = 0.54).

Conclusion: Metabolic syndrome is significantly associated with complicated gallstone disease, highlighting a potentially high-risk group. Early identification of patients with asymptomatic gallstones and metabolic syndrome may help prevent progression to complicated disease, emphasizing the need for integrated metabolic and gastrointestinal risk management.

Keywords: Gallstone disease, Complicated gallstones, Metabolic syndrome, Obesity, Dyslipidemia

Introduction

Gallstone disease (GSD) is a common gastrointestinal disorder characterized by marked geographical variation in prevalence. While its incidence is or all lower in developing countries than in the Western populations, recent trends suggest increasing burden in these areas. The incidence of gall stones in India is estimated to be about 4% as compared to almost 10% in the western nations.^[1] Despite this overall lower prevalence, very large differences exist by region of the country. Epidemiological studies that rely predominantly on surgical and autopsy findings^[1–3], are likely to underestimate the true burden in the population, since community-based data remains limited^[4–11]. In fact, higher prevalence was reported from North India than South India; Malhotra et al. In a study, [12] reported that the prevalence of gallstones, in North Indian populations was almost seven times higher than South Indian residents with no explanation for this discrepancy. Although much has been achieved in understanding the pathophysiology of the development of gallstones, the epidemiological factors, especially in relation to the Indian population, have not received enough attention. Various factors, including age, gender, obesity, and metabolic disorders, have all been shown to contribute towards the development of gallstones, but the interplay of all these factors in relation to the Indian population needs further research. The epidemiological situation in India is such that the population is currently experiencing a rapid epidemiological transition, with an increased incidence of metabolic disorders. India is also termed the “diabetic capital of the world.” The incidence of metabolic syndrome is very high in this population, which is

attributed to urbanization, increased prevalence of an “unhealthy diet,” and a “sedentary lifestyle.” Over the past two decades, the availability of ultrasonography has increased, thereby enhancing the detection rate of gallstones, thus emphasizing the importance of the condition.

Gallstone disease is a significant contributor to healthcare expenditure, and it is also associated with considerable morbidity, including potentially serious complications such as acute cholecystitis, pancreatitis, and biliary obstruction. Although most people suffering from gallstones are asymptomatic, a minority do experience symptomatic or complicated gallstone disease, for which they seek medical attention. It is, therefore, critical for early identification of people at increased risk of developing complicated gallstone disease. The cluster of metabolic disorders, including obesity, type 2 diabetes mellitus, dyslipidemia, and hypertension, known as metabolic syndrome, is now recognized as an important factor in the development of gallstones^[7,8]. The physiological function of the gallbladder, which is bile concentration, is also a predisposing factor for gallstones. However, it is also clear that bile supersaturation is not sufficient, suggesting the influence of other metabolic and environmental factors.^[13]

There is a growing body of evidence suggesting a strong association between metabolic syndrome and gallstone disease. Alteration in lipid composition and insulin resistance are key components in the development of cholesterol gallstones, and glucose metabolism can also contribute to the development of cholelithiasis. Several research works have established metabolic syndrome as a risk factor for the

development of gallstones [15]. Recent research have established the association between metabolic syndrome and complicated gallstone disease [8]. The clinical implications of this association are significant, as the presence of metabolic syndrome in gallstone disease can increase the risk of disease progression in affected individuals. In this context, the present study was designed to assess and compare the prevalence of metabolic syndrome in complicated and uncomplicated gallstone disease, with the aim of understanding the role of metabolic syndrome in disease progression and clinical outcome.

Methodology

This prospective observational study was carried out in the Department of Surgery, Heritage Institute of Medical Sciences (HIMS), Varanasi, over a period of two years. The study population included adult patients suffering from gallstone disease (GSD), who either underwent surgical intervention for their disease or were managed conservatively in the event of complications. The study adopted a purposive sampling technique for selecting the study participants. All adult patients who were ≥ 18 years old and who attended the Outpatient Department (OPD) or Emergency Unit of the Surgery Department with ultrasonographically proven gallstones were included in the study. Patients with a history of prior abdominal surgery, associated abdominal pathologies, suspicion of malignancy in the gallbladder, or bleeding diatheses were excluded from the study. A thorough clinical evaluation was carried out for all the study participants, which included taking a detailed case history and physical examination. The assessment of metabolic syndrome included measuring the waist circumference (WC), blood pressure (BP), fasting blood glucose (FBS), glycated hemoglobin (HbA1c), lipid profile consisting of triglycerides (TG), and high-density lipoprotein (HDL).

Patients were categorized into two groups:

- Complicated gallstone disease (CGSD)
- Uncomplicated gallstone disease (UGSD)

Metabolic syndrome was defined according to established criteria (NCEP ATP III), taking into account the presence of at least three out of the five metabolic components: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, hypertension, and impaired fasting glucose. Statistical analysis was done using SPSS software version 26.0. Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. The Chi-square test was done for the assessment of the relationship between the variables. Odds ratio with 95% confidence interval was computed where appropriate. A p-value of less than 0.05 was considered statistically significant.

Result

A total of 100 patients with gallstone disease were included in the study. The mean age was 33.49 ± 17.99 years, with a majority in the age group of 31-40 years. Females outnumbered males (male:female = 0.3:1). The mean duration of symptoms was 5.29 ± 7.34 months. There was a significant correlation between age and symptom duration ($p < 0.05$). All patients had abdominal pain as a symptom. Abdominal tenderness was the most common symptom (58%), followed by fever (21%), abdominal mass (15%), and icterus (7%). The mean BMI was 26.57 ± 3.97 kg/m², with a significant correlation between age, BMI, and waist circumference ($p < 0.00001$). The mean waist circumference was 96.67 ± 14.78 cm. Most patients had multiple gallstones (Figure 1). Ultrasonography revealed an edematous gallbladder with calculi (Figure 2). Intraoperative findings revealed adhesions in Calot's triangle. Metabolic syndrome was found to have a significant association with complicated gallstone disease (OR 3.986; 95% CI: 2.142-6.872; $p < 0.001$). Metabolic syndrome was present in 29/43 complicated and 24/57 uncomplicated cases (Table 3). Among the components of metabolic syndrome, fasting hyperglycemia and low HDL had significant correlations ($p < 0.001$ and $p < 0.05$, respectively (Table 5). HbA1c was significant on univariate analysis ($p = 0.033$), while other components were insignificant (Table 4). ROC analysis revealed a poor predictive value (AUC = 0.54). The hospital stay was 5.44 ± 6.91 days.

Tables

Table 1: Correlation of Age, BMI and WC

VARIABLES	AGE	BMI	WC
N	100	100	100
$\sum X$	2829	1727.3	6284
Mean	43.5231	26.5738	96.6769
$\sum X^2$	133867	46911.01	621512
Std.Dev.	12.9544	3.9726	14.7871

Table 2: Correlation of metabolic syndrome with complicated gall stone disease

Metabolic syndrome	Complicated gall stone disease (43)	Uncomplicated gall stone disease (57)	Odd ratio at 95% confidence interval	P value
Present	29	24	OR 3.986 (CI: 2.142-6.872)	<0.001
Absent	14	86		

Table 3: Univariate Linear Regression

Coefficient B	Constant	Standard error	z	p	Odds Ratio	95% conf. interval
HBA1C	-2.48	1.16	2.13	0.033	0.08	0.01 - 0.82
TG	0.39	0.29	1.32	0.187	1.48	0.83 - 2.63
FBS	0.03	0.18	0.17	0.867	1.03	0.72 - 1.48
HDL	0.12	0.16	0.74	0.458	1.12	0.83 - 1.52

Table 4: Correlation of metabolic syndrome with other parameters

Components of Metabolic Syndrome	Complicated Gallstones (n)	Uncomplicated Gallstones (n)	Odds Ratio (95% CI)	P Value
Hypertriglyceridemia (TG ≥ 150 mg/dL) (n=92)	30	22	1.031 (CI: 1.064–1.045)	0.71
Large waist circumference (≥102 cm in men, ≥88 cm in women)	27	17	0.90 (CI: 0.504–1.605)	0.834
Systolic hypertension (BP >130 mm Hg)	29	20	1.585 (CI: 0.918–2.735)	0.12
Diastolic hypertension (BP >85 mm Hg)	31	17	1.285 (CI: 0.818–1.735)	0.2
Lower serum HDL-C (≤30 mg/dL in men, ≤35 mg/dL in women)	22	8	1.846 (CI: 1.048–3.25)	<0.05
Fasting plasma glucose ≥100 mg/dL or previously diagnosed type 2 DM	28	12	2.800 (CI: 1.609–4.874)	<0.001

Figures

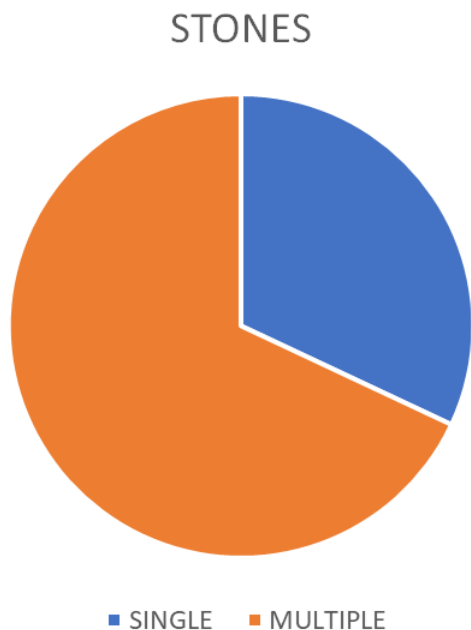


Fig 1: Presence of single or multiple stones

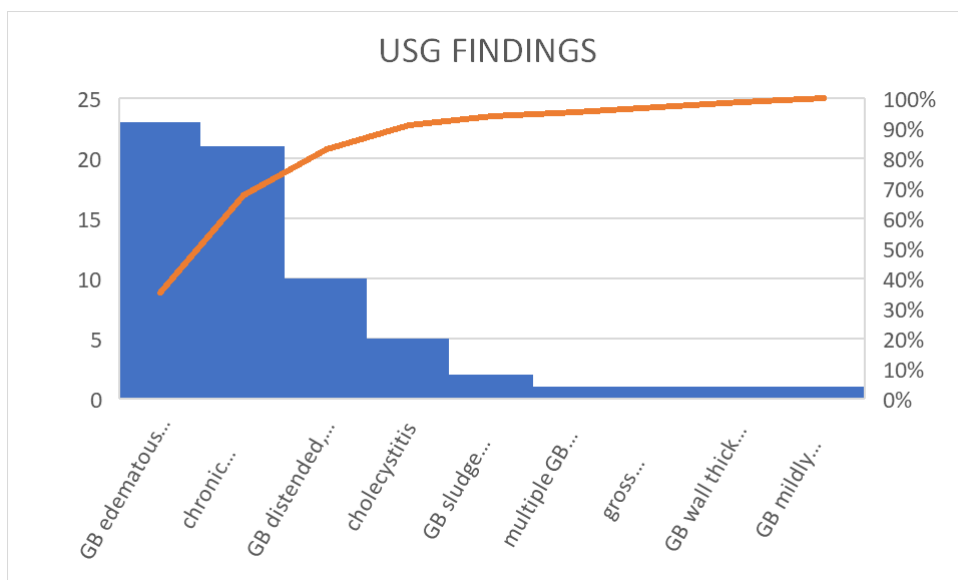


Fig 2: USG findings

Discussion

The present study demonstrated a significant association between metabolic syndrome and gallstone disease, especially complicated gallstone disease. With an increased prevalence of obesity and

metabolic syndrome in India, gallstone disease is being increasingly recognized as part of a spectrum of metabolic disorders.

The demographic profile of gallstone disease observed in our study, i.e., increased prevalence in females and a higher prevalence in the

31-40 years age group, was similar to previous studies. However, the mean age of our study was less compared to previous studies by Kumar et al. and Zhu et al.

The significant association between metabolic syndrome and complicated gallstone disease observed in our study (OR \approx 4) was similar to previous studies. Our study and previous studies by Ata et al. and Mendez-Sanchez et al. demonstrated metabolic syndrome to be a significant risk factor for gallstone disease.

The pathophysiological link between metabolic syndrome and gallstone disease may be explained by insulin resistance causing increased hepatic cholesterol secretion and hence supersaturation of bile. Dyslipidaemia due to increased triglycerides and decreased HDL is an additional factor for cholesterol crystal formation. Abdominal obesity is an important factor for gallstone disease formation.

In the present study, fasting hyperglycemia and low HDL were found to have significant correlations with complicated gallstone disease, thereby supporting the hypothesis that altered glucose and lipid metabolism play a crucial role in the development of complications. However, the lower AUC may also imply that individual factors may not play a crucial role in the prediction of complications; rather, a combined effect may be observed with the help of a condition such as metabolic syndrome.

From a clinical point of view, the present study has significant implications. It may help in identifying a high-risk group with asymptomatic gallstones and metabolic syndrome who may develop complications in the future.

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