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Efficacy of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio as Potential Biomarkers for Severity of Acute Calculous Cholecystitis

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ABSTRACT

Background: Acute calculous cholecystitis is a common presentation requiring surgical management. The decision for the line of treatment depends upon the degree of inflammation and severity of the disease. Therefore, the determination of severity is crucial. The objective of the present study was to assess the utility of Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) in determining the severity of disease.

Methods: This retrospective study analyzed 120 patient records with confirmed acute calculous cholecystitis admitted between October 2023 and March 2024. Demographic details, clinical history, laboratory investigations, and ultrasound findings were reviewed. Disease severity was graded according to Tokyo Guidelines 2018 (TG18). Operative details, type of surgery (laparoscopic vs open), conversion rates, and perioperative complications were recorded.

Results: The mean age was 49.9 years, with a female predominance (71.7%). Most patients presented with Grade II severity. Laparoscopic cholecystectomy was the mainstay (92.5%), with 9% requiring conversion to open surgery, while 7.5% underwent upfront open surgery. A strong positive correlation was noted between NLR and PLR ($r=0.88$, $p<0.001$). Mean NLR increased from 3.23 in Grade I to 17.07 in Grade III, while PLR rose from 146.4 to 340.3 across the same grades ($p<0.001$). Both ratios were significantly higher in patients undergoing open surgery compared to laparoscopic surgery ($p=0.004$ for NLR; $p<0.001$ for PLR). No major postoperative complications were observed.

Conclusion: NLR and PLR correlate well with the severity of acute calculous cholecystitis and may be used as early biomarkers for predicting disease severity. As they are inexpensive and widely available, they can also aid in guiding the choice of surgical management (laparoscopic vs open surgery) and help reduce unfavourable surgical outcomes.

Key-words: Acute calculous cholecystitis, Cholecystectomy, Inflammation, NLR, PLR, Tokyo guidelines

INTRODUCTION

Cholecystitis is a common disease, with acute calculous cholecystitis often requiring surgical management [1,2]. Abdominal ultrasound is the investigation of choice for diagnosis. However, the treatment plan is based on the patient's condition, the severity and type of cholecystitis, and the presence of complications. Accordingly, guidelines have been developed to grade the severity of the disease. Tokyo guidelines (TG) are the most widely used for grading of cholecystitis, with the most recent revision in 2018 (TG18) [3]. They include a combination of findings of patient history and examination, and results of the laboratory tests.

Surgical management remains the mainstay. With the advent of laparoscopic techniques, it has become the modality of choice and gold standard for

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cholecystectomies [4]. However, even the laparoscopic methods are associated with 0.1 to 1% mortality rate and 6 to 9% rate of significant complications [4], which include conversion to open surgery due to a lack of critical view because of adhesions and fibrosis.

Understandably, the degree of underlying inflammation is of the essence for diagnosis and treatment. Complete blood count (CBC) is a readily available and inexpensive test. There has been a recent interest in the assessment of the efficacy of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) as a biomarker of systemic inflammation in diseases such as appendicitis, ulcerative colitis and malignancies [5-8]. Utilization of NLR and PLR in diagnosing and grading acute cholecystitis using a simple test such as CBC is of importance, particularly in a developing country like ours, with limited health resources and restricted availability of trained Specialists. Therefore, the present study was conducted to evaluate the efficacy of NLR and PLR in predicting the severity of acute calculous cholecystitis.

MATERIALS AND METHODS

Place of study and Research design- The present hospital-based retrospective study was conducted under the Department of Surgery, Shri Vasantrao Naik Government Medical College, Yavatmal, Maharashtra, on records of patients admitted between October 2023 and March 2024 with a confirmed diagnosis of acute calculous cholecystitis. Consecutive patient records fulfilling the inclusion and exclusion criteria were analyzed until the desired sample size was achieved.

Methodology- A total of 120 records meeting the inclusion and exclusion criteria and having complete treatment records were included in the study. A detailed history was taken with demographic details and history of present illness. Findings of the ultrasound of the abdomen were noted. Findings of all the laboratory tests were recorded. The severity grade of acute calculous cholecystitis as per the TG18 guidelines was noted [3].

The details of operative management were recorded. Details of intraoperative and postoperative complications (if any) were noted. The conversion to open surgery was recorded.

Inclusion criteria

- ✓ Patients whose complete records were available
- ✓ Records of patients of either gender and aged >18 years
- ✓ Records indicating diagnosis with acute calculous cholecystitis and indicating surgical management, either laparoscopic or open cholecystectomy.

Exclusion criteria

- ✓ Patients with incomplete records
- ✓ Records of patients indicating other types of cholecystitis
- ✓ Records indicating significant comorbidities including malignancy, haematological disorders
- ✓ Records indicating history of previous abdominal surgery
- ✓ Records indicating pregnancy.

Statistical Analysis- Descriptive statistics, including measures of central tendency and standard deviation, were applied. Analytical statistics were performed using Chi-square test/Fisher's exact test for quantitative data and Unpaired t-test for qualitative data. The Pearson Correlation test assessed correlation. The p-value of less than 0.05 was considered "statistically significant".

RESULTS

The mean age of the study population was 49.99±16.42 years. A female preponderance was observed in the study (71.67%). The age distribution (p=0.72) was similar in both genders. When assessed according to the severity, it was observed that many of the cases belonged to Grade II (Table 1).

There was no age (p=0.52) and gender difference (p=0.27) in the severity of acute calculous cholecystitis. When assessed according to the type of operative management, it was observed that 92.50% of the cases underwent laparoscopic surgery, while 7.50% of the cases underwent open surgery. Of the cases undergoing laparoscopic surgery, 9.01% required conversion to open surgery. There was no difference in the age (p=0.40) and gender distribution (p=0.90) according to the surgical procedure.

There was a strongly positive significant correlation between NLR and PLR (r=0.88; p<0.001). Neither NLR nor PLR values correlated with age or gender (p>0.05). When assessed according to the disease, it was observed that the mean NLR and PLR values increased with an increase in severity of the disease (Table 2).

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Table 1: Distribution of the surgical management as per severity of disease

Surgery	Grade I	Grade II	Grade III	p-value
Laparoscopic cholecystectomy	30 (93.75%)	45 (93.75%)	26 (65%)	0.001
Converted to open surgery	0 (0%)	3 (6.25%)	7 (17.5%)	
Open cholecystectomy	2 (6.25%)	0 (0%)	7 (17.5%)	

Table 2: Distribution of the NLR and PLR findings as per severity of disease

Parameter	Grade I (Mean±SD)	Grade II (Mean±SD)	Grade III (Mean±SD)	p-value
NLR	3.23±1.21	10.81±2.13	17.07±2.03	<0.001
PLR	146.44±25.02	213.35±21.09	340.26±27.72	<0.001

The mean NLR values were significantly higher in cases requiring open surgery (and converted laparoscopic cases) than in laparoscopic surgery cases (p=0.004). A similar trend was observed with PLR, with higher mean values in open surgery cases (and converted laparoscopic cases) than in laparoscopic surgery cases (p<0.001) (Table 3). There were no significant post-operative complications in any Group requiring treatment.

Table 3: Distribution of the NLR and PLR findings as per surgical management

Parameter	Laparoscopic surgery (Mean±SD)	Converted to open surgery (Mean±SD)	Open surgery (Mean±SD)	p-value
NLR	10.14±5.47	14.17±4.42	15.44±6.17	0.004
PLR	223.25±72.13	313.55±67.46	317.07±105.74	<0.001

DISCUSSION

It was noted that most of the admitted cases belonged to Grade II as per TG18 [3]. Laparoscopic surgery was the most common mode of treatment. In Grade I cases, laparoscopic surgery was successfully performed in most of the cases (93.75%) as compared to 65% cases with Grade III disease. In 2 cases with Grade I disease and 7 cases with Grade III disease, the decision of open surgery was made as per the ASA grade of the patient and imaging data showing abscess and complicated cholecystitis. The reasons for conversion of laparoscopic surgery to open surgery include the presence of inflammation and adhesions, which can obscure the visualization of anatomy and the critical view of safety, as noted in the study by Serban *et al.* [9].

Both NLR and PLR showed an increasing trend with the increase in severity of the disease. We also noted that cases where laparoscopic surgery could be successfully performed had lower NLR and PLR as compared to cases requiring open surgery.

Serban *et al.* included a total of 235 patients with acute calculous cholecystitis [9]. They observed a female preponderance (71.40%). The mean age was 54.6±16.3 years. They assessed the correlation of NLR and PLR and observed an increase in both NLR and PLR with an increase in the severity of disease as per TG13/TG18 grading (p<0.01). They observed that NLR was lowest in the cases undergoing laparoscopic surgery and highest in the cases undergoing open surgery. The levels in the cases requiring conversion of laparoscopic surgery to open surgery were intermediate (p=0.001). However, they did not find PLR to be significantly different (p=0.82). These findings were almost like the present study.

Turhan *et al.* also found significantly higher mean values of NLR and PLR in complicated cholecystitis than in the uncomplicated cases [10]. They found both ratios to be independent predictors of complications. Some other studies have found similar results [11-14].

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Kubat *et al.* compared the inflammatory markers between overdue urgent cholecystectomy and delayed cholecystectomy [15]. They observed NLR to be significantly higher in the cases requiring urgent cholecystectomy as compared to those planned for conservative management and delayed cholecystectomy ($p<0.001$).

In the study by Balbaloglu *et al*. they reported higher values of NLR and PLR in cases requiring conversion of laparoscopic cholecystectomy to open surgery as compared to cases undergoing laparoscopic surgery successfully [16].

Gall bladder inflammation is a major underlying factor in grading the severity of the disease, predicting complications, and requiring open surgery. Gall bladder stones lead to blockage of the duct and stasis of bile, leading to an inflammatory response which includes the secretion of inflammatory cytokines, platelet-activating factor, immunomodulatory cytokines [17,18], all of which lead to a state of relative lymphopenia, which is effectively measured by the increase in NLR and PLR.
may limit the generalization of results.

LIMITATIONS

The limitation of the present study was the sampling of single-centre indoor admission of patients with acute calculous cholecystitis, which may limit the generalization of results. Being retrospective, it depended on existing records and could not fully account for factors influencing NLR and PLR values. Larger multicentre prospective studies are needed to confirm these findings.

CONCLUSIONS

This study concluded that NLR and PLR correlate significantly well with each other and with the severity of acute calculous cholecystitis. Thus, they can be used as early biomarkers of inflammation in cases of acute calculous cholecystitis. Both tests are inexpensive and can be independently used as a reliable predictor of severity. Furthermore, they may also aid in deciding the modality of surgical management (laparoscopic vs open surgery) based on the degree of inflammation, thereby reducing the chances of unfavourable surgical outcomes.

CONTRIBUTION OF AUTHORS

Research concept-Ram V. Tongale, Vishal Yelke
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