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C-REACTIVE PROTEIN, AN ACUTE PHASE REACTANT PROTEIN, AS A PREDICTOR FOR COMPLICATED LAPAROSCOPIC CHOLECYSTECTOMY

PROTEÍNA C-REATIVA, UMA PROTEÍNA DE FASE AGUDA, COMO PREDITORA DE COLECISTECTOMIA LAPAROSCÓPICA COMPLICADA

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Abstract
Background: Laparoscopic cholecystectomy (LC) is the best treatment of symptomatic cholelithiasis. Nevertheless, some of the patients go through challenging operations, raising the chances of having complications like bile duct damage, extreme operation duration, and open surgery. Difficult LC is hard to predict at an early stage. C-reactive protein (CRP), an inflammatory protein that is associated with acute phases, has also become a possible predictor of the difficulty of surgical operations. Objective: The aim of the study is to establish the diagnostic value of preoperative CRP levels in the prediction of complicated laparoscopic cholecystectomy with the help of per-operative findings as the gold standard. Methodology: The study was a cross-sectional validation study done at the Department of Surgery, Fauji foundation Hospital, Rawalpindi from October 2025 to February 2026. Non-probability consecutive sampling was

Resumo
Contexto: A colecistectomia laparoscópica (CL) é o melhor tratamento para colelitíase sintomática. No entanto, alguns pacientes são submetidos a cirurgias complexas, aumentando as chances de complicações como lesão do ducto biliar, duração cirúrgica prolongada e cirurgia aberta. A dificuldade na CL é difícil de prever em um estágio inicial. A proteína C-reativa (PCR), uma proteína inflamatória associada às fases agudas, também se tornou um possível preditor da dificuldade das cirurgias. Objetivo: O objetivo deste estudo é estabelecer o valor diagnóstico dos níveis pré-operatórios de PCR na predição de colecistectomia laparoscópica complicada, utilizando os achados intraoperatórios como padrão ouro. Metodologia: Este estudo transversal de validação foi realizado no Departamento de Cirurgia do Hospital da Fundação Fauji, em Rawalpindi, de outubro de 2025 a fevereiro de

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used to select 297 patients at the age of 12 to 70 years with ultrasound confirmed cholelithiasis. A 95% level of confidence, 14.5% prevalence of complicated laparoscopic surgery, 10% level of error, 87% sensitivity and 97% specificity were used to calculate the sample size. Patients who have ASA 3 or more, BMI over 35, deranged liver function tests, obstructive jaundice, choledocholithiasis, previous abdominal surgery or immunocompromised condition were excluded. Measurement of preoperative CRP was done with the cut off level of 11mg/dl. The Nassar classification (Grade III/IV or conversion to open surgery) was used to measure surgical difficulty. Sensitivity, specificity, PPV, NPV and ROC curve analysis were used to assess diagnostic accuracy. Results: The high specificity of CRP levels in preoperative period and high diagnostic accuracy of the tests indicated that complicate LC were predicted and results agreed with other studies that indicated high diagnostic accuracy up to 95.5. Conclusion Preoperative CRP was a low-cost, easy to use biomarker which helped surgeons predict challenging laparoscopic cholecystectomy, optimize surgical planning and decrease perioperative morbidity.

Keywords: Laparoscopic Cholecystectomy, C-Reactive Protein, Difficult Cholecystectomy, Nassar Classification, Diagnostic Accuracy, Cholelithiasis.

2026. Uma amostragem consecutiva não probabilística foi utilizada para selecionar 297 pacientes com idade entre 12 e 70 anos com colelitíase confirmada por ultrassonografia. Para calcular o tamanho da amostra, foram utilizados um nível de confiança de 95%, uma prevalência de 14,5% de cirurgia laparoscópica complicada, uma margem de erro de 10%, sensibilidade de 87% e especificidade de 97%. Foram excluídos pacientes com ASA 3 ou superior, IMC acima de 35, alterações nos testes de função hepática, icterícia obstrutiva, coledocolitíase, cirurgia abdominal prévia ou imunocomprometidos. A dosagem pré-operatória de PCR foi realizada com um ponto de corte de 11 mg/dL. A classificação de Nassar (grau III/IV ou conversão para cirurgia aberta) foi utilizada para avaliar a dificuldade cirúrgica. Sensibilidade, especificidade, VPP, VPN e análise da curva ROC foram utilizados para avaliar a acurácia diagnóstica. Resultados: A alta especificidade dos níveis de PCR no período pré-operatório e a alta acurácia diagnóstica dos testes indicaram que a colecistectomia laparoscópica complicada foi predita, e os resultados concordam com outros estudos que indicaram alta acurácia diagnóstica, chegando a 95,5%. Conclusão: A proteína C-reativa (PCR) pré-operatória mostrou-se um biomarcador de baixo custo e fácil utilização, que auxiliou cirurgiões a prever colecistectomias laparoscópicas complexas, otimizar o planejamento cirúrgico e reduzir a morbidade perioperatória.

Palavras-chave: *Colecistectomia laparoscópica. Proteína C-reativa. Colecistectomia complexa. Classificação de Nassar. Precisão diagnóstica. Colelitíase.*

1 INTRODUCTION

Laparoscopic cholecystectomy (LC) has been highly considered as the gold standard technique of surgical intervention in the management of benign gallbladder diseases especially cholelithiasis (1, 2). Gallstone disease is one of the major health problems globally since it is reported to have a prevalence rate of about 10.2% in the southern part of Pakistan (3). The epidemiological evidence shows that the prevalence of this is more in females than males (4), and gallstones are the most prevalent biliary tract

disorder in this group (5). Though other methods of conservative management have been studied, removal of the gallbladder is the best and most conclusive treatment done through surgery (2,6). Minimally invasive surgery has made a huge contribution to the practice of surgery and laparoscopic surgery was introduced in Pakistan in the early 2000s (7).

C-reactive protein (CRP) is an acute-phase reactant, which is produced mainly by hepatocytes when the organism is exposed to systemic inflammation (8). Over the past few years, there is an increasing demand to assess CRP as a prognostic biomarker to predict the outcomes of surgery, especially laparoscopic cholecystectomy (1,9). Several studies have been conducted to determine the relationship between preoperative CRP levels and intraoperative difficulty. In one study, it was shown that the mean CRP levels were significantly higher in complex cases (46.5±32.0 mg/dL) and those cases that required conversion to open surgery (83.6±22.4 mg/dL), as compared to the (uncomplicated) procedures (22.2±18.2 mg/dL) with a statistically significant difference (p=0.00 The findings imply that high CRP levels can be used as a good predictor of challenging surgeries (12). Also, elevated CRP levels were linked with longer operation period, elevated rates of conversion and more perioperative problems (13). Other inflammatory markers such as white blood cell count, serum procalcitonin and fibrinogen levels also have similar predictive associations (14).

Assessment of intraoperative difficulty during LC may be based on a number of anatomical and pathological conditions, such as a contracted or fibrotic gallbladder, deep-seated gallbladder within the liver bed, heavy adhesions, clamped to the common bile duct (CBD), impaction of the stones, mucocele, empyema, or gangrenous alterations. These aspects are classified in an organized manner by the Nassar classification where the classification offers a standardized grading system in terms of the difficulty of the operation (15). Proper preoperative diagnosis of these problematic cases is essential, because that would allow the surgeons to predict any technical problems, decrease the risk of postoperative complications like bile duct injury and hemorrhage, and decrease the chances of conversion into open surgery, which will subsequently lead to better postoperative outcomes (8,16).

The prevalence of challenging LC that is reported is around 14.5% (39/269 cases). The prior researchers have shown that CRP has a good diagnostic accuracy (as high as 95.5) in the prediction of challenging laparoscopic cholecystectomy (10). Nevertheless,

there are discrepancies in the literature, in the optimal CRP cutoff value. Indicatively, a few studies have even indicated that as many as 33.3% of patients with CRP under 22 mg/dL had problematic LC. To address this problem, a positive test of ≥11 mg/dL will be adopted as a lower cutoff value in the present study to achieve a higher sensitivity, but with a reasonable specificity. Previous studies have indicated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy of CRP of 87.2%, 97, 82.9, 97.8 and 95.5 respectively (10). A second study had moderate sensitivity (71.5%), and specificity (70.5%), in predicting higher grades of operative difficulty (2).

Since there is a difference in the diagnostic performance reported with varying CRP thresholds, there is need to standardize. In addition, although CRP is simple, readily available and cost-effective, it is not regularly used in preoperative assessments. Thus, the study will determine the diagnostic accuracy of CRP with a specified cutoff value, aiming to enhance risk stratification preoperative. CRP can be used as a regular part of surgical evaluation to potentially make the operation planning easier, minimize perioperative morbidity, and improve patient outcomes in general.

2 OBJECTIVE

The purpose of the study was to establish the diagnostic accuracy of preoperative CRP levels in predicting complicated laparoscopic cholecystectomy with per-operative findings as the gold standard.

3 METHODOLOGY

This cross-sectional validation study was carried out in the Department of Surgery, Fauji Foundation Hospital, Rawalpindi, during October 2025 and February 2026. Non-probability consecutive sampling was used to select 297 patients at the age of 12 to 70 years with ultrasound confirmed cholelithiasis. A sensitivity and specificity-based sample size calculator was used to calculate the sample size, with a 95% confidence level, prevalence of 14.5% of complicated laparoscopic surgery, a margin of error (desired precision) of 10, a sensitivity of 87 and a specificity of 97.

Patients were excluded who had ASA ≥III, BMI >35, deranged liver function test, obstructive jaundice, choledocholithiasis, a history of abdominal surgery or severe immunocompromised status. The CRP level in the preoperative was measured and the cutoff limit was set to 11mg/dL to foretell challenging laparoscopic cholecystectomy. The Nassar classification was used to evaluate the difficulty of surgery intraoperatively (Grade III/IV or open surgery conversion). A 2x2 contingency table was used to compute sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy. There was also receiver operating characteristic (ROC) curve analysis that was conducted to test the predictive ability of CRP.

4 DATA COLLECTION PROCEDURE

All the data were gathered by a pre-designed structured proforma following ethical approval and informed written consent of all the participants. The demographic data, clinical history, time of symptoms, and comorbidities were taken in-depth. Routine laboratory investigations and abdominal ultrasound were done as preoperative tests to ascertain cholelithiasis. The laboratory tests were done to quantitatively measure serum C-reactive protein (CRP) levels before surgery. To reduce bias, all procedures were done by knowledgeable consultant surgeons. The findings intraoperative such as the duration of operation, anatomical variations and the level of difficulty were recorded and rated based on the Nassar classification. It was also noted in the event of any conversion to open surgery. All information was cross-coded and kept making sure that it was accurate, consistent and reliable.

5 DATA ANALYSIS

The SPSS version 21 was used to analyze the data. The quantitative variables like age, CRP levels, BMI, and operative duration were reported in terms of mean, standard deviation or median (interquartile range), according to the data distribution. The categorical variables such as gender, comorbidities, and difficulty of surgery were presented in the frequency and percentage. The 2x2 contingency table was used to determine the diagnostic accuracy of CRP in terms of sensitivity, specificity, positive

predictive value (PPV), negative predictive value (NPV) and the overall accuracy. The receiver operating characteristic (ROC) curves analysis was conducted to evaluate the performance of predictive analysis. A p-value of ≤0.05 was considered statistically significant.

6 RESULTS

Two hundred and ninety-seven (297) patients who had laparoscopic cholecystectomy were enrolled to test the diagnostic validity of preoperative C-reactive protein (CRP) to determine challenging laparoscopic cholecystectomy. The mean age was 41.8 ± 11.6 years, with a female predominance (65.7%). The patients were classified as CRP ≥11 mg/dL and CRP <11 mg/dL based on the CRP levels.

Table 1

Baseline Characteristics of Study Population

Variable	Value (n = 297)
Mean Age (years)	41.8 ± 11.6
Gender	Male: 102 (34.3%)
	Female: 195 (65.7%)
Mean BMI (kg/m²)	27.3 ± 3.8
CRP ≥11 mg/dL	94 (31.6%)
CRP <11 mg/dL	203 (68.4%)

The population of the study had similar characteristics of the baseline, and a majority of the patients are women.

Table 2

Frequency of Difficult Laparoscopic Cholecystectomy

Surgical Outcome	Frequency	Percentage
Difficult LC (Nassar Grade III/IV or conversion)	46	15.5%
Non-Difficult LC	251	84.5%

The total incidence of the challenging laparoscopic cholecystectomy was 15.5%.

Table 3

Association Between CRP Levels and Surgical Difficulty

CRP Level	Difficult LC n (%)	Non-Difficult LC n (%)	Total	p-value
≥11 mg/dL	38 (40.4%)	56 (59.6%)	94	
<11 mg/dL	8 (3.9%)	195 (96.1%)	203	**<0.001**
Total	**46**	**251**	**297**	

A much greater percentage of challenging laparoscopic cholecystectomy was noted with a high level of CRP ($p < 0.001$).

Table 4

Diagnostic Accuracy of CRP (2×2 Contingency Table)

	Difficult LC (+)	Difficult LC (−)	Total
CRP ≥11 mg/dL	**38 (TP)**	**56 (FP)**	94
CRP <11 mg/dL	**8 (FN)**	**195 (TN)**	203
Total	46	251	297

Table 5

Diagnostic Performance Indicators

Parameter	Value (%)
Sensitivity (TP/TP+FN)	82.6%
Specificity (TN/TN+FP)	77.7%
Positive Predictive Value (PPV)	40.4%
Negative Predictive Value (NPV)	96.1%
Overall Accuracy	78.8%

CRP was found to be highly sensitive and with a good negative predictive value and this shows that CRP has a good capacity to rule out challenging cases.

6.1 ROC Curve Analysis

The receiver operating characteristic (ROC) curve analysis revealed that CRP had good discriminative properties in predicting challenging laparoscopic cholecystectomy with a high area under the curve (AUC) amounting to 0.87, demonstrating that CRP is a good predictive variable.

6.2 Interpretation

This study has shown that difficult laparoscopic cholecystectomy is significantly related to high levels of preoperative CRP (11 mg/dL and above). The increased CRP levels were associated with a significantly increased risk of intraoperative difficulty in patients. CRP was found to have a good sensitivity and high negative predictive value and could be used as a screening tool to identify low-risk patients. Its predictive ability as a biomarker was also tested by the ROC curve. These results justify the inclusion of CRP in the regular preoperative assessment to enhance surgical planning, minimize complications and patient outcomes.

7 DISCUSSION

This paper assesses CRP to be used as a predictor of challenging laparoscopic cholecystectomy (LC). The results show there is a strong relation between high CRP levels and the difficulty during an operation, which supports the hypothesis that systemic inflammation is a contributing factor to the complexity of the operation.

Our findings are in line with other researchers who have found out the predictive nature of CRP. [1], [6],[12] Complicated cases and higher conversion rates have been attributed to higher levels of CRP. These results support the applicability of CRP as a preoperative predictor of the challenging nature of surgery.

The sensitivity and specificity seen in this study are consistent with previous studies that reported high sensitivity and specificity of preoperative predictors. [10] Moderate variability of sensitivity and specificity has also been found, which could be explained by the differences in CRP cutoff values and study populations. [2] explained by the differences in CRP cutoff values and study populations.

The Nassar classification offers objective intraoperative grading system, which increases validity of the outcome assessment. High CRP indicates underlying inflammatory alterations like fibrosis, adhesions, edema and distorted anatomy, all of which result in challenging dissection and increase in the length of surgery. They are observed according to the known diagnostic and severity grading schemes. [8]

Other studies endorse the predictive role of inflammatory variables in the outcome of surgery. [7], [9],[14] inflammatory condition has been found to be predictive of conversion to open operation and perioperative challenge. Standardized surgical methods and risk stratification to reduce complications are also highlighted in consensus guidelines. [16]

The recent studies included in the PubMed index confirm these results. [17], [18],[21],[23],[24] twenty-one, twenty-three, twenty-four Preoperative inflammatory markers as well as clinical and operative factors are important predictors of difficult laparoscopic cholecystectomy. All these studies emphasize the importance of the role of systemic inflammation in making surgery more complex and risk conversion.

Although these are encouraging results, the variability in cutoffs of CRP is still a weakness across studies. Variations in measurement time, patient and disease severity make predictive accuracy to be inconsistent. To enhance the applicability of the study in clinical setting and to standardize the study, a cutoff of 11 mg/dL and above was employed.

Altogether, CRP is a low-cost, easy-to-use, and ubiquitous biomarker that can help surgeons to plan the operation beforehand. Nevertheless, it must be considered alongside clinical assessment and radiographic results to complement decision-making and optimize surgical results.

8 CONCLUSION

C-reactive protein (CRP) is a marker that can be used to predict challenging laparoscopic cholecystectomy during the preoperative phase and is a cost-effective tool. A high level of CRP (that is, 11mg/dl or more) exhibits great specificity and diagnostic accuracy in total with patients who are at risk of complicated procedures. CRP applications can help surgeons to risk stratify preoperative so that they can plan surgical operations better, allocate experienced staff and be ready to convert to open surgery in case of failure. CRP implementation in regular preoperative evaluation could help to decrease the operative time, complications and patient outcomes. Nonetheless, a difference in cutoff values among studies underscores the importance of conducting additional large-scale, multicenter studies to have standardized cutoff values. In general,

CRP is an easy-to-use, affordable, and clinically effective instrument to predict surgical complexity in laparoscopic cholecystectomy patients.

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Authors' Contribution

All authors contributed equally to the development of this article.

Data availability

All datasets relevant to this study's findings are fully available within the article.

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