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PRE-OPERATIVE NEUTROPHIL-LYMPHOCYTE RATIO TO PREDICT OUTCOMES IN ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT **Background:** Many scoring systems exist to predict operative difficulty and outcomes of laparoscopic cholecystectomy in acute cholecystitis. In elective laparoscopy where ambulatory/ outpatient surgery is considered, few studies are available. Neutrophil-lymphocyte ratio (NLR) can be used as an effective pre-operative predictive marker in elective laparoscopic cholecystectomy. **Materials and Methods:** A single center prospective observational study was done over a period of one year in 72 patients undergoing elective laparoscopic cholecystectomy. Only those patients with predicted easy/ moderate laparoscopic cholecystectomy were included. NLR ≥ 3 was considered high. Intraoperative and postoperative outcomes were studied in normal and high NLR patients. **Results:** Normal neutrophil-lymphocyte ratio (NLR) was noted in 46 patients (63.9%) and high NLR (≥ 3) in 26 patients (36.1%). Rates of previous cholecystitis/ cholangitis and ERCP with stenting were similar in both groups. Mean G10 intra-operative score was 1.98 (easy group) in normal NLR group vs 3 (moderate group) in high NLR group ($p < 0.05$). None of the patients who participated in the study needed conversion to open procedure or had adverse intra-operative outcomes. Post-operatively, patients with normal NLR had significantly low pain score at day 1 compared to high NLR group (1.91 vs 4.5; $p < 0.001$). Patients with high NLR also had significantly increased length of hospital stay (1.19 days in normal NLR vs 2.77 days in high NLR, $p < 0.001$). Positive predictive value (PPV) of high NLR in estimating hospitalization post-surgery of more than 1 day is 92.3%. **Conclusion:** Pre-operative NLR can be used as a cost-effective and useful tool in predicting outcomes in elective laparoscopic cholecystectomy, even in carefully selected group of patients. In settings of outpatient cholecystectomy, this will help in decision making and patient selection.

KEYWORDS : NLR Ratio, Ambulatory Laparoscopic Cholecystectomy, Predictive Factor, Operative Outcome

INTRODUCTION

Laparoscopic cholecystectomy (LC) is one of the most common laparoscopic procedures in daily surgical practice. It is the gold standard in the treatment of gallstone disease.[1] It has proven to be a safe procedure, with morbidity rates less than 3% and mortality rates around 0.2%.[2] Outpatient laparoscopic cholecystectomy (OLC) was first promoted in 1990 by Reddick and Olsen. Since then, surgeons around the world have been gradually implementing the outpatient regimen, and, together with the laparoscopic approach, advantages such as lower hospital costs and surgical waiting times have been added.[3]

Many surgical studies have been conducted to identify predictors of conversion from laparoscopic cholecystectomy to open cholecystectomy. Various scoring systems have been developed to assess the difficulty of laparoscopic cholecystectomy both pre-operatively and intra-operatively. Most popular among them include modified Randhawa and Pujahari system for pre-operative scoring and G10 scoring system for intraoperative scoring.[4,5,6]

However, in patients undergoing elective laparoscopic cholecystectomy, and having no features of acute cholecystitis on pre-operative assessment, less studies have been done to identify pre-operative prognostic parameters. Before planning for outpatient laparoscopic cholecystectomy, it becomes important to determine predictors that might help counsel patients regarding complications or hospital stay that may be longer than intended.

Surgery induces an acute inflammatory response, and many complications can occur in the early postoperative period.[7] Neutrophil-lymphocyte ratio (NLR) is derived from the ratios of counts of circulating neutrophils and lymphocytes, both of which are major leukocyte subpopulations. The inflammation-triggered release of arachidonic acid metabolites and platelet-activating factors results in neutrophilia, and cortisol-induced stress results in relative lymphopenia, and thus, the NLR accurately represents the underlying inflammatory process. In addition, it is simple to calculate and requires no additional tests or cost escalation.[8]

AIMS AND OBJECTIVES

We conducted a prospective observational study to determine the utility of neutrophil-lymphocyte ratio as pre-operative predictive factor for determining outcomes in elective laparoscopic cholecystectomies.

OBJECTIVES

1. To estimate the frequency of high neutrophil-lymphocyte ratio (NLR) in study population
2. To determine intraoperative difficulty in low and high NLR group
3. To determine number of hospitalization days post-surgery and post-operative complications in low and high NLR group

MATERIALS AND METHODS

All patients requiring elective laparoscopic cholecystectomy for gallstone disease between November 2022 to November 2023 were included in the study. Exclusion criteria were:

1. Age <18 years
2. Patients with ongoing acute cholecystitis
3. Patients undergoing other surgical procedures in the same setting.
4. Patients who have had ERCP done less than 6 weeks ago.
5. Patients with ASA grades 3 and higher
6. Patients with modified Randhawa and Pujahari scoring of more than 5 (only pre-operative scoring predictive of easy laparoscopic cholecystectomy are included in the study)

Study was conducted after clearance from institutional Ethics Committee. Informed consent regarding study details was obtained from all participants. All patients fulfilling the study criteria and consenting for the study were enrolled in the study. Relevant demographic and clinical data, pre-operative investigations such as complete blood counts, liver function tests, serum amylase, and radiological findings were studied. NLR was calculated for all patients by dividing either absolute or percentage differential of neutrophil to absolute/ percentage differential of lymphocyte, as per blood counts obtained pre-operatively. According to literature, NLR <3 was considered normal and NLR ≥ 3 was considered high. Patients were divided into high and normal NLR groups.

Intra-operatively, difficulty was studied using G10 scoring system and included gallbladder's operative appearance, whether distended or contracted, ease of access and the presence of sepsis in the peritoneal cavity, either biliary peritonitis or purulent fluid, and/or a cholecysto-enteric fistula. Post-operatively, pain score using visual analog scale was studied at day 1. All patients received similar post-operative care with intravenous antibiotics, fluids, and non-opioid analgesia. Length of hospital stay after surgery, incidence and details of any post-operative complications were noted as well. As per hospital protocols, all patients with uncomplicated course of surgery were discharged the day after surgery.

All data was entered in Microsoft Excel and statistical analysis was done using SPSS software. Descriptive statistics such as frequency and percentage were used to study the data. Data comparing high and normal NLR groups were analyzed using unpaired t-tests and Chi square test, as appropriate. A p value of <0.05 was considered significant in all the tests.

RESULTS

Total of 72 patients fulfilling the study criteria were included in the study. Most of the study participants were females (n = 49; 68.1%). Mean age group of participants was 47.1 years. Normal neutrophil-lymphocyte ratio (NLR) was noted in 46 patients (63.9%). High NLR (≥ 3) was noted in 26 patients (36.1%). Previous attack of cholecystitis and/ or cholangitis was noted in 18 patients (39.1%) in normal NLR group vs 12 patients in high NLR group (46.1%) (p > 0.05). Previous ERCP and stenting was done in 5 patients (10.9%) in normal NLR group vs 2 patients in high NLR group (7.7%) (p > 0.05). Average size of calculus was 9.7 mm vs 10.2 mm in normal vs high NLR groups respectively (p>0.05).

Table 1: Comparison of pre-operative predictive factors in normal and high NLR groups

	NORMAL NLR (n=46)	HIGH NLR (n=26)	P value
Previous history of cholecystitis or cholangitis	18 (39.1%)	12 (46.2%)	0.34
Previous history of ERCP with stenting	5 (10.9%)	2 (7.8%)	0.19
Average size of calculus	9.7 mm	10.1 mm	0.41
Presence of diabetes mellitus	5 (10.9%)	3 (11.5%)	0.93
Age > 50 years	21 (45.7%)	9 (34.7%)	0.36

Intra-operatively, adhesions involving <50% of gall bladder was seen in patients 28 (60.9%) in normal NLR group vs 3 patients in high NLR group (11.5%), and adhesions involving >50% of gall bladder was seen in 2 patients (4.3%) in normal NLR group vs 21 patients in high NLR group (80.8%). Other parameters in G10 intra-operative score were studied and elaborated in table 2. Mean G10 intraoperative score was 1.98 in normal NLR group vs 3. In high NLR group (p <0.05). However, both these mean scores fall under easy and moderate category respectively. None of the patients who participated in the study needed conversion to open procedure, incurred any injury to bile duct or had any significant intra-operative adverse outcome.

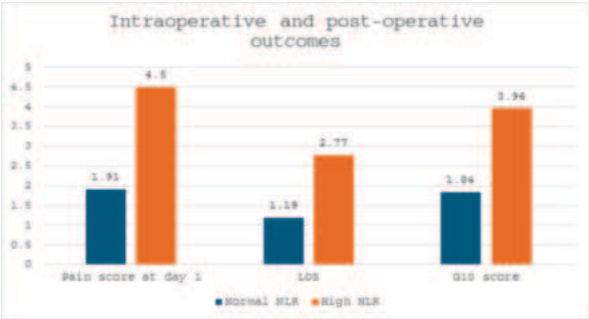
Table 2: G10 score in normal and high NLR groups. p value <0.001

G10 SCORING PARAMETERS	NORMAL NLR (n = 46)	HIGH NLR (n = 26)
Adhesions involving <50% GB	28 (60.9%)	3 (11.5%)
Adhesions involving >50% GB	2 (4.3%)	21 (80.8%)
Completely buried GB	0	0
Distended or contracted DB	34 (73.9%)	22 (84.6%)
Inability to grasp without decompression.	2 (4.3%)	8 (30.8%)
Stone >1 cm impacted in Hartmann's pouch.	5 (10.9%)	4 (15.4%)
BMI >30	5 (10.9%)	3 (11.5%)
Adhesions from previous surgery limiting surgery.	4 (8.7%)	2 (7.7%)
Free bile or pus outside the gallbladder	0	0
Fistula	0	0
Total score: (Max 10)	1.84	3.96

Post-operatively, patients with normal NLR had significantly low pain score at day 1 compared to high NLR group. (1.91 vs 4.5; p <0.001). Patients with high NLR also had significantly increased length of hospital stay (1.19 days in normal NLR vs 2.77 days in high NLR, p <0.001). In normal NLR group, 3 patients experienced hypoxia in post-operative period. In high NLR group, 12 patients had complications that included fever, vomiting or hypoxia. One patient among the high NLR required ICU stay for respiratory deterioration. Table 3 elaborates post-operative outcomes in the study. From our study results, positive predictive value (PPV) of high NLR in estimating hospitalization post-surgery of more than 1 day is 92.3%. PPV of high NLR in predicting occurrence of any post-operative complication is, however, 46.15% only.

Table 3: Post-operative outcomes in normal and high NLR group. Both length of hospital stay, and pain score have significant difference in mean with p <0.001.

Post-operative outcomes	Normal NLR (n= 46)	High NLR (n = 26)
Length of hospital stay post-surgery	1.19 days	2.77 days
Complications	Fever - 0 Hypoxia - 3	Fever - 5 Hypoxia – 3 Vomiting - 3 Respiratory distress requiring ICU admission - 1
Pain score at day 1	1.91	4.50



Graph 1: Summary of difference in mean outcomes in normal and high NLR groups

DISCUSSION

In the current era of improved laparoscopic techniques and instruments, difficult laparoscopic cholecystectomy can still result in longer operative time, and higher complication rate such as intraoperative bleeding, bile leakage, or bile duct injury.[5] Moreover, the conversion to open cholecystectomy might be inevitable in concern of patients' safety with varying range of 1%-15% in all LC.[9] In current literature, there had been many previous studies to identify significant factors affecting the difficulty and conversion of LC.

Randhawa and Pujahari's model is one of the preferable and practical scoring systems, using pre-operative information.[4] However, this model was established for LC at episode of acute cholecystitis. Tongyoo A et al.[5] had modified few terms in Randhawa's model to be eligible for delayed LC after any acute problems subsided. This modified Randhawa and Pujahari system includes the following: age >50 years, male, history of previous biliary inflammation and procedure, BMI 25-27.5, >27.5, abdominal scar, clinically palpable gallbladder or radiologically contracted gallbladder, wall thickness >4mm, pericholecystic collection and impacted stone.[5] In our study, we eliminated sonological predictive factors for difficult cholecystectomy even at patient selection. In addition, only patient with score of 0-5 were eligible for study participation.

Outpatient laparoscopic cholecystectomy has proven to be a safe and cost-effective technique; however, it is not yet a universally widespread procedure. Several studies have been done to assess factors determining failure of outpatient laparoscopic cholecystectomy. A meta-analysis study was done by Balciscueta et al.[3] on predictors of failure in ambulatory laparoscopic cholecystectomy. The predictors of outpatient laparoscopic cholecystectomy failure (any admission that required spending at least 1 night in hospital, even if discharge was given before the first 24 postoperative hours) were: age > 65 years, body mass index > 30 , American Society of Anesthesiologists score > 3, previous complicated biliary pathology, gallbladder wall thickening, surgical time exceeding 60 minutes, and the beginning of surgery after 1:00 PM. Sex and history of abdominal surgery in the supra-mesocolic compartment were not associated with outpatient laparoscopic cholecystectomy failure.

Based on the above-mentioned studies, we did a careful patient selection that would predict easy laparoscopic cholecystectomy. However, even in such circumstances, to further predict outcomes, we sought to use neutrophil-lymphocyte ratio. Several studies had been done to prove the utility of NLR in acute cholecystitis and in emergency settings. Studies by Beliaev et al.[10], and Mahmood et al.[11],

concluded that NLR can be used as an independent biomarker in predicting severity of acute cholecystitis. Kuon Lee et al.[12], also studied use of NLR in acute cholecystitis. NLR ≥3.0 was significantly associated with severe cholecystitis and prolonged LOS in patients undergoing cholecystectomy.

In the study, "The clinical utility of pre-operative neutrophil-to-lymphocyte ratio as a predictor of outcomes in patients undergoing elective laparoscopic cholecystectomy" by Moloney et al.[13], PNLR cut-off value of 3 was utilized. Those patients with PNLR>3 had associated prolonged operation time ($p < 0.005$), prolonged LOS ($p < 0.005$), and higher rates of conversion to open surgery ($p < 0.005$). It was thus concluded that PNLR correlates with outcomes following LC and that it is useful in delineating patients that have higher risk of conversion or prolonged length of hospital stay.

Our study shows similar results to study by Moloney et al.[13] in that NLR ≥ 3 is associated with prolonged length of stay. It was also associated with worse pain outcomes and complication rates after surgery. High NLR in our study also has high positive predictive value for length of hospital stay more than 1 day. Therefore, even in carefully selected group of patients with uncomplicated predicted course of laparoscopic cholecystectomy, NLR can serve as an important pre-operative marker in assessing outcomes. This helps us further our decision making and patient selection in advising ambulatory/ outpatient LC for the patient.

CONCLUSION

Neutrophil-lymphocyte ratio can serve as a useful independent predictive factor in determining post-operative pain, post-operative complications and length of hospital stay in patients undergoing elective laparoscopic cholecystectomy. This is an easy tool with no escalation of costs, and even in cases where careful selection has been done based on existing pre-operative scoring systems, it serves as an efficient tool in predicting outcomes. In settings where ambulatory/ outpatient laparoscopic cholecystectomy is considered, NLR will prove integral in decision making and patient selection.

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