ORIGINAL ARTICLE

Role of Neutrophil to Lymphocyte Ratio in Diagnosis of Cholecystitis

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ABSTRACT

Aim: To determine diagnostic accuracy of preoperative predictivity of neutrophil-to lymphocyte ratio in patients with acute cholecystitis taking histopathology as a gold standard.
Methods: This was a multi-centric study conducted at different tertiary care hospitals of Lahore. A retrograde record of CBC and Histopathology reports was taken of 52 cases of cholecystectomies. The report of NLR (≥ 3) was compared with their final diagnosis on histopathology. All the data was entered and analyzed on SPSS version 23 to find out mean and standard deviation of age. The Sensitivity, Specificity, PPV, NPV and Diagnostic Accuracy was calculated to assess the diagnostic role of NL Ratio in diagnosing cholecystitis.
Results: In our study the average age of the patients was 52 years, the male to female ratio was 1: 1.41. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of NLR was 79.31%, 78.26%,82.14%,75% and 78.84%.
Conclusion: According to our results the preoperative neutrophil-to lymphocyte ratio(NLR)≥3 is useful and reliable predictor of severe cholecystitis in patients with acute cholecystitis.
Keywords: Cholecystitis, Neutrophil, Lymphocyte, Predictor,

INTRODUCTION

Cholelithiasis is a worldwide problem due to crystalline deposits in the gallbladder leading to impaired excretion of bile into the gut.[1] Gallstones are present in 10-15% adults of the western world, and only 1-4% of these develop symptoms in a year.[2]

Cholesterol and calcium bilirubinate are the main chemical compounds present in gall stones and their precipitation in bile is induced by multiple etiological factors.[3,4] It is also reported that women are twicely susceptible to develop gall stone as compared to men, due to increased biliary secretion by the effect of estrogen during their child bearing age.[5] The other reasons lie in ethnicity, old age, female sex and family involvement of gall stone, which cannot be modified. While obesity, rapid weight loss and sedentary lifestyle have more risk of developing gall stones but these can be modified to avoid gall stone formation.[6]

The sign and symptoms, which are helpful in the diagnosis of acute cholecystitis, are pain and tenderness at right upper abdominal area lasting more than 6 hours, nausea or vomiting, temperature (>100°F), and findings of distended gall bladder, stones and thickened gall bladder wall on sonography. Presence of positive Murphy's sign, and peri-cholecystic fluid collection.[7] The neutrophil to lymphocyte ratio (NLR) has also been found to be correlated with the degree of inflammation in COPD cases.[8]

In a study of 632 cases (503 with simple cholecystitis and 129 with severe cholecystitis), the NLR ≥3.0 was reliably diagnostic of severity of gall bladder infection (sensitivity 70.5% and specificity 70%). More-over it was also observed that this ratio is raised as the age advances as well as in males reflecting severity of infection[9].

According to different oncological letters as well as studies the NLR was evaluated as diagnostic indicator of metastatic spread and independently shows an inverse association with prognosis, and clinically a reliable survival marker[15-20].

Received on 28-04-2019
Accepted on 14-09-2019

Rationale: We planned this study to determine reliability of NLR ≥ 3 in diagnosing severe cholecystitis in our population. As no local study is available and international data is also lacking. However Davis et al[11] recommended routine preoperative NLR calculation in every patient with cholecystitis. If we find higher accuracy of NLR ≥ 3 in our study, then in future this simple biomarker can be utilized to diagnose the severity of cholecystitis.

Operational Definitions

Neutrophil to Lymphocyte Ratio (NLR): NLR was calculated at admission as the absolute neutrophil count divided by the absolute lymphocyte count, using their standard complete blood count test. NLR ≥ 3.0 was considered as prediction of severe cholecystitis (Positive).

Acute cholecystitis:- It is defined as patient having pain right hypochondrium, fever >100 F for two days and one or more vomitings, tenderness RHC, increased TLC or increased gall bladder wall thickness(>5mm) on USG.

MATERIALS AND METHODS

This retrospective, cross-sectional, analytic study was conducted at multiple tertiary care hospitals of Lahore.

Samplings: A data of CBC and histopathologic reports of retrospective 52 cases of cholecystectomies of acute cholecystitis was collected. All adults of either gender, except any acute infection other than cholecystitis, were included in study.

Data Analysis: SPSS version 23 was used for analysis of quantitative variables like age, mean ± S.D. For qualitative variables like gender of patients, severity of cholecystitis on NLR and histopathology was presented as frequency and percentage. Final diagnosis of cholecystitis on NLR and histopathology was tabulated in the form of 2×2 table. Sensitivity, Specificity, PPV and NPV along with diagnostic accuracy was calculated for NLR≥3 (as per operational definite) taking final diagnosis as gold standard. Data was stratified for gender and age to address the effect of modifiers.

RESULTS

Table 1: Descriptive statistics of age (years)

Age (years)	n	52
	Mean	51.15
	SD	16.09
	Minimum	25
	Maximum	78

Table 2: Comparison of NLR with Histopathology

NLR	**Histopathology**		**Total**
	Positive	**Negative**	
Positive	23	5	28
Negative	6	18	24
Total	29	23	52

Sensitivity	79.31%
Specificity	78.26%
PPV	82.14%
NPV	75.00%
Diagnostic Accuracy	78.84%

Table 3: Comparison of NLR with Histopathology in Males

NLR	Histopathology		Total
	Positive	Negative	
Positive	9	2	11
Negative	4	6	10
Total	13	8	21

Sensitivity	69.23%
Specificity	75.00%
PPV	81.81%
NPV	60.00%
Diagnostic Accuracy	71.43%

Table 4: Comparison of NLR with Histopathology in Females

NLR	**Histopathology**		**Total**
	Positive	**Negative**	
Positive	14	3	17
Negative	2	12	14
Total	16	15	31

Sensitivity	87.50%
Specificity	80.00%
PPV	82.35%
NPV	85.71%
Diagnostic Accuracy	83.87%

Table 5: Age and Gender wise distribution of NLR with Histopathology

Age in Years	**21-40**		**41-60**		**61-80**	
Gender	**M**	**F**	**M**	**F**	**M**	**F**
Number of patients	8	7	9	12	4	12
Sensitivity %	66.67	75.00	80.00	85.71	100.00	83.33
Specificity %	80.00	100.00	50.00	80.00	100.00	83.33
PPV %	66.67	100.00	57.14	85.71	100.00	83.33
NPV %	80.00	75.00	50.00	80.00	100.00	83.33
Diagnostic Accuracy %	75.00	85.71	55.55	83.33	100.00	83.33

DISCUSSION

This retrospective study was conducted at different tertiary care hospitals of Lahore to determine diagnostic accuracy of preoperative NLR in predicting severity of gall bladder infection in patients with acute cholecystitis taking histopathology as gold standard. Due to adverse clinical status of severe cholecystitis as compared to simple one, there is urgent need of diagnosis and surgical treatment before advancing to any complication[10].

Due to systemic response in inflammations and malignancy, some researchers have found a linkage of pro inflammatory cytokines with NLR. They observed higher level of plasma interleukins (e.g., IL-1ra, IL-6,IL-7,IL-8,and IL-12) with raised NLR[11-13].

As per Kelly M.E et al[14] NLR is also a helpful tool in assessing severity of appendicitis to avoid unnecessary delay of surgery (Sang Kuon Lee et al).[9] determined on the ROC curve, that NLR 0.3 was a reliable cut-off value for severe cholecystitis having sensitivity of 70.5% and specificity of 70%. Some other studies as well as oncology letters depicts NLR as prognostic indicator in metastasis. NLR has invers association with the prognosis of skeletal spread of cancer[15-19]. While in our study, these values were higher than 78%, reflecting better diagnostic reliability of NLR for cholecystitis.

Age and sex are other confounders which may affect NLR association with severity of infection of gall bladder, Sang Kuon Lee et al[9]. Another study depicts that Age, Gender, CRP and NLR independently associated with the severity and complications of gall bladder infection. Although, there was high morbidity as well as mortality after emergent surgery[20]. Like-wise in our study 21(40.38%) patients were males and 31(59.61%) patients were females. A difference was found between the comparison of NLR and histopathology stratified by age and gender and has high sensitivity and specificity value of NLR. The incidence of cholecystitis in males is maximal upto 60 years of age and is declining afterwards, but the diagnostic accuracy of NLR is increasing after 60 years of age. But the incidence in females increases as the age advances while the diagnostic accuracy of NLR slightly falls as the age advances. It is also observed the NLR has better predictivity in females (>80%) than in males (<80%).

It is however, imperative for further studies to assess optimal neutrophil to lymphocyte ratio that could be diagnostic of severity of gall bladder infection in Pakistan.

CONCLUSION

According to our results, the preoperative neutrophil-to lymphocyte ratio is very good and reliable marker of severe cholecystitis. So in future, we can rely on NLR value for prediction of severe cholecystitis.

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