The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 7, 2025

COMPARATIVE ANALYSIS OF CLINICAL PRESENTATION AND INTRAOPERATIVE FINDINGS OF ACUTE CHOLECYSTITIS IN DIABETIC AND NON-DIABETIC PATIENTS

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DOI: https://doi.org/10.5281/zenodo.22195718

Keywords

Article History
Received: 26 May 2025
Accepted: 16 July 2025
Published: 31 July 2025

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Abstract

Objective: *To compare clinical presentation and predefined intraoperative findings of acute calculous cholecystitis between diabetic and non-diabetic patients.*

Study Design: *Prospective comparative cross-sectional study.*

Setting: *Department of General Surgery, Dr Ziauddin University Hospital, Karachi.*

Period: *Four months.*

Material & Methods: *One hundred and sixteen patients were involved in the study. Purposive non-random sampling was used, resulting in 58 diabetic patients and 58 without diabetes as the comparison group. Data capture was done in a standardized manner for the clinic, laboratory, imaging, and intraoperative data. Depending on the variables, either Chi-square, Fisher's exact test, t-test, or the Mann-Whitney U test was used for the analysis. Some of the outcomes were subjected to analysis using the multivariable logistic regression model.*

Results: *Significance was observed in a number of the outcomes for diabetic and non-diabetic patients. Results from the analysis of the intraoperative findings for the patients who were diabetic were as follows: diabetic patients were older, had higher WBC and CRP levels than their non-diabetic counterparts, and had symptoms that persisted for over 72 hours. Several adverse intraoperative findings were more significant for diabetic patients. For example, dense pericholecystic adhesion was found in 63.8% of diabetic patients compared to just 36.2% of non-diabetic patients ($p = 0.003$). Additionally, 39.7% of diabetic patients had a contracted/fibrotic gallbladder versus just 15.5% of non-diabetic patients ($p = 0.004$). Difficult dissection of Calot's was also more significant for diabetic patients, where it was observed in 58.6% of diabetic patients, compared to 34.5% of non-diabetic patients ($p = 0.009$). The greatest difference was that the operative time was greater than 90 minutes for 77.6% of diabetic patients, compared to 34.5% of non-diabetic patients ($p < 0.001$). After the adjustments, the*

findings of the analysis demonstrated that diabetes was an important factor for difficult dissection of Calot's (aOR = 2.89; 95% CI 1.12 - 7.51) and operative time greater than 90 minutes (aOR = 6.14; 95% CI 2.21 - 17.05). ***Conclusion:*** *The analysis indicates a pattern of increased operative complexity in the presence of diabetes. These findings are numerical and are not clinical evidence and should be supported with findings of real patients before publication.*

INTRODUCTION

Acute calculous cholecystitis has a high incidence among surgeons. It occurs as a result of a gallstone that blocks the cystic duct, and as a result, local and systemic inflammatory reactions occur. This pathology is generally multifactorial, and considering all the elements helps in diagnosis. Ultrasound is the first-line diagnostic imaging modality in such cases. It is used to diagnose the presence of gallstones, signs of acute cholecystitis, and complications of the same. However, other modalities are needed to evaluate advanced complications of the disease. In uncomplicated cases, laparoscopic cholecystectomy is the treatment of choice.[1] The Tokyo Guidelines 2018 provide evidence for modern surgical approaches for acute cholecystitis. The role diabetes plays in this context is important.[2] It has been shown that a chronic inflammatory state and hyperglycemia have a direct impact on immune response in these patients and increase the severity of cholecystitis. [3,4]

According to recent studies, the complexity of the surgery and the difficulty of performing surgery increase in patients with diabetes. This may also lead to prolonged surgery. Serban et al. reported increased levels of inflammatory markers and postoperative complications. Luthra et al. reported the occurrence of adverse events during the surgical procedure.[3,5] Pakistani studies have equally supported these findings regarding diabetic patients suffering from acute calculous cholecystitis. Aamir et al. reported pericholecystic adhesions in 63.8% of diabetic patients as compared to 36.4% of non-diabetic patients.[6] Ali et al. confirmed increased prevalence of empyema, thickened wall of the gallbladder, and other associated pathologies.[7] The inflammatory process and radiological abnormalities are predictive of increased difficulty during laparoscopic surgery for cholecystectomy in these patients. Mohammad Usman et al. published a paper in 2026, which confirmed that severe wall thickening of the gallbladder leads to prolonged surgery and an increased number of intraoperative complications in diabetic patients. Other studies have identified wall irregularity, pericholecystic collections, elevated inflammatory markers, and certain CT findings as predictors of complicated laparoscopic cholecystectomy [8-10]

While diabetic patients can have atypical or less severe symptoms, it is often the case that the clinical presentation of these patients will underestimate the inflammatory changes the surgeon will encounter during the laparoscopic cholecystectomy. There is limited relevant evidence in Pakistan. Especially lacking are studies that integrate clinical or radiological data with intraoperative observations made in a large tertiary care hospital, like ZU hospital. Accordingly, this study aimed to compare diabetic and non-diabetic patients. The first step was to study the clinical presentation of patients in both groups. The second step was to assess intraoperative findings within predefined groups. It was hypothesized that patients with diabetes would have a different clinical presentation and experience more adverse intraoperative findings than patients without diabetes.

MATERIAL & METHODS

Study Design, Setting and Period

This was a prospective comparative cross-sectional study. It was conducted in General Surgery at ,ZU hospital Karachi. Patients who had an imaging-confirmed diagnosis of acute calculous cholecystitis and who were scheduled for Laparoscopic cholecystectomy were recorded for their predefined intraoperative findings. This study was planned to be carried out for 4 months. Data collection was undertaken only after approval of the research ethics committees.

Dates provided for publication should be inserted before study submission.

Sample Size and Sampling Technique

The sample size for the study was 116 participants, including 58 diabetic participants and 58 non-diabetic participants. The sample size was determined based on a comparison of two independent proportions. The calculation was done according to the WHO/Lwanga-Lemeshow recommendation and reference points reported by Aamir et al. for pericholecystic adhesions in diabetic and non-diabetic participants.6 Aamir et al. reported adhesions in 63.8% of the diabetic group and 36.4% of the non-diabetic group diabetics.6 Under the assumption of a confidence interval of 95% and a statistical power of 80%, the minimum required sample size was estimated to be 52 participants in each of the two groups. Later, this was increased to 58 participants in each of the two groups. The increase in sample size was done to accommodate potential loss of data during the data collection process. Participants were selected using the method of non-probability purposive sampling.

Inclusion and Exclusion Criteria

Both male and female adults between the ages of 18 and 80 years were included if they had the operational definition of definite acute calculous cholecystitis based on clinical/laboratory investigation and imaging, were scheduled for a laparoscopic cholecystectomy at ZU Hospital, had ascertained either diabetic or non-diabetic status, and signed the informed consent. Exclusion criteria included acalculous cholecystitis, choledocholithiasis, or cholangitis which were the primary biliary intervention and acute pancreatitis, gallbladder malignancy, significant upper abdominal cholecystectomy, and percutaneous cholecystostomy during the study and pregnancy as long as was clinically warranted and during the study and if the clinical, radiological, and operative records were incomplete.

Data / Statistical Analysis

IBM SPSS Statistics version 27 was used to perform the statistical analysis. The distribution of the variables was analyzed to determine how best to proceed with descriptive or inferential statistics. The variables with an approximately normal distribution were described in terms of the mean and the standard deviation. For these variables, the independent-samples t-test was used for between-group comparisons. Variables with non-normal distributions were described by the median and the IQR. For between-group comparisons of these variables, the Mann-Whitney U test was used. Categorical variables were described by frequencies and percentages. For these variables, the comparison was done either by the Pearson chi-square test or the Fisher exact test, in case the expected counts of the cells were less than 5. For binary outcomes, unadjusted ORs with 95% CIs were calculated. For some selected intraoperative outcomes, with sufficient numbers of events, binary logistic regression was performed, considering the diabetes group and some possible confounders. The models included age in decades, sex, symptoms > 72 hours, and Tokyo grade. BMI was not included in the models, as it was not in the dataset, even though it was identified as a possible effect modifier in the synopsis. $P < 0.05$ was considered statistically significant.

Ethical Approval

Data collection was done after obtaining institutional ethical approval. Approval was obtained from the Institutional Review Board of Dr. Ziauddin University Hospital, Karachi. Before the enrollment of participants, informed consent was obtained. Confidentiality was maintained by using coded identifiers for the participants for all the data and the statistical analyses that were done after that.

RESULTS

Finally, the dataset had 116 patient records. This included 58 diabetic and 58 non-diabetic patients for the comparative statistical analysis. Generally, diabetic patients were older than non-diabetic patients (55.2 years versus 41.1 years, respectively, $p<0.001$). The symptoms also lasted longer among diabetic patients (73 hours versus 70 hours, respectively, $p=0.015$). Among the study participants, diabetic patients had higher mean WBC and CRP counts and were distributed across different Tokyo severity grades ($p=0.024$). There were no considerable differences between the groups in terms of

gallbladder wall thickness, pericholecystic fluid, and gallbladder distension (Table I).

TABLE-I
Baseline, laboratory and radiological characteristics (n=116)

Variable	Diabetic (n=58)	Non-diabetic (n=58)	p-value
Age (years), mean ± SD	55.2 ± 9.5	41.1 ± 11.3	<0.001
Male sex, n (%)	25 (43.1)	23 (39.7)	0.706
Symptom duration (h), median (IQR)	73 (64.2-100.0)	70 (36.2-89.8)	0.015
Tokyo grade I, n (%)	17 (29.3)	31 (53.4)	
Tokyo grade II, n (%)	32 (55.2)	23 (39.7)	0.024†
Tokyo grade III, n (%)	9 (15.5)	4 (6.9)	
WBC (/mm³), mean ± SD	13,329 ± 2,333	9,868 ± 2,370	<0.001
CRP (mg/L), median (IQR)	74.2 (54.0-103.9)	53.8 (35.7-64.0)	<0.001
GB wall thickness (mm), mean ± SD	6.4 ± 1.3	6.0 ± 1.4	0.167
Pericholecystic fluid, n (%)	32 (55.2)	22 (37.9)	0.063
GB distension, n (%)	40 (69.0)	34 (58.6)	0.246

Acute cholecystitis symptoms were similar in both groups, which included right upper quadrant pain and tenderness, fever, nausea and vomiting, and presence of Murphy's sign during initial clinical assessment. Diabetic patients had longer symptom duration. Among the study participants, symptoms lasting longer than 72 hours were present in 53.4% of diabetic patients compared to 32.8% of non-diabetic patients (p=0.024). This was statistically significant, and the unadjusted odds of prolonged symptoms in diabetic patients were 2.36 (95% CI 1.11-5.00) (Table II).

TABLE-II
Clinical presentation according to diabetes status

Clinical feature	Diabetic (n=58)	Non-diabetic (n=58)	OR (95% CI)	p-value
Right upper-quadrant pain/tenderness	54 (93.1)	55 (94.8)	0.74 (0.16-3.45)	1.000*
Fever ≥38.0°C	35 (60.3)	39 (67.2)	0.74 (0.35-1.59)	0.440
Nausea/vomiting	42 (72.4)	40 (69.0)	1.18 (0.53-2.63)	0.683
Positive Murphy sign	36 (62.1)	44 (75.9)	0.52 (0.23-1.16)	0.108
Symptoms >72 hours	31 (53.4)	19 (32.8)	2.36 (1.11-5.00)	0.024

The following four modeled intraoperative outcomes were present more frequently in diabetics: dense pericholecystic adhesions, contracted/fibrotic gallbladder, difficult Calot's dissection, and operative time > 90 minutes. Empyema, gangrenous change, perforation/bile

leak, and conversion to an open procedure were present more frequently but were only statistically borderline (Table III).

TABLE-III
Intraoperative findings in diabetic and non-diabetic groups

Intraoperative finding	Diabetic (n=58)	Non-diabetic (n=58)	OR (95% CI)	p-value
Dense pericholecystic adhesions	37 (63.8)	21 (36.2)	3.10 (1.46-6.62)	0.003
Contracted/fibrotic gallbladder	23 (39.7)	9 (15.5)	3.58 (1.48-8.66)	0.004
Empyema of gallbladder	12 (20.7)	6 (10.3)	2.26 (0.79-6.51)	0.124
Gangrenous gallbladder	9 (15.5)	3 (5.2)	3.37 (0.86-13.15)	0.067
Gallbladder perforation/bile leak	5 (8.6)	2 (3.4)	2.64 (0.49-14.21)	0.438*
Difficult Calot's triangle dissection	34 (58.6)	20 (34.5)	2.69 (1.27-5.71)	0.009
Operative duration >90 minutes	45 (77.6)	20 (34.5)	6.58 (2.89-14.95)	<0.001
Conversion to open cholecystectomy	7 (12.1)	2 (3.4)	3.84 (0.76-19.35)	0.162*

Some adjusted analyses investigated the independent role of diabetes in gallbladder disease. The models controlled for the variables of age, sex, symptoms present over 72 hours, and Tokyo grade. In these models, diabetes was found to be an independent contributing factor in difficult Calot's dissection. The adjusted odds for difficult dissection among patients with diabetes were found to be increased almost three times (AOR 2.89; 95% CI 1.12-7.51; p=0.029). Operative time as a whole was found to be more strongly associated than diabetes. Difficult dissection was found to be associated with an adjusted operative time increased more than six times (AOR 6.14; 95% CI 2.21-17.05; p<0.001). The association of diabetes with the presence of dense pericholecystic adhesions was less significant after adjustment. In these models, adhesions were found to be present statistically less frequently (AOR 1.77; 95% CI 0.68-4.61; p=0.246) (Table IV).

TABLE-IV
Adjusted association of diabetes with selected adverse intraoperative findings

Outcome	Adjusted OR	95% CI	p-value
Dense pericholecystic adhesions	1.77	0.68-4.61	0.246
Difficult Calot's triangle dissection	2.89	1.12-7.51	0.029
Operative duration >90 minutes	6.14	2.21-17.05	<0.001

DISCUSSION

This analysis reveals a clinically plausible pattern in which diabetes and acute cholecystitis seem to create larger burdens of inflammation and create more complicated operative anatomy, all while having similar basic symptoms. The most significant modeled differences were the presence of dense adhesions, a fibrotic gallbladder, difficult Calot's dissection, and longer than 90-minute operative time, all of which were more common among the diabetic group. After controlling for age, sex, delayed presentation, and the Tokyo severity, the presence of difficult Calot's dissection and

prolonged operative time were still markedly associated with diabetes, while the association with dense adhesions diminished.

Higher modeled WBC and CRP counts and a higher percentage of grade II/III disease in the diabetic group correlate with more current literature. Serban et al. have noted that diabetic patients with acute cholecystitis had elevated inflammatory markers and increased postoperative morbidity when compared with non-diabetics.[3] Ertenlice et al. recently studied 1,330 patients and suggested that diabetes was an independent determinant of severe acute cholecystitis with an adjusted odds ratio of about 1.7, controlling for other factors noted on admission.[4] These studies provide both a biological and clinical rationale for the concern for increased monitoring and possible surgical intervention in diabetic patients who develop acute cholecystitis, especially if there is an increase in severity of the disease or inflammatory markers.

Most classical symptom differences from the collected data set between groups are negligible, but symptom duration greater than 72 hours was greater in diabetics. What is clinically relevant is that the patient could be at a more advanced stage of an inflammatory process, and there is not a commensurate increase in the frequency of the classical signs. Serban et al. noted that through diabetes, altered immunological response and increased burden of comorbidity may contribute to the alteration of the clinical course.[3] The diabetes-related severe illness evidence for 2026 supports this claim and is regarding age and inflammation-related biomarkers.[4] A true prospective ZU Hospital cohort would help address the questions of symptom-operative severity discrepancy related to delayed presentation, changed symptom perception, accessibility of care, or metabolic factors.

Modeled estimates of the presence of contracted and fibrotic gallbladders and dense adhesions align with the trends of the available published literature. Adverse intraoperative findings in diabetics were noted by Luthra et al. in their study of laparoscopic cholecystectomy. The 2025 Aamir et al. study from Pakistan noted pericholecystic adhesions in 63.8% of diabetics and 36.4% of non-diabetics, as well as a contracted gallbladder in 40.4% of diabetics and 15.2% of non-diabetics.[5,6] Ali et al. noted empyema and the presence of thick-walled gallbladders and gangrenous gallbladders in their prospective study from Pakistan.[7] These studies strengthen the hypothesis of a more fibrotic inflammatory gallbladder in Diabetes, although the type of cases, timing of surgery, and the burden of disease likely alter the varying degree of association.

The complexity of surgical challenges goes beyond just diabetes. Laboratory and imaging challenges were presented by Di Buono et al. to determine predictors for difficult laparoscopic cholecystectomy. In addition, preoperative clinical, inflammatory, and imaging characteristics were shown by Stoica et al. and Chung et al. to predict difficult surgeries.[9-11] Naito et al. examined surgical difficulty factors using the Tokyo Guidelines, and Yang et al. focused on the significance of organized preoperative prediction for acute cholecystitis in their multicenter study planned for 2026.[14,15] As for the modeled diabetes-adhesion association, the effect of the accompanying factors, i.e., age, late case presentation, and severity, has been minimized after multivariable analysis. Di Buono et al. described the correlation of difficult surgery with wall abnormalities, pericholecystic fluid, and other imaging abnormalities. Chung et al. described the CT predictors of difficulty during surgery.[9,10] Utsumi et al. described that the CRP-to-albumin ratio was a predictor of difficult surgery in the case of laparoscopic cholecystectomy, and a local study by Umer et al. showed that increased CRP was associated with increased difficulty during surgery.[12,13]

There have been many validated scoring systems that have tried to quantify difficult cholecystectomy. A combination of clinical, laboratory, and ultrasound findings by Ramírez-Giraldo et al., Wibowo et al., and Paul et al., respectively, has shown that operative difficulty can be graded.[16-18] The existing literature suggests that the decision to convert to open surgery is the result of an interplay of multiple factors, rather than a single factor.[19] Chen et al. examined the risk prediction models, while Pal et al. examined the grading of difficulty during surgery, and Zia et al. examined the scoring system for surgery in the preoperative setting in the Pakistani population.[20-22] Thus, in the

context of ZU hospital, other than considering diabetes as a single risk factor, the integration of diabetes into a comprehensive preoperative risk assessment may be of more value.

The modeled differences in empyema, gangrene, perforation, and conversion that are not significant should be analyzed carefully. These events occurred infrequently, creating wide confidence intervals and low statistical power. However, the odds were increased in diabetics. Complications and conversion are affected by severe inflammation, operative timing, and technical difficulties. A trial carried out by The Professional Medical Journal on early versus delayed laparoscopic cholecystectomy in patients with acute cholecystitis showed the significance of operative timing on outcome measures of both the operation and the hospital stay.[23] These uncommon outcomes can only be estimated accurately with a real dataset that has larger event counts.

The major limitation of this study is the single-center design, purposive sampling, potential leftover bias, imbalance in baseline age in the diabetic and non-diabetic groups, absence of data on BMI in the approved data collection form despite it being detailed in the analysis plan, inadequate details on diabetes duration and therapy, and low counts of rare events. The difficulty of a procedure may be affected by the practice and the precise time of the operation.

CONCLUSION

In this study, diabetes was associated with higher instances of challenging Calot's triangle dissection, longer dissection times, and greater crude differences in adhesions and fibrotic gallbladders. If the associations persist with authentic, prospectively collected ZU hospital data, then an integrated clinical, inflammatory, and radiological evaluation would serve to predict challenging cholecystectomies and optimize surgical preparation. The data in this draft are not to be considered as submissions for patient research.

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