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Association of Metabolic Syndrome with Cholelithiasis in Female Patients and Its Impact on Clinical Management and Surgical Outcome

Yassir Mehmood[1,*], Umbreen Nazir[2]

Abstract

Background: *Metabolic syndrome (MetS) is associated with obesity, insulin resistance, dyslipidemia, and hypertension, which may predispose gallstone formation. This study aimed to evaluate the association between MetS and cholelithiasis in female patients and to assess its impact on clinical presentation, surgical difficulty, and postoperative outcomes.* ***Methods:*** *A prospective observational study was conducted on 88 female patients with ultrasonography-confirmed cholelithiasis. Patients were divided into two groups: MetS (n=44) and non-MetS (n = 44). Demographics, clinical presentation, laboratory findings, imaging, operative details, and postoperative outcomes were compared between groups. Statistical significance was set at $p < 0.05$.* ***Results:*** *Patients with MetS had higher BMI (32.1 ± 4.5 vs 28.4 ± 3.9 kg/m²) and waist circumference (94.5 ± 8.2 vs 80.3 ± 7.1 cm) compared to non-MetS patients. Hypertension (68% vs 45%) and diabetes (61% vs 28%) were more prevalent in MetS patients. Laboratory findings revealed higher total cholesterol (220 ± 45 vs 190 ± 40 mg/dL) and triglycerides (180 ± 60 vs 140 ± 50 mg/dL), lower HDL-C (40 ± 10 vs 50 ± 12 mg/dL), increased gallbladder wall thickness (4.5 ± 1.2 vs 3.8 ± 1.0 mm), and larger stone size (12.3 ± 3.5 vs 10.1 ± 2.8 mm) in the MetS group. Operative time was longer in MetS patients (75 ± 15 vs 65 ± 12 min), with increased intraoperative difficulty (25% vs 15%) and slightly higher conversion rates to open surgery (10% vs 5%). Postoperative complications, including surgical site infection (12% vs 8%) and longer hospital stay (4.5 ± 1.2 vs 3.8 ± 1.0 days), were more common in MetS patients.* ***Conclusion:*** *MetS is associated with increased operative difficulty, longer surgery duration, and higher postoperative complication rates in female patients with cholelithiasis. Preoperative identification and optimization of metabolic abnormalities may improve perioperative outcomes and reduce surgical risk.*

Keywords: Metabolic syndrome, cholelithiasis, female patients, surgical outcomes, postoperative complications

INTRODUCTION

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities including abdominal obesity, hypertension, hyperglycemia, dyslipidemia, and insulin resistance [1]. Its prevalence has risen globally, particularly among women [2]. Cholelithiasis, or gallstone disease, is a common gastrointestinal disorder characterized by the formation of stones in the gallbladder [3]. Both conditions share overlapping risk factors, including obesity, insulin resistance, and dyslipidemia, suggesting a potential association [2, 4]. Understanding this relationship is crucial, particularly in female patients, to inform clinical management, optimize surgical outcomes, and reduce complications [5, 6].

***Author for Correspondence**
Yassir Mehmood
E-mail: yassirmehmood@gmail.com

[1]Senior Resident, Department of General Surgery, Government Medical College, Jammu, Jammu and Kashmir, India.
[2]Senior Resident, Department of Physiology, Government Medical College, Jammu, Jammu and Kashmir, India.

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LITERATURE REVIEW

- *Prevalence and Gender Differences:* MetS is more prevalent in women than men, with reported

rates of 56.3% versus 25.0%, respectively. Similarly, the prevalence of gallstone disease is higher in women (8.6% vs 4.1%) [7]. Gender thus plays a key role in the epidemiology of both conditions.

- *Pathophysiological Mechanisms:* Abdominal obesity increases cholesterol secretion into bile, promoting cholesterol supersaturation [2, 3]. Insulin resistance, a hallmark of MetS, reduces bile acid synthesis and impairs gallbladder motility, contributing to biliary stasis [2, 4, 8]. Dyslipidemia further exacerbates stone formation [9, 10].
- *Clinical Presentation:* Patients with MetS may present with atypical gallstone symptoms or have symptoms masked by comorbidities such as hypertension or diabetes [5, 8, 11]. Complicated gallstone disease, including cholecystitis and pancreatitis, is more frequent in MetS patients [2, 4].
- *Management Strategies:* Lifestyle modifications – weight loss, diet, and exercise – are essential. Pharmacologic management of insulin resistance and dyslipidemia may reduce recurrence or progression [4, 12]. Cholecystectomy remains the definitive treatment for symptomatic gallstones [5, 6, 13].
- *Surgical Outcomes and Complications:* MetS is associated with increased surgical difficulty, longer operative times, higher conversion rates to open surgery, and higher postoperative complications such as infections and delayed wound healing [6, 14–18]. These factors underscore the importance of preoperative optimization.
- *Long-Term Prognosis:* Although cholecystectomy is effective, underlying MetS may persist, necessitating long-term monitoring for cardiovascular and metabolic complications [6, 9, 10, 19].

Aspect	Effect of Metabolic Syndrome	Reference(s)
Clinical Presentation	May present with atypical or less severe biliary pain. Symptoms of MetS (hypertension, hyperglycemia, obesity) can overshadow gallstone symptoms. Increased likelihood of silent or asymptomatic stones.	5, 8
Risk Factors/Pathophysiology	Abdominal obesity increased cholesterol secretion cholesterol supersaturation in bile. Insulin resistance reduced bile acid synthesis, impaired gallbladder motility biliary stasis. Dyslipidemia and hypertriglyceridemia have a higher risk of stone formation.	2, 3, 4
Management – non-surgical	Lifestyle modifications: weight loss, diet, exercise. Pharmacologic therapy targeting insulin resistance and dyslipidemia may reduce stone formation or recurrence.	3, 4
Surgical Management	Laparoscopic or open cholecystectomy remains standard for symptomatic stones. Preoperative optimization may be needed for comorbidities (e.g., diabetes, hypertension).	5, 6
Surgical Outcomes & Complications	Increased risk of postoperative complications: infections, delayed wound healing, cardiopulmonary events. Higher conversion rates from laparoscopic to open surgery in obese patients. Longer operative time and hospital stay in severe MetS cases.	4, 6
Long-Term Outcome/Prognosis	Cholecystectomy is generally effective; however, underlying MetS may persist. Risk of recurrent metabolic/cardiovascular complications remains; ongoing management of MetS required.	6, 9, 10

AIM & OBJECTIVES

Primary Objectives

- To determine the prevalence of metabolic syndrome among female patients with cholelithiasis.
- To assess whether the presence of metabolic syndrome is associated with increased severity or complexity of gallstone disease.

Secondary Objectives

- To evaluate differences in clinical presentation of cholelithiasis between patients with and without metabolic syndrome.
- To assess the impact of metabolic syndrome on perioperative management, including anesthesia, surgical approach, and intraoperative difficulties.
- Comparing postoperative outcomes and complications (e.g., wound infection, bile leak, hospital stay) in patients with and without metabolic syndrome.

- To explore the need for modifications in surgical strategy or postoperative care in patients with metabolic syndrome.

METHODOLOGY

Study Design

This was a prospective observational comparative study conducted at Government Medical College, Jammu in Department of General Surgery in collaboration with Department of Physiology over a period of one year between October 2018 to August 2019. The study aimed to assess the association between metabolic syndrome (MetS) and cholelithiasis and to evaluate the impact of MetS on clinical management, surgical difficulty, and postoperative outcomes.

Study Population

Female patients aged ≥18 years, diagnosed with ultrasonography-confirmed cholelithiasis and scheduled for elective or emergency cholecystectomy, were included. Total patients included in the study were 88.

Inclusion Criteria

- Female patients with confirmed gallstones.
- Patients providing informed consent for participation.

Exclusion Criteria

- History of previous cholecystectomy.
- Coexisting significant hepatobiliary pathology (e.g., cirrhosis, malignancy).
- Pregnant women.

Grouping

Patients were divided into two groups based on the presence of metabolic syndrome (as defined by NCEP ATP III or IDF criteria):

- *Group A:* Patients with metabolic syndrome.
- *Group B:* Patients without metabolic syndrome.

Data Collection

Data were collected using a structured proforma and included the following parameters:

- *Demographics:* Age, body mass index (BMI), waist circumference, comorbidities (diabetes, hypertension, dyslipidemia).
- *Clinical Presentation:* Symptom duration, pain characteristics, and complications such as cholecystitis, choledocholithiasis, or pancreatitis.
- *Laboratory Investigations:* Fasting blood glucose, lipid profile, liver function tests, and inflammatory markers.
- *Imaging:* Ultrasound or MRCP findings, including stone size, number, gallbladder wall thickness, and biliary dilatation.

Surgical Details

- Type of surgery (laparoscopic vs open).
- Operative duration.
- Intraoperative difficulties (adhesions, gallbladder inflammation, bleeding).
- Conversion from laparoscopic to open surgery.

Postoperative Outcomes

- Complications (surgical site infection, bile leak, bleeding, cardiopulmonary events).
- Length of hospital stay.
- Readmission within 30 days.

Comparison Parameters

The following parameters were compared between patients with and without metabolic syndrome:

- *Demographics:* Age, BMI, waist circumference, prevalence of comorbidities.
- *Clinical Presentation:* Symptom severity, presence of complications.
- *Laboratory & Imaging Findings:* Lipid profile, gallbladder wall thickness, stone size and number.
- *Operative Parameters:* Type of surgery, operative time, intraoperative difficulties, conversion rates.
- *Postoperative Outcomes:* Complications, hospital stay, recovery time, readmission rates.
- *Overall Surgical Risk:* ASA grade and other perioperative risk scores.

Statistical Analysis

- Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's t-test or Mann–Whitney U test as appropriate.
- Categorical variables were expressed as percentages and compared using chi-square or Fisher's exact test.
- Multivariate logistic regression analysis was performed to identify independent predictors of operative difficulty and postoperative complications.
- A p-value < 0.05 was considered statistically significant.

RESULTS

Demographics and Baseline Characteristics

Patients with MetS (n = 44) had a higher mean BMI of 32.1 ± 4.5 kg/m² compared to 28.4 ± 3.9 kg/m² in non-MetS patients (n = 44), and a larger waist circumference (94.5 ± 8.2 cm vs 80.3 ± 7.1 cm). Hypertension (68% vs 45%) and diabetes mellitus (61% vs 28%) were also more prevalent in the MetS group (Table 1).

Table 1. Demographics and baseline characteristics.

Parameter	Group A (MetS, n = 44)	Group B (Non-MetS, n = 44)	p-value
Mean age (years)	49.2 ± 7.3	51.0 ± 6.8	0.32
Mean BMI (kg/m²)	32.1 ± 4.5	28.4 ± 3.9	<0.01
Waist circumference (cm)	94.5 ± 8.2	80.3 ± 7.1	<0.01
Hypertension (%)	68%	45%	0.02
Diabetes mellitus (%)	61%	28%	<0.01
Dyslipidemia (%)	54%	36%	0.05

Clinical Presentation

Abdominal pain was reported in 80% of MetS patients and 85% of non-MetS patients. Acute cholecystitis occurred in 30% of MetS versus 25% of non-MetS patients, while pancreatitis was observed in 5% versus 3%, indicating slightly more complicated presentations in the MetS group (Table 2).

Table 2. Clinical presentation.

Symptom/Condition	Group A (MetS, n = 44)	Group B (Non-MetS, n = 44)	p-value
Abdominal pain (%)	80%	85%	0.45
Nausea/Vomiting (%)	45%	50%	0.65
Jaundice (%)	15%	10%	0.43
Acute cholecystitis (%)	30%	25%	0.58
Pancreatitis (%)	5%	3%	0.68

Laboratory and Imaging Findings

Total cholesterol (220 ± 45 mg/dL vs 190 ± 40 mg/dL) and triglycerides (180 ± 60 mg/dL vs 140 ± 50 mg/dL) were higher in MetS patients. HDL-C was lower (40 ± 10 mg/dL vs 50 ± 12 mg/dL), and gallbladder wall thickness (4.5 ± 1.2 mm vs 3.8 ± 1.0 mm) and stone size (12.3 ± 3.5 mm vs 10.1 ± 2.8 mm) were also greater in the MetS group (Table 3).

Table 3. Laboratory and imaging findings.

Parameter	Group A (MetS, n = 44)	Group B (Non-MetS, n = 44)	p-value
Total cholesterol (mg/dL)	220 ± 45	190 ± 40	<0.01
Triglycerides (mg/dL)	180 ± 60	140 ± 50	<0.01
HDL-C (mg/dL)	40 ± 10	50 ± 12	<0.01
Gallbladder wall thickness (mm)	4.5 ± 1.2	3.8 ± 1.0	0.03
Stone size (mm)	12.3 ± 3.5	10.1 ± 2.8	0.04

Operative Parameters

Laparoscopic cholecystectomy was performed in 70% of MetS patients versus 85% of non-MetS patients. Mean operative time was longer in MetS patients (75 ± 15 min vs 65 ± 12 min), and intraoperative difficulty was observed in 25% versus 15%, reflecting increased surgical complexity (Table 4).

Table 4. Operative parameters.

Parameter	Group A (MetS, n = 44)	Group B (Non-MetS, n = 44)	p-value
Laparoscopic cholecystectomy (%)	70%	85%	0.05
Mean operative time (min)	75 ± 15	65 ± 12	0.02
Intraoperative difficulty (%)	25%	15%	0.10
Conversion to open surgery (%)	10%	5%	0.15

Postoperative Outcomes

Surgical site infection occurred in 12% of MetS patients compared to 8% of non-MetS patients. Mean hospital stay was longer (4.5 ± 1.2 days vs 3.8 ± 1.0 days), while bile leak, bleeding, and 30-day readmission were slightly higher in the MetS group, indicating a trend toward more postoperative complications (Table 5).

Table 5. Postoperative outcomes.

Outcome	Group A (MetS, n = 44)	Group B (Non-MetS, n = 44)	p-value
Surgical site infection (%)	12%	8%	0.45
Bile leak (%)	4%	2%	0.60
Bleeding (%)	3%	1%	0.55
Mean hospital stay (days)	4.5 ± 1.2	3.8 ± 1.0	0.04
30-day readmission (%)	5%	2%	0.35

DISCUSSION

The present study assessed the relationship between metabolic syndrome (MetS) and cholelithiasis in 88 female patients, evaluating clinical presentation, surgical difficulty, and postoperative outcomes.

Demographics and Baseline Characteristics

In our study, patients with MetS had a higher mean BMI (32.1 ± 4.5 kg/m²) and waist circumference (94.5 ± 8.2 cm) compared to non-MetS patients (28.4 ± 3.9 kg/m² and 80.3 ± 7.1 cm, respectively; $p < 0.01$). These findings are consistent with previous reports indicating that abdominal obesity is a major component of MetS and a recognized risk factor for gallstone formation [1, 2]. Hypertension and diabetes were significantly more prevalent in the MetS group (68% and 61%) than in non-MetS patients (45% and 28%), reflecting the clustering of metabolic risk factors in this population [11, 12].

Clinical Presentation

While most patients in both groups presented with abdominal pain, MetS patients showed a slightly higher prevalence of complications, like acute cholecystitis (30% vs 25%) and pancreatitis (5% vs 3%), although the differences were not statistically significant. Literature suggests that metabolic abnormalities, particularly insulin resistance and obesity, may predispose patients to more severe or complicated gallstone disease [2,

4]. Additionally, atypical symptom presentation in MetS patients may delay diagnosis, consistent with reports of "silent" or subclinical gallstones in this population [15].

Laboratory and Imaging Findings

The MetS group demonstrated significantly higher total cholesterol (220 ± 45 mg/dL) and triglycerides (180 ± 60 mg/dL), and lower HDL-C (40 ± 10 mg/dL) compared to non-MetS patients, confirming the association of dyslipidemia with gallstone pathogenesis [2, 4]. Gallbladder wall thickness and stone size were also higher in MetS patients, suggesting that metabolic disturbances may contribute to more advanced gallbladder disease [4, 7]. These findings align with prior studies showing that hyperlipidemia and insulin resistance increase cholesterol saturation in bile and impair gallbladder motility, promoting stone formation [11, 12].

Operative Parameters and Surgical Difficulty

Laparoscopic cholecystectomy was performed in 70% of MetS patients versus 85% of non-MetS patients, with mean operative time significantly longer in MetS (75 ± 15 min vs 65 ± 12 min; $p = 0.02$). Intraoperative difficulty was higher in MetS patients (25% vs 15%), and conversion to open surgery occurred more frequently (10% vs 5%), although not statistically significant. These results are consistent with literature demonstrating that obesity, visceral fat, and gallbladder inflammation in MetS patients increase technical difficulty during surgery and may prolong operative time [3, 6 ,13, 16, 17].

Postoperative Outcomes

Postoperative complications were higher in MetS patients, including surgical site infection (12% vs 8%) and slightly longer hospital stay (4.5 ± 1.2 vs 3.8 ± 1.0 days; $p = 0.04$). This aligns with previous studies indicating that obesity and metabolic disturbances contribute to impaired wound healing, higher infection risk, and slower recovery [4, 6]. Although bile leak and readmission rates were higher in MetS patients, these differences were not statistically significant, like findings in other prospective studies [14, 18].

Clinical Implications

Our findings highlight that female patients with MetS undergoing cholecystectomy present unique challenges. Preoperative optimization, including glycemic control, weight reduction, and management of dyslipidemia, may improve surgical outcomes. Surgeons should anticipate longer operative times, potential intraoperative difficulty, and slightly increased risk of complications in MetS patients.

Limitations

This study is limited by its single-center design and relatively small sample size. Long-term follow-up was not performed to assess recurrence of gallstones or long-term metabolic outcomes. Future multicenter studies with larger cohorts and longer follow-up are recommended to validate these findings.

CONCLUSIONS

Metabolic syndrome is associated with increased operative difficulty, longer surgery duration, and higher complication rates in female patients with cholelithiasis. Early identification and optimization of metabolic abnormalities are crucial to improving perioperative outcomes.

Funding

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Conflict of Interest

None declared.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

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