C-Reactive Protein as A Useful Predictor of Difficult Laparoscopic Cholecystectomy

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ABSTRACT

Objective: To determine the ability of C-reactive protein as a useful predictor of difficult laparoscopic cholecystectomy.

Study Design: Cross sectional study.

Place and Duration of Study: General Surgery unit of Combined Military Hospital, Rawalpindi Pakistan, from Nov 2021–Nov 2022.

Methodology: Fifty-six patients who underwent emergency or early laparoscopic cholecystectomy were made part of this study. After an informed consent age, gender, Body Mass Index and C-Reactive Protein levels were documented. Patients then underwent surgery and operative time along with "Nassar Difficulty Grade" was documented to define difficult cholecystectomy.

Results: A total of 56 patients who were scheduled to undergo laparoscopic cholecystectomy were included with mean age of 44.32±5.37 years. 23(41.10%) were male patients while 33(58.90%) were female patients. Mean CRP levels were 20.00±8.81 mg/L. Frequency of "difficult laparoscopic cholecystectomy" in patients who had high preoperative CRP was 15/22(68.18%) while in patients who had low preoperative CRP it was 13/34(38.23%). Additionally, bivariate analysis of CRP levels and mean operative time showed that Pearson correlation coefficient (r) value was 0.355 showing a significant positive correlation (p=0.007).

Conclusion: C-reactive protein levels in patients undergoing laparoscopic cholecystectomy for gallstones or any of its related problems are helpful in predicting whether or not the patient will have a challenging laparoscopic cholecystectomy.

Keywords: Cholecystectomy, C-reactive protein, Frequency, Laparoscopic cholecystectomy.

INTRODUCTION

Having a comprehensive grasp of anatomical distinctions is crucial when performing surgery on the gallbladder as it presents a wide variety of potential changes in anatomy.[1] Gallstones develop in the gallbladder when bile crystallizes and accumulates there; they are made up of a vast variety of substances.[2] Age over 40 years, pregnancy, female gender, obesity, thyroid dysfunction, and hypercholesterolemia are just few of the many documented and catalogued risk factors for gallstone formation.[3,4] Clinically, one of the most common symptoms that these patients report with is discomfort in the upper right quadrant of the abdomen, with or without jaundice.[5] One highly prevalent acute surgical condition is "acute cholecystitis" which presents characteristically with upper abdominal pain, fever and high count of white blood cells. The clinical diagnosis of "acute cholecystitis" is frequently confirmed using ultrasonography of the abdomen and hepatobiliary system.[6]

Laparoscopic cholecystectomy is a gold standard surgical treatment for management of cholelithiasis.[7] Some surgeons consider that the laparoscopic cholecystectomy procedure can be considered difficult if it lasts for more than 1 hour.[8] There are several methods to predict occurrence of "difficult cholecystectomy" that have been mentioned in the previous literature one of which is serum CRP levels.

C-reactive protein (CRP) is a marker of presence and severity of inflammation.[9] It is hypothesized that presence of raised CRP prior to surgery may indicate ongoing inflammation which may lead to adhesions at the surgical site, making surgery difficult. However, whether or not should it be used as standard of care for this purpose is still a debate. This study was thus aimed at determining the ability of C-reactive protein (CRP) as a useful predictor of difficult laparoscopic cholecystectomy.

METHODOLOGY

The cross-sectional study was conducted at General Surgery Unit of Combined Military Hospital Rawalpindi, Pakistan from November 2021 to

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November 2022 after obtaining approval from the Ethical Committee (IERB approval certificate number:306). Sample size was calculated using WHO sample size calculator by assuming the anticipated frequency of difficult cholecystectomy with high CRP 78.1% and anticipated frequency of not difficult cholecystectomy with low CRP 42.2%.[10]

Inclusion Criteria: Patients aged of 18 and 70, of either gender who underwent emergency or early (<72 hours after admission) laparoscopic cholecystectomy for acute cholecystitis were included.

Exclusion Criteria: Patients who had a history of respiratory disease such as asthma, patients who had a history of coagulation issue, patients with conditions

utilizing the four-port approach and carbon dioxide at a pressure of 12 mmHg to create "pneumoperitoneum." The gallbladder was dissected with the use of a "harmonic scalpel." Titanium clips were used to close and seal the cystic duct and the cystic artery. Any bleeding or biliary leakage that was immediately noticeable was halted before the gall bladder was removed from its location in the gall bladder bed. Operative time was recorded in order to determine the occurrence of "difficult laparoscopic cholecystectomy" and patients were labelled as having "difficult laparoscopic cholecystectomy" if it took more than 60 minutes [13]. Alongside this "Nassar Difficulty Grade" (Table-I) was also documented to define

Table-I: "Nassar Difficulty Grade"

Condition of GB	Condition of "Cystic Pedicle"	Adhesions
Non-adherent Floppy	Clear and thin	Up to the neck of GB or "Hartmann's pouch" Simple
Stone packed Mucocele	Laden with fat	Up to the GB body
Deep fossa Contracted and fibrosis Acute cholecystitis CBD and "Hartmann's pouch" adherent Impaction	Obscured, short or dilated "Cystic duct" with abnormal anatomy	Dense Up to fundus of GB, duodenum and/or hepatic flexure
Gangrenous and completely obscured GB Empyema GB Mass	Impossible to clear	Dense Fibrosis Difficult to be separated Wrapped around GB

that can lead to raised CRP levels like infection and/or drugs, and patients who were deemed unfit for surgery were all excluded.

We recruited patients using non-probability consecutive sampling. After obtaining informed consent, baseline demographic characteristics of all the included study participants, including age, gender, BMI and pre-operative CRP levels were documented.

For CRP levels, quantitative CRP was used which was performed in our hospital laboratory using Roche cobas c 501 analyzer with twice daily quality control. Two ml serum, collected in gel tube was used for each sample. Traditionally CRP levels of 1.0 to 10.0 mg/dL (10 to 100mg/L) are considered moderate elevation, levels more than 10mg/dl (100mg/L) are considered marked elevation and CRP levels of 50mg/dl(500mg/L) or more are considered severe elevation.[11] We used a mid-value of 22mg/L as cut-off with values > 22mg/L considered as high pre-operative CRP while value ≤ 22 mg/L considered as low pre-operative CRP .[12] A laparoscopic cholecystectomy was then performed on patients

"difficult cholecystectomy (Grade III and IV)".[14,15]

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 22. Normality of data was checked by Shapiro-Wilk test. Quantitative data was represented using mean with standard deviation and the median (IQR). Qualitative data was represented by using percentage and frequency. Data was stratified by age, gender, BMI and pre-operative CRP levels to see the effect on frequency of difficult cholecystectomy. Chi-square test (for qualitative variables) and unpaired t-test (for quantitative variables) were applied and p-value of ≤ 0.05 was taken as significant.

RESULTS

In our study a total of 56 patients who underwent laparoscopic cholecystectomy were included. Baseline characteristics of the included patients is tabulated below (Table-II):

As far as post-operative parameters (Table-III) are concerned it was found that mean operative time was

63.03±13.96 minutes. Mean operative time in patients with high levels of preoperative CRP was

68.14±14.36 minutes while in patients with low preoperative CRP mean operative time was 59.73±12.86 minutes (*p*=0.027). Composite frequency of Nassar difficulty grade-1 was 15/56(26.78%), grade-2 was 13/56(23.21%), grade-3 was 16/56(28.57%) and grade-4 was 12/56(21.42%). Amongst patients with high levels of preoperative CRP most common "Nassar Difficulty Grade" was grade-4 9/22(40.91%) followed by grade-3 6/22(27.27%), grade-1 5/22(22.72%) and grade-2 2/22(9.09%). On the other hand, patients with low preoperative CRP, common "Nassar Difficulty Grade" was grade-2 11/34(32.35%) followed by grade-1 10/34(29.41%), grade-3 10/34(29.41%) and grade-4 3/34(8.82%).

Table-II: Baseline Characteristics of Patients (n=56)

Characteristics	n(%)
Mean age (years) Mean±SD	44.32±5.37
Gender	
Male	23(41.10%)
Female	33(58.90%)
Mean BMI a (kg/m²) Mean±SD	28.37±4.12
Mean pre-operative CRP b mg/L Mean±SD	20.00±8.81
High preoperative CRP (>22mg/L)	22(39.30%)
Low preoperative CRP (≤ 22mg/L)	34(60.70%)

a = body mass index
b = C-reactive protein

Table-III: Post-operative Parameters of Patients (n=56)

Post-operative Parameters				*p-value*
Mean operative time (minutes) Mean±SD	63.03±13.96			------
Mean operative time (minutes) Mean±SD	High CRP	Low CRP		------
68.14±14.36	59.73±12.86		0.027	
"Nassar Difficulty Grade"				
1	15/56(26.78%)			
2	13/56(23.21%)			
3	16/56(28.57%)			
4	12/56(21.42%)			
High CRP		Low CRP		
Grade	Value	Grade	Value	
1	5/22(22.72%)	1	10/34 (29.41%)	
2	2/22(9.09%)	2	11/34 (32.35%)	0.021
3	6/22(27.27%)	3	10/34 (29.41%)	
4	9/22(40.91%)	4	3/34 (8.82%)	

Composite frequency of patients who had "difficult laparoscopic cholecystectomy" was 28(50%). Amongst these patients, frequency of "difficult laparoscopic cholecystectomy" in male participants was 12/28(42.85%) while in female patients it was 16/28(57.14%).

Frequency of "difficult laparoscopic cholecystectomy" in patients who had high preoperative CRP was 15/22(68.18%) while remaining 7/22(31.81%) had "simple laparoscopic cholecystectomy". On the other hand, frequency of "difficult laparoscopic cholecystectomy" in patients who had low preoperative CRP was 13/34(38.23%) while remaining 21/34(61.76%) had "simple laparoscopic cholecystectomy" (*p*=0.029), depicted below in Table-IV.

Table-IV: Frequency of "Difficult Laparoscopic Cholecystectomy" Based on CRP Levels (n=56)

	Difficult Laparoscopic Cholecystectomy (n=28)	Simple Laparoscopic Cholecystectomy (n=28)
High CRP (> 22mg/L)	15/22(68.18%)	7/22(31.81%)
Low CRP (≤ 22mg/L)	13/34(38.23%)	21/34(61.76%)
p=0.029		

Additionally, bivariate analysis of CRP levels and mean operative time showed that Pearson correlation coefficient (r) value was 0.355 showing a significant positive correlation (*p*= 0.007).

DISCUSSION

We found that there was a strong positive correlation between difficult laparoscopic cholecystectomy and pre-operative CRP levels. Frequency of "difficult laparoscopic cholecystectomy" and mean operative time in patients who had high preoperative levels of CRP was more than those with low levels of preoperative CRP and this difference was statistically significant. In our study, cut off value of high CRP was > 22mg/L which showed a significant correlation with difficult laparoscopic cholecystectomy.

In line with the findings of our study are the results of a previous study which was conducted by Kaushik *et al*.[14] with the similar aim to assess the preoperative CRP ability to predict "difficult laparoscopic cholecystectomy". They also reported that there was a statistically significant difference in the mean operative time and the frequency of "difficult laparoscopic cholecystectomy" in those patients who had high levels of preoperative CRP (> 22mg/L) than those with low levels of CRP (*p*=0.003). Another study reported that higher the levels of preoperative CRP, higher is the "Nassar Difficulty Grade" of the patient and vice versa which is also

consistent with the findings of our study.[15] In one study, cut-off value for high CRP level was > 6mg/L [16] which was much lower than our study.

An international study had similar results to our study, it was found that the frequency of "difficult laparoscopic cholecystectomy" was much higher in patients with high preoperative CRP as compared to those with low preoperative CRP with the difference being statistically significant (0.041) but in their study, cut-off value for high CRP level was > 100mg/dl (1000mg/L) which was much higher than our study.[17] However, much lower cut off value for high CRP i.e., ≥ 11mg/dl (110mg/L), that may predict difficult cholecystectomy was observed by Díaz-Flores *et al*.[18]

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CONCLUSION

C-reactive protein (CRP) levels in patients before undergoing laparoscopic cholecystectomy for gallstones or any of its related problems are helpful in predicting whether or not the patient will have a challenging laparoscopic cholecystectomy.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

WU & RQN: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

FS & MT: Study design, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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