MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.7.416.420

Neutrophil-to-Lymphocyte Ratio as A Predictor for Severe Acute Cholecystitis

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Abstract

Acute cholecystitis(AC) is a frequent surgical emergency case. Preoperative inflammation and metabolic problems as well as an extended hospital stay are the outcomes of cholecystitis progression from basic to severe. The neutrophil to lymphocyte ratio (NLR) is a novel, low-cost predictive biomarker for severe AC that can be used to stratify patients for the best course of treatment. The NLR appropriately reflects the underlying inflammatory reaction since inflammation causes the production of arachidonic acid metabolites as well as platelet-activating agents, which leads to neutrophilia. Cortisol-induced stress causes relative lymphopenia. To evaluate the utility of the NLR as a prognostic indicator in patients with cholecystitis and to observe the patterns of preoperative NLR in simple and severe cholecystitis. The present study was a cross-sectional study was conducted at Sree Mookambika Institute of medical sciences from July 2023 to January 2024. In this study, 60 individuals with acute cholecystitis who were older than 18 were enrolled. The clinical characteristics and demographic data of the patients who were enrolled were gathered. Tokyo standards were used to categorize patients into groups with mild, moderate, or severe acute cholecystitis; the NLR was computed as the absolute neutrophil count divided by the absolute lymphocyte count. The information was gathered and input into SPSS Statistics version 22. Student's t-test was used to assess the variation between the severe and non-severe AC groups in order to analyze continuous variables. The relationship between the category variables was assessed using the chi-square test. P-values less than 0.05 were regarded as significant. According to the Tokyo guidelines classification of AC, 34 (56.67%) had mild cholecystitis, 16 (26.67%) had intermediate cholecystitis 10 (16.67%) had severe AC. The mean total WBC count, NLR, HbA1c, CRP and total bilirubin level all rose ($p<0.05$) in proportion to the severity of cholecystitis. The majority of patients with severe cholecystitis had pericholecystic fluid accumulation and fat stranding. Compared to the other two subgroups, individuals with severe cholecystitis had a higher mean hospital stay ($p = 0.003$). ICU stays were required by patients with severe cholecystitis ($p<0.001$). Patients with severe cholecystitis had mortality rate ($p<0.001$). In patients with AC, NLR has shown to be a prognostic marker for assessing the severity of the disease, which will aid in effective care and improve patient prognosis.

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Key Words

Acute cholecystitis, gall bladder, neutrophil lymphocyte ratio, prognosis

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Received: 20 April 2024
Accepted: 19 June 2024
Published: 23 June 2024

Citation: Pallamala Lasya and G. Divya, 2024. Neutrophil-to-Lymphocyte Ratio as A Predictor for Severe Acute Cholecystitis. Res. J. Med. Sci., 18: 416-420, doi: 10.36478/makrjms.2024.7.416.420

INTRODUCTION

Acute cholecystitis (AC) is one of the most frequent gastrointestinal disorders that presents to emergency department which in tern requires hospitalization and surgical treatment[1]. AC is characterized as gallbladder inflammation brought on by stones obstructing the cystic duct, sludge causing bile stasis ensuing mechanical, chemical, or infections affecting the gallbladder wall[2].

Cholecystitis is more common in conditions including burns, severe trauma, diabetes mellitus (DM), sepsis, organ failure, substantial surgical intervention vasculitis, yet its exact origin is still unknown. Upon clinical examination, patients with AC often exhibit upper right quadrant discomfort, nausea and vomiting[3]. AC is characterized by right upper quadrant (RUQ) discomfort, guarding, fever, Murphy's sign, high leukocyte count C reactive protein (CRP), according to Tokyo recommendations from 2007 that were revised in 2018[4].

The symptoms of cholecystitis, or gall bladder inflammation, include fever, vomiting, nausea upper abdominal pain. In the event of a perforation, peritonitis could be present. Most often, gall bladder inflammation results from gall stones obstructing the cystic duct. The final course of treatment involves cholecystectomy. Severe cholecystitis may worsen and potentially result in death if it is accompanied by gallbladder gangrene, pus accumulation in the gallbladder, or even gallbladder perforation[5,6].

Delayed treatment might worsen the illness, increasing morbidity owing to progression to severe cholecystitis, such as gangrene, abscess formation, gallbladder perforation so on[7]. Since the clinical symptoms of severe cholecystitis can vary and imaging scans are frequently ambiguous, making a diagnosis in these patients can be challenging, both clinically and radiologically. Consequently, in order to prevent complications, patients who are at increased risk for developing severe cholecystitis must be appropriately diagnosed and treated[8].

The complete blood count (CBC) is an easy, quick reasonably priced test. Total white blood cell (WBC) count, neutrophil-lymphocyte levels platelet count are commonly utilized as indicators of inflammation and as measures to determine the severity of an illness. The ratio of neutrophils to lymphocytes, as obtained by a full blood count, can be used to simply compute the neutrophil lymphocyte ratio (NLR)[9]. According to recent research, NLR is a good indicator of inflammation in a variety of conditions, including appendicitis, chronic inflammation, systemic lupus erythematosus (SLE), rupture risk in tubal ectopic pregnancy, ulcerative colitis the majority of cancers.

The NLR is a better indicator of the immunological and inflammatory responses than the total WBC count. Because of the release of platelet activating factors and metabolites of arachidonic acid, inflammation causes neutrophilia, but stress generated by cortisol causes relative lymphopenia. Thus, the inflammatory process at the root of many disorders is reflected in the neutrophil to lymphocyte ratio[10]. Nevertheless, in south India, very few research has looked into the connection between the NLR and severe acute cholangitis.

Aims and Objectives: The aim of the present study was to evaluate the utility of the NLR as a prognostic indicator in patients with cholecystitis and to observe the patterns of preoperative NLR in simple and severe cholecystitis.

MATERIALS AND METHODS

The present study was a prospective observational study, conducted in Department of General Surgery, Sree Mookambika Institute of Medical Sciences, Kulasekharam for a period of 7 months from July 2023-January 2024. The study included 60 patients over the age of 18 who were diagnosed with acute cholecystitis. Those with uncontrolled hypertension and diabetes mellitus, severe systemic infections, immunocompromised states, antibiotic use within seven days prior to the visit, pregnant or nursing mothers, either acute or chronic inflammatory illnesses patients unwilling to engage in the study were not included in the study.

The clinical characteristics and demographic data of the patients who were enrolled were gathered. We applied the global consensus-derived severity grading standards of the TG Tokyo guidelines to assess the degree of AC. 11 As a result, three groups of patients with AC were identified: grade 1 (mild), grade 2 (moderate) grade 3 (severe).

- Grade I subjects had minimal Gall bladder inflammatory alterations and no organ damage.
- Patients with WBC count >18,000/mm3, pain duration >72 hours, palpable painful mass in the RUQ, or evident local inflammation were classified as Grade II.
- Patients with AC and organ/system impairment were considered Grade III. The confirmation of severe Grade III AC has been established when one or more organ or functional failure signs were seen.

The preoperative biochemical findings were acquired by taking 1 mL of venous blood from the participant on an empty stomach 12 hours before the procedure. An automatic blood analyzer performed routine blood tests the NLR was calculated. NLR was computed at the time of admission by dividing the

absolute neutrophil count by the absolute lymphocyte count. After presentation, ultrasonography (USG) was completed in six hours. The duration of hospital and intensive care unit stays, as well as the death rates, were statistically analyzed and compared between the groups.

Microsoft Excel was used to collect and store the data. Data analysis was done with SPSS 20.0. The range of continuous variables was expressed as mean ± standard deviation / median. Frequency was used to represent categorical variables. The Chi square test was employed to examine the relationship between the attributes. P<0.05 were regarded as statistically significant.

RESULTS AND DISCUSSIONS

There were 26 (43.33%) females and 34 (56.67%) males in the study. The patients ranged in age from 28 to 63 years old, with a mean age of 42.31±4.51 years. The age group most frequently affected was 31-50 years in 47 (71.67%) of the study population. According to the Tokyo standards, 34 (56.67%) patients had mild cholecystitis, 16 (26.67%) had moderate cholecystitis 10 (16.67%) had severe AC.

Comparison of mean age and gender with different grades of cholecystitis showed no statistical significance. (Table 1)

The mean WBC count, NLR, HbA1c, CRP total bilirubin level increased (p<0.05) in proportion to the severity of cholecystitis. This was regarded as statistically significant. However, as the severity increased, the mean platelet count dropped (p = 0.009). (Table 2) Diabetes mellitus (glycated hemoglobin >6.5) was present in three patients (30%) and was related with severe cholecystitis (p = 0.01, statistically significant).

According to USG findings, 6 patients (10%) had acute acalculous cholecystitis, while the remaining 54 patients (90%), had calculous cholecystitis. The gallbladder was grossly enlarged in 28 patients (46.67%). A thick gallbladder wall was seen in 32 (53.33%) patients. The mean thickness of the gallbladder wall was 2.42 mm in mild cholecystitis, 3.16 mm in moderate cholecystitis, as well as 5.47 mm in severe cholecystitis. Pericholecystic fat stranding was identified in 18 (30%) patients, while pericholecystic collection of fluid was seen in 17 (28.33%) patients. Comparison of USG finding with grades of cholecystitis was given in (Table 3).

Mean hospital stay of patients was high in patients with severe cholecystitis when compare to other 2 subgroups(p = 0.003). Patients with severe cholecystitis required ICU stays(p<0.001). Mortality rate was observed in patients who had severe cholecystitis (p<0.001). (Table 4)

Severe cholecystitis is related with more negative clinical characteristics than uncomplicated cholecystitis. Therefore, it is crucial to identify severe cholecystitis early and take action to stop it from getting worse in order to prevent problems. Patients in this category are more likely to sustain damage to the biliary ducts, damage to the right hepatic artery during surgery, etc.

According to the Tokyo standards, 34 (56.67%) of the patients had mild cholecystitis, 16 (26.67%) had moderate cholecystitis 10 (16.67%) had severe cholecystitis.

In their study, Çetinkaya[12] reported that 9 (16.67%) people had severe cholecystitis and 45 (83.33%) people had simple cholecystitis.

Prabhu[13] found that 30.91% had moderate AC, 45.45% had mild AC 23.64% had severe AC. Severe cholecystitis patients had longer mean hospital stays and stays in intensive care units. A prevalent comorbidity with severe cholecystitis was diabetes mellitus (35.48%). This was similar to the current study. Inflammatory indicators can be identified by values such as the WBC count and the neutrophil, lymphocyte platelet counts in this test. The NLR value has been shown to be correlated with the degree of inflammation in the current investigation, where it was found to be quite high in patients having severe cholecystitis and beneficial in differentiating between mild and severe cholecystitis. Pro-inflammatory cytokines (such as IL-1ra, IL-6, IL-7, IL-8 IL-12) have been discovered to be elevated in the plasma of individuals with NLR, which is based on the underlying molecular basis of the condition. Moreover, cancer patients with increased NLR showed substantial peritumoral infiltration of macrophages. As a result, increased NLR seems to be a reliable sign of an activated innate immune response[14].

The study by Turhan[15] included 229 individuals who underwent surgery for acute cholecystitis. There were 78 cases of intra operative and pathologically complex acute cholecystitis and 151 cases in the control group. There was a significant difference in the NLR and PLR levels between the complicated and simple groups (4.18±4.53 vs. 15.23±20.99, 145.34±87.58 251.92±245.93, respectively, p<0.01).

conducted[16] a study that included 359 patients with uncomplicated cholecystitis (69.63%) as well as 109 patients with severe cholecystitis (30.36%). Greater age (p = 0.001), male gender (p = 0.001), emergency department admission (p<0.001), longer operation time (p<0.001), greater frequency of postoperative complications (p = 0.056) longer length of hospital stay (LOS) (p<0.001) were all significantly correlated with a higher NLR (=3.0). The study found that preoperative NLR appeared to be a helpful

Table 1: Demographic characteristic among subgroups

Parameters		Mild	Moderate	Severe	p-value
Mean Age		37.3±6.5	42.5±5.3	39.5±4.7	0.0563
Gender	Male	16(47.06%)	11(32.35%)	7(20.59%)	0.081
	Female	18(69.23%)	5(19.23%)	3(11.54%)	

Table 2: Comparison of haematological and biochemical features among subgroups

Parameters (Mean)	Mild	Moderate	Severe	p-value
WBC count/µl	8476±246	11220±382	15360±473	<0.001
NLR	4.23±3.2	10.72±3.8	19.56±4.3	<0.001
Platelet x 103/µl	340.33±90.33	227.27±92.45	168.14±107.21	0.009
HBA1c	5.1±0.7	5.3±0.8	6.9±1.1	0.004
CRP	4.63±1.82	8.41±1.76	11.56±2.22	0.001
Total Bilirubin (mg/dl)	2.76±1.32	3.03±1.56	4.63±1.17	0.052

Table 3: Comparison of USG findings among subgroups

USG findings	Mild(n = 34)	Moderate(n = 16)	Severe(n = 10)	p-value
Gallbladder stone	32(94.1%)	13(81.25%)	9(90%)	0.0135
Gallbladder distension	13(38.23%)	8(50%)	7(70%)	0.004
Gallbladder wall thickening	21(61.76%)	8(50%)	3(30%)	0.873
Perihepatic hyper attenuation	6(17.65%)	5(31.25%)	3(30%)	0.614
Increased pericholecystic fat stranding	3(8.82%)	7(43.75%)	8(80%)	<0.001
Pericholecystic fluid collection	4(11.76%)	6(37.5%)	7(70%)	<0.001

Table 4: Comparison of mean hospital stay and mortality among subgroups

	Mild	Moderate	Severe	p-value
ICU stay	0(0%)	0(0%)	4(40%)	<0.001
Mean duration of hospital stay	5.4±0.4	6.3±0.8	8.5±1.7	0.003
Mortality	0(0%)	0(0%)	2(20%)	<0.001

surrogate measure for severe cholecystitis in patients undergoing cholecystitis.

In the study by Ünal[17] there were 40 patients (7.6%) in the severe AC group, 102 patients (19.3%) in the moderate AC group 386 patients (73.1%) in the mild AC group. The authors found that the WBC, NLR, CRP IG% were useful indicators for differentiating between mild, moderate severe AC.

In their study, Prakash[18] found that the mean NLR for patients with severe AC was 18.6500±2.32655. On CT scans, 29 (72.5%) patients had gallbladder distension, 31 (77.5%) had increased pericholecystic fat stranding 18 (45%) had pericholecystic fluid accumulation. The results of the CT scan and the NLR readings were substantially correlated. The current study also revealed that, with a p-value of less than 0.001, the majority of patients with severe cholecystitis had pericholecystic fluid collection (17.33%) and pericholecystic fat stranding (18%).

When patients with severe cholecystitis were compared to the other two groupings, their mean hospital stay, ICU stay fatality rate were higher ($p<0.05$). This was comparable to the studies conducted by Vela-Polanco[19] Serban[20] and Durgesh[21]

CONCLUSION

Early diagnosis of AC severity at the time of initial hospital admission results in appropriate and successful treatment, as well as decreased rates of morbidity and mortality, shorter hospital stays fewer medical expenses. In individuals with AC, NLR has shown to be a prognostic sign for assessing the severity of the condition. Preoperative NLR calculation is a low-cost, trustworthy test that can provide information about the degree of cholecystitis and forecast the prognosis at the time of admission. Based on the patient's NLR at admission, it can be determined if the patient can be handled conservatively or if a laparoscopic or percutaneous cholecystectomy is required to decompress the gallbladder and reduce complications.

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