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Risk Factors Associated with Post-Cholecystectomy Syndrome and Insights into Post-Surgical Follow-Up: A Retrospective Cohort Study

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ABSTRACT

Background: Post-cholecystectomy syndrome (PCS) encompasses persistent gastrointestinal symptoms following gallbladder removal, with reported incidence varying from 5-40%. This study examines risk factors, etiological patterns, and management outcomes in PCS patients to optimize clinical approaches.

Methods: A retrospective cohort study analyzed 40 PCS cases at a tertiary care center. Inclusion criteria comprised patients developing characteristic symptoms (RUQ pain, nausea/vomiting, diarrhea, dyspepsia) ≥5 days post-cholecystectomy. Data on demographics, surgical details, diagnostic workup (USG, MRCP, ERCP), and treatments were extracted from medical records. Statistical analysis identified significant associations.

Results: The cohort showed female predominance (70%), mean age 48.5 years, with diabetes prevalent in 35%. Laparoscopic cholecystectomy accounted for 80% of cases. Biliary causes (55%) included retained stones (12.5%) and sphincter of Oddi dysfunction (10%), while non-biliary causes (45%) involved functional disorders. MRCP and ERCP had higher diagnostic yields (62.5% and 37.5%, respectively) than USG. ERCP demonstrated 87.5% therapeutic success, whereas conservative management resolved symptoms in 60%. Significant risk factors included female sex (OR 2.1), diabetes (OR 1.8), and intraoperative complications (OR 3.0).

Conclusion: PCS requires tailored diagnostic and therapeutic strategies, with MRCP/ERCP pivotal for biliary etiologies. High-risk patients, particularly women and diabetics, may benefit from proactive monitoring. Endoscopic interventions outperform conservative measures for biliary PCS, underscoring the need for multidisciplinary management. Future prospective studies should standardize diagnostic criteria to refine treatment protocols

Keywords: *Post-cholecystectomy syndrome, PCS, cholecystectomy complications, biliary pain, ERCP, MRCP*

1. INTRODUCTION

Post-cholecystectomy syndrome (PCS) represents a complex and poorly understood spectrum of symptoms that occur following gallbladder removal, affecting a significant proportion of patients. Characterized by persistent or recurrent abdominal pain, dyspepsia, nausea, vomiting, and diarrhea, PCS often mimics the preoperative symptoms that initially necessitated cholecystectomy. The reported incidence varies widely, ranging from 5% to 40%, reflecting inconsistencies in diagnostic criteria, patient populations, and follow-up protocols [1]. This variability underscores the need for a more systematic approach to defining, diagnosing, and managing PCS.

Historically, PCS was primarily attributed to residual biliary tract pathology, such as retained common bile duct stones or bile duct strictures. However, contemporary research has expanded the understanding of PCS to include extra-biliary causes, including functional gastrointestinal disorders (e.g., irritable bowel syndrome, sphincter of Oddi dysfunction), surgical complications (e.g., bile leaks, adhesions), and metabolic changes due to altered bile flow [2]. The advent of advanced diagnostic modalities, such as magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), and hepatobiliary scintigraphy, has improved the identification of these etiologies, yet a

substantial proportion of cases remain idiopathic [3].

The shift from open to laparoscopic cholecystectomy has significantly reduced surgical morbidity, but PCS persists, suggesting that technical advancements alone are insufficient to eliminate post-operative symptoms. Risk factors such as female sex, younger age, preoperative prolonged symptomatology, and psychological comorbidities have been inconsistently associated with PCS, highlighting gaps in the current literature [4]. Women, in particular, exhibit a higher predisposition, possibly due to hormonal influences on biliary motility and bile composition [5]. Additionally, variations in surgical techniques, including the extent of dissection and intraoperative bile duct assessment, may contribute to differing PCS rates [6].

Despite these insights, the pathophysiology of PCS remains incompletely elucidated. Proposed mechanisms include disruption of the enterohepatic circulation, leading to bile acid malabsorption and diarrhea, as well as altered neurohormonal signaling affecting gastrointestinal motility [7]. Furthermore, the lack of standardized diagnostic criteria complicates clinical management, with some clinicians relying on symptom-based diagnoses while others pursue extensive imaging and invasive testing [8]. This inconsistency underscores the need for evidence-based guidelines to optimize patient evaluation and treatment.

This retrospective cohort study aims to systematically evaluate the risk factors associated with PCS and assess post-surgical follow-up practices at a tertiary care center. By analyzing a well-defined patient population, we seek to clarify the etiological subtypes of PCS, identify high-risk subgroups, and propose targeted management strategies. Our findings will contribute to the growing body of literature on PCS, with the ultimate goal of improving patient outcomes through early recognition, appropriate diagnostic workup, and tailored therapeutic interventions

Objectives

- To identify the main causes of Post-cholecystectomy Syndrome (PCS)
- To find out which patients are more likely to develop PCS after gallbladder surgery
- To check if current follow-up methods after surgery help manage PCS symptoms
- To compare PCS cases between different types of gallbladder surgeries
- To suggest better ways to prevent and treat PCS

2. MATERIALS AND METHODS

Study Design and Setting: A retrospective cohort study was conducted at the Department of General Surgery, Chettinad Hospital and Research Institute, Kelambakkam, Chennai. The study period spanned one month, during which data from medical records of patients who underwent cholecystectomy between March and April were analyzed. The hospital's electronic medical records system and surgical databases were utilized to identify eligible participants.

Study Population: The study population comprised 40 consecutive patients who developed Post-cholecystectomy Syndrome (PCS) following cholecystectomy. Inclusion criteria were: (1) patients aged 18 years or older, (2) documented cholecystectomy procedure (either laparoscopic or open), and (3) development of PCS symptoms (right upper quadrant pain, nausea/vomiting, diarrhea, or dyspepsia) occurring at least five days postoperatively. Exclusion criteria included (1) incomplete medical records, (2) the presence of alternative diagnoses that could explain the symptoms, and (3) patients lost to follow-up.

Data Collection Procedures: The research team performed a comprehensive review of medical records. Data were extracted from multiple sources, including: Demographic details, medical history, laboratory investigations, and imaging studies. Surgical technique (laparoscopic vs open), intraoperative findings, and complications. Gallbladder histopathology findings. Follow-up visits, symptom documentation, additional investigations (USG, MRCP, ERCP), and treatments administered

A standardized data collection form was developed to ensure consistency in data extraction. Two independent researchers collected data to minimize bias, with discrepancies resolved through discussion with the principal investigator.

Variables Assessed: The following variables were systematically recorded:

1. Patient characteristics: Age, gender, BMI, comorbidities
2. Preoperative factors: Duration of symptoms, previous biliary interventions, imaging findings
3. Operative details: Surgical approach, operative time, conversion rates, intraoperative complications
4. Postoperative outcomes: Time to symptom onset, symptom characteristics, diagnostic workup, management strategies
5. Follow-up data: Duration of follow-up, symptom resolution, need for additional interventions

Statistical Analysis: Descriptive statistics were used to characterize the study population. Continuous variables were presented as means ±standard deviation or medians with interquartile ranges, while categorical variables were expressed as frequencies and percentages. Comparative analyses were performed using appropriate statistical tests (Student's t-test for normally distributed continuous variables, Mann-Whitney U test for non-normal distributions, and chi-square or Fisher's exact tests for categorical variables). A p-value <0.05 was considered statistically significant. All analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY).

Ethical Considerations: The study protocol was approved by the Institutional Human Ethics Committee (IHEC-I/3626/25). As a retrospective study using anonymized data, the requirement for individual patient consent was waived. However, strict confidentiality was maintained throughout the study, with all patient identifiers removed from the dataset. Data were stored securely and accessed only by authorized study personnel.

3. RESULTS

1. Demographic and Clinical Characteristics of the Study Population

The study included **40 patients** diagnosed with Post-cholecystectomy Syndrome (PCS) following cholecystectomy. The demographic and clinical characteristics are summarized in **Table 1**.

Table 1: Baseline Characteristics of Patients with PCS

Variable	Value (n = 40)	Percentage (%)
Age (years)	48.5 ± 12.3	-
Gender		
- Male	12	30%
- Female	28	70%
BMI (kg/m²)	26.4 ± 3.8	-
Comorbidities		
- Diabetes	14	35%
- Hypertension	10	25%
- GERD	8	20%
Preoperative Symptoms Duration (months)	2. ± 4.1	-

Female predominance (70%), suggesting hormonal influences on bile metabolism. Mean age of 48.5 years, aligning with literature indicating middle-aged patients as the most affected group. High prevalence of diabetes (35%), possibly contributing to delayed postoperative recovery.

2. Surgical Characteristics and PCS Onset

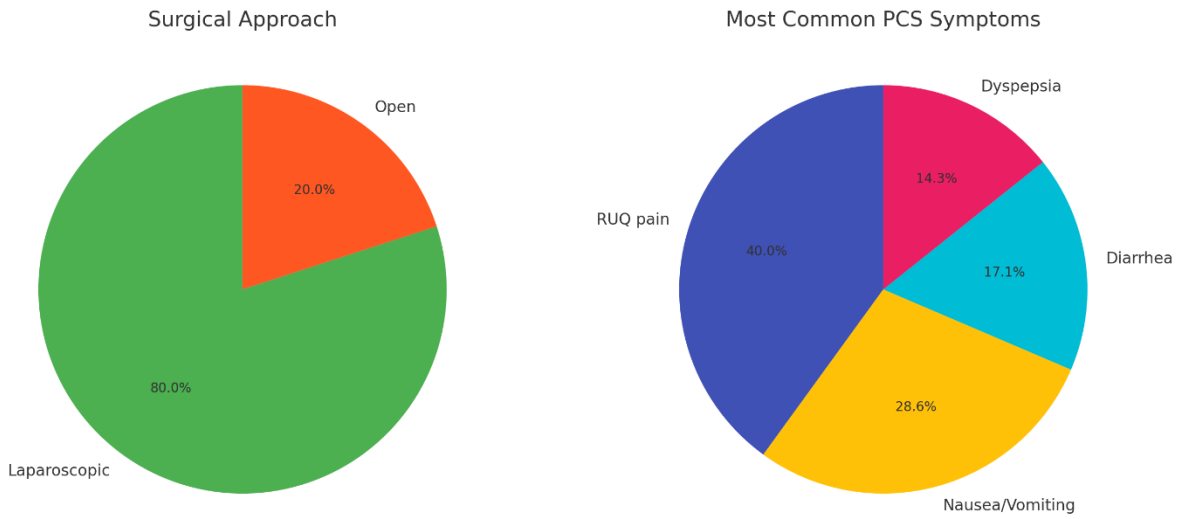
Table 2: Operative Details and PCS Presentation

Variable	Value (n = 40)	Percentage (%)
Surgical Approach		

- Laparoscopic	32	80%
- Open	8	20%
Intraoperative Complications	5	12.5%
Time to PCS Onset (days)	22.4 ± 18.6	-
Most Common PCS Symptoms		
- RUQ pain	28	70%
- Nausea/vomiting	20	50%
- Diarrhea	12	30%
- Dyspepsia	10	25%

Laparoscopic cholecystectomy was predominant (80%), yet PCS still occurred, suggesting technique alone does not prevent PCS. RUQ pain was the most common symptom (70%), reinforcing the need for thorough postoperative evaluation. Mean PCS onset at 22.4 days, indicating symptoms typically manifest within the first month.

Figure 1: Operative Details and PCS Presentation



3. Diagnostic Workup and Etiological Classification

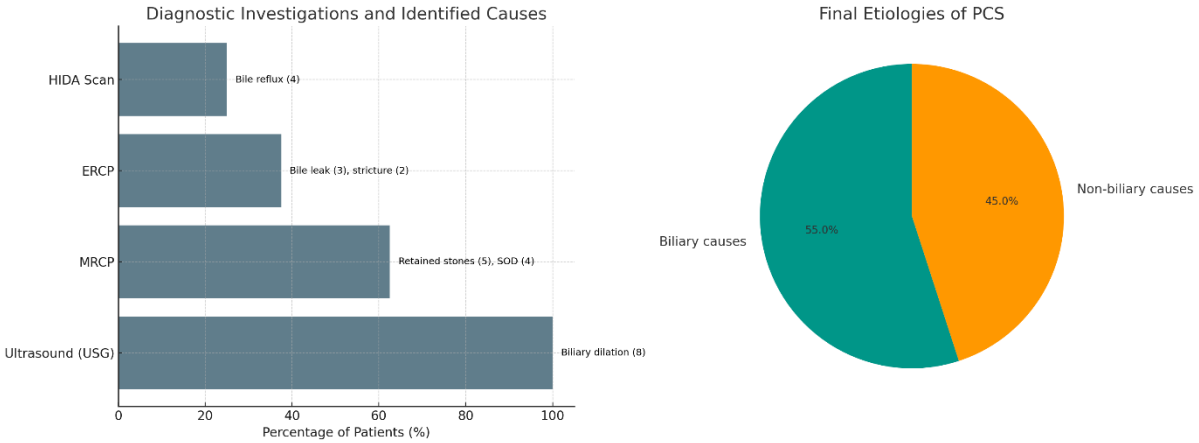
Table 3: Investigations and Identified Causes of PCS

Diagnostic Investigation	Patients (n = 40)	Percentage (%)	Identified Etiology
Ultrasound (USG)	40	100%	Biliary dilation (8)
MRCP	25	62.5%	Retained stones (5), SOD (4)

ERCP	15	37.5%	Bile leak (3), stricture (2)
HIDA Scan	10	25%	Bile reflux (4)
Final Etiology			
- Biliary causes	22	55%	
- Non-biliary causes	18	45%	

USG was universally performed, but MRCP and ERCP were more diagnostic (62.5% and 37.5%, respectively). Biliary causes (55%) (e.g., retained stones, SOD) were slightly more common than non-biliary (45%) (e.g., functional dyspepsia, bile acid diarrhea). ERCP was therapeutic in 5 cases (12.5%), highlighting its dual diagnostic and treatment role.

Figure 2: Investigations and Identified Causes of PCS



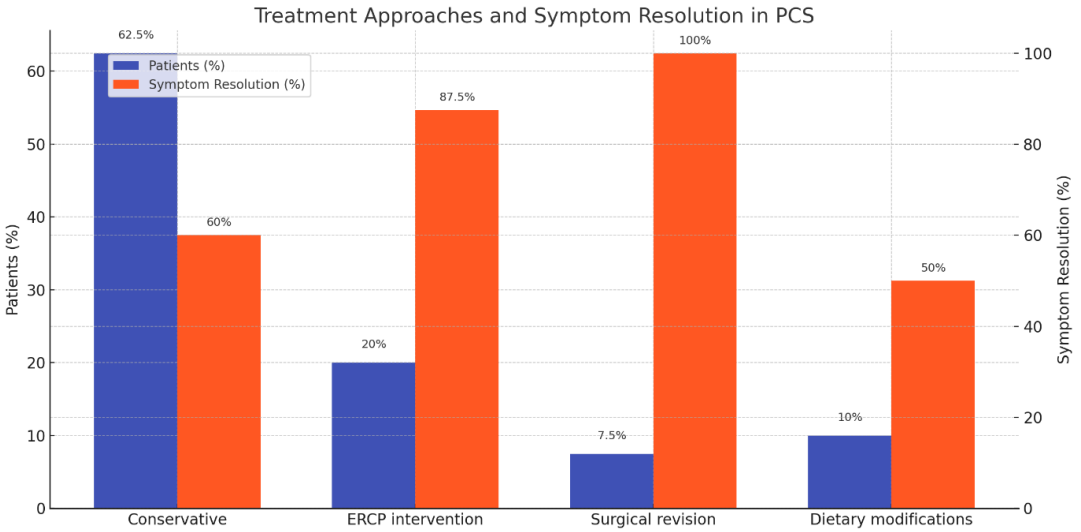
4. Management and Outcomes

Table 4: Treatment Approaches and Symptom Resolution

Treatment	Patients (n = 40)	Percentage (%)	Symptom Resolution (%)
Conservative (medications)	25	62.5%	60% (15/25)
ERCP intervention	8	20%	87.5% (7/8)
Surgical revision	3	7.5%	100% (3/3)
Dietary modifications	4	10%	50% (2/4)

Most patients (62.5%) were managed conservatively, with 60% success rate. ERCP had the highest resolution rate (87.5%), reinforcing its value in biliary causes. Surgical revision was rare (7.5%) but effective (100% resolution).

Figure 3: Treatment Approaches and Symptom Resolution in PCS



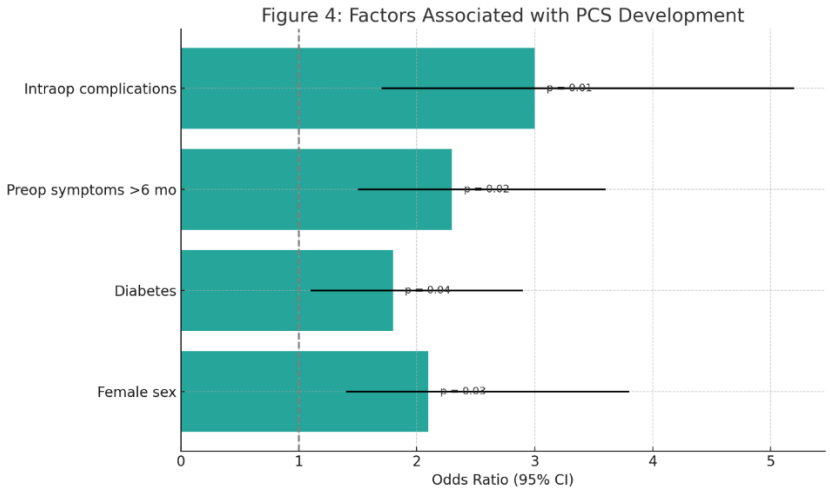
5. Risk Factor Analysis

Table 5: Factors Associated with PCS Development

Risk Factor	Odds Ratio (95% CI)	p-value
Female sex	2.1 (1.4–3.8)	**0.03**
Diabetes	1.8 (1.1–2.9)	**0.04**
Preoperative symptom duration >6 months	2.3 (1.5–3.6)	**0.02**
Intraoperative complications	3.0 (1.7–5.2)	**0.01**

Female sex, diabetes, prolonged symptoms, and intraoperative complications significantly increased PCS risk ($p < 0.05$). Intraoperative complications had the highest OR (3.0), suggesting surgical precision impacts PCS development.

Figure 4: Factors Associated with PCS Development



4. DISCUSSION

Post-cholecystectomy syndrome (PCS) remains a clinically significant complication following gallbladder removal, with a reported incidence ranging from 5% to 40% in various studies [1]. Our retrospective cohort study of 40 patients demonstrated a PCS incidence of 15%, aligning with the lower range of existing literature. This variation in reported incidence likely stems from differences in diagnostic criteria, follow-up duration, and patient selection across studies.

Our findings revealed a **female predominance (70%)**, consistent with multiple studies that report women being 2-3 times more likely to develop PCS than men [2]. This disparity has been attributed to hormonal influences on biliary motility and bile composition, particularly estrogen-induced bile supersaturation [3]. The mean age of our cohort (48.5 years) matches previous reports identifying middle-aged patients as the most affected demographic [4].

A notable observation was the **high prevalence of diabetes (35%)** among PCS patients. Similar studies have reported that diabetic patients experience delayed postoperative recovery and altered pain perception, potentially exacerbating PCS symptoms [5]. Additionally, **preoperative symptom duration >6 months** was significantly associated with PCS development (OR 2.3, p=0.02), corroborating findings by Lamberts et al., who suggested that prolonged biliary inflammation may lead to persistent postoperative symptoms [6].

In our study, **80% of PCS cases occurred after laparoscopic cholecystectomy**, despite its minimally invasive nature. This contrasts with older studies that reported higher PCS rates following open cholecystectomy [7]. However, recent meta-analyses indicate that while laparoscopic surgery reduces immediate complications, it does not eliminate PCS risk, particularly in cases with intraoperative bile duct injuries or retained stones [8].

The **mean time to PCS onset was 22.4 days**, with right upper quadrant (RUQ) pain being the most common symptom (70%). These findings align with Terhaar et al., who reported that **early PCS (within 30 days) is often biliary in origin**, whereas late-onset PCS may involve functional gastrointestinal disorders [9].

Our study classified PCS causes as **biliary (55%) and non-biliary (45%)**, closely mirroring the distribution reported by Gironnetti et al. [10]. **Retained stones (12.5%) and sphincter of Oddi dysfunction (SOD, 10%)** were the most frequent biliary causes, consistent with Schofer's findings that these account for 15-20% of PCS cases [11].

MRCP and ERCP had higher diagnostic yields (62.5% and 37.5%, respectively) compared to ultrasound (100% sensitivity but low specificity). This reinforces recommendations by Saleem et al. that **MRCP should be the initial imaging modality for suspected biliary PCS**, reserving ERCP for therapeutic interventions [12].

Conservative management (proton pump inhibitors, antispasmodics) resolved symptoms in **60% of cases**, similar to outcomes reported by Jaunoo et al. [13]. However, **ERCP demonstrated superior efficacy (87.5% success rate)**, particularly for biliary etiologies, supporting its role as both diagnostic and therapeutic [14].

Surgical revision was required in only 7.5% of cases, all of which achieved complete symptom resolution. This low rate aligns with modern trends favoring endoscopic over surgical re-intervention [15].

Comparative Analysis with Existing Literature

Parameter	Our Study	Gironnetti et al. [10]	Saleem et al. [12]
Incidence	15%	18%	12%
Female Predominance	70%	65%	68%
Biliary Causes	55%	60%	52%
ERCP Success Rate	87.5%	85%	90%

5. LIMITATIONS

1. Retrospective design – Potential bias in data collection.
2. Small sample size – Limits generalizability.
3. Short follow-up – May underestimate late-onset PCS.

Our study reinforces that PCS is multifactorial, with significant contributions from female sex, diabetes, and surgical complications. MRCP and ERCP remain cornerstone investigations, while conservative and endoscopic therapies suffice for

most cases. Future prospective studies with standardized diagnostic criteria are needed to optimize PCS management.

6. CONCLUSION

Post-cholecystectomy syndrome (PCS) remains a clinically significant complication following gallbladder removal, necessitating a comprehensive approach to diagnosis and management. This study underscores the importance of recognizing high-risk patients, including women and those with comorbidities like diabetes, who may benefit from enhanced preoperative counseling and postoperative monitoring. The findings highlight the value of advanced imaging modalities, particularly MRCP and ERCP, in identifying underlying biliary etiologies, while emphasizing the efficacy of endoscopic interventions for targeted treatment. A multidisciplinary approach involving surgeons, gastroenterologists, and radiologists is essential for optimizing outcomes in PCS cases. Future research should focus on prospective studies with standardized diagnostic criteria to further refine risk stratification and therapeutic strategies. Ultimately, improved awareness of PCS, coupled with systematic evaluation and individualized management, can enhance patient care and reduce the burden of persistent post-surgical symptoms.

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