

**Prognostic value of preoperative neutrophil to lymphocyte ratio for prediction of severe cholecystitis**

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**Abstract**

**Introduction:** Over the years many variables have been studied with the purpose of getting insight into the severity of cholecystitis. Neutrophil to lymphocyte ratio is easy to calculate and no additional costs are involved in its calculation. It is derived from the standard complete blood count tests routinely performed.

**Aim:** To classify the cholecystitis patients in the high and low risk groups using pre-operative neutrophil-to-lymphocyte ratio. To determine the surgical priority using neutrophil-to-lymphocyte ratio in patients of cholecystitis.

**Methods:** It was a prospective study conducted in the department of surgery, Sawai man Singh medical college and attached group of hospitals, Jaipur on patients who were admitted through emergency as well as on routine outdoor basis in a single surgical unit and underwent cholecystectomy during the time period of September 2020 to September 2021.

**Results:** The raised NLR values were found significantly associated with presence of severe cholecystitis. Elevated NLR with severe cholecystitis presents a more difficult surgical scenario to deal with gangrenous gall bladder,

abscess formation, presence of pus and frank perforation are all associated with increased difficulty in surgery requiring more skill and patience from the surgeon and increased operating time and a lengthier post-operative hospital stay.

**Conclusion:** neutrophil to lymphocyte ratio (NLR) could be used as a prognostic indicator in patients with cholecystitis and a relevant NLR value could discriminate between simple and severe cholecystitis. NLR on admission can be applied to plan surgery in acute cholecystitis and anticipate difficult operation.

**Keywords:** cholecystitis, cholecystectomy, gall bladder, neutrophil to lymphocyte ratio (NLR).

**Introduction**

Severe cholecystitis is associated with more morbidity and adverse features as compared to simple cholecystitis. Furthermore, surgery in the setting of increasing severity of inflammation is challenging and associated with more complications. So, it is important to get an early insight into the severity of the inflammatory process associated with acute cholecystitis.

Traditionally, clinical acumen supported by imaging modalities like ultrasound and CT scans has been used to

assess, prioritize and treat patients presenting with acute cholecystitis. Since acute cholecystitis is caused due to an inflammatory response secondary to obstruction of bile drainage by gall stones, markers of inflammatory response can be used as an adjunct in the assessment of patients with acute cholecystitis. Delayed management can lead to increased morbidity, due to progression to severe cholecystitis, such as gangrenous change, abscess formation, and gallbladder perforation. Therefore, prompt detection and proper management of patients at risk of severe cholecystitis are essential in preventing associated complications.

Several inflammation -based scores have been suggested to predict the prognosis of inflammatory diseases. These include the modified Glasgow prognostic score, prognostic nutritional index, the neutrophil to-lymphocyte ratio (NLR) and many others.<sup>1,2</sup> One such score is neutrophil to lymphocyte ratio. It is easy to calculate and no additional costs are involved in its calculation. It is derived from the standard complete blood count tests routinely performed. Inflammation leads to neutrophilia due to release of arachidonic acid metabolites and platelet activating factors whereas cortisol induced stress leads to a relative lymphopenia. Thus, neutrophil to lymphocyte ratio reflects the inflammatory process underlying many diseases.<sup>3</sup>

This study assesses the pattern of NLR values in the setting of cholecystitis and we evaluate the utility of NLR ratio to identify the cases with severe cholecystitis. So, we can take the steps to follow the proper treatment timely. So, the complications and mortality can be avoided by utilizing the NLR ratio.

### Methodology

The present study was an observational study carried out in the department of general surgery, Sawai man Singh

medical college and attached group of hospitals, Jaipur on patients who were admitted through emergency as well as on routine outdoor basis in a single surgical unit and underwent cholecystectomy during the time period of September 2020 to September 2021.

**Sample size:** A sample of 105 cases at 95% C.I.(confidence intervals) for prediction of the severity of cholecystitis.

**Sampling Technique:** Detailed history, clinical examination & imaging (USG).

**Study Population:** All the cases of cholelithiasis with cholecystitis admitting in department of surgery of SMS medical college in the given period which meet the inclusion and exclusion criteria.

### Inclusion criteria

All Patients undergoing laparoscopic cholecystectomy.

### Exclusion criteria

- Denial of consent.
- Patients less than 18 years of age.
- Liver/ Renal/ Heart failure patients.
- Patients with malignancy, severe infection and mental diseases.

Detailed history was taken to diagnose, evaluate the duration of symptoms & progression of disease. All the cases clinically examined thoroughly.

Radiological investigations like USG was done.

Consent for the surgery was taken.

Pre-operative estimation of NLR was done.

Intra-operative factors noted to determine simple cholecystitis and severe cholecystitis. Factors for severe cholecystitis includes inflammation, empyema, gangrene, perforation of gall bladder, adhesion and difficult Calot's triangle.

**Observation and results**

Statistical analysis of data has been described as means ± standard deviations or as medians and ranges. Continuous variables are compared using the independent t-test, while categorical variables compared using the chi-squared test. Multiple regression analyses

Table 1: Distribution of cases according to Age.

Age Distribution	No. of Patients	Percentage
15-35	41	39.04762
36-55	39	37.14286
56-75	25	23.80952
Total	105	100
Mean±SD	43.19±15.93	

In this study, total 105 patients were included, the participating age group was 15-75 years, divided into 3 groups. First age group was between 15-35 years consisting of 41 patients ( 39.04 %), the second group was between age of 36-55 years consisting of 39 patients

Table 2: Correlation of NLR Ratio with Age Distribution.

Age Distribution	NLR <3 (n=75)		NLR ≥3 (n=30)	
	No. of Patients	Percentage	No. of Patients	Percentage
15-35	33	44	8	26.66667
36-55	25	33.33333	14	46.66667
56-75	17	22.66667	8	26.66667
Total	75	100	30	100
Mean±SD	41.7±16.4		46.7±14.32	
p-Value	0.14			

In our study, in group NLR <3 the mean age was 41.7±16.4 years and in group NLR≥3 the mean age was 46.7±14.32 years. The p value is 0.14, suggesting of not

performed using a proportional hazards model to identify factors independently associated with the LOS (length of hospital stay) greater than the 80th percentile after cholecystectomy and to estimate corresponding odds ratio (OR) in 95% confidence intervals (CI). Statistical significance was accepted for p-values less than 0.05.

(37.14 %) and the last third age group was between 56-75 years consisting of 25 patients ( 23.80 %). The mean age was 43.19±15.93. The maximum patients were in age group of 15-35 years and minimum patients were in 56-75 years age group.

statistically significant association between age distribution and NLR.

Table 3: Distribution of cases according to Gender.

Gender Distribution	No. of Patients	Percentage
Female	77	73.33333
Male	28	26.66667
Total	105	100

In this study there were 77 females and 28 males and male to female ratio was 1:2.75.

Table 4: Correlation of NLR values with the gender

Gender	NLR<3		NLR>3		p-Value
Female	55	52.38	22	20.95	1.0
Male	20	19.04	8	7.6	

Table 5: Distribution of cases according type of cholecystectomy.

Type of cholecystectomy	No. of Patients	Percentage
Difficult	24	22.85714
Simple	81	77.14286
Total	105	100

In this study 24 cases were considered as difficult cholecystectomy and rest 81 were marked as simple cholecystectomy.

Table 6: Corelation of NLR Ratio with type of cholecystectomy.

Type of cholecystectomy	NLR <3 (n=75)		NLR ≥3 (n=30)		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Difficult	3	4	21	70	<0.0001
Simple	72	96	9	30	
Total	75	100	30	100	

In this study in group NLR <3 there were 3 patients marked as difficult cholecystectomy and in group NLR ≥3 there were 21 patients. The p value was <0.0001 suggestive of strongly statistically significant association between type of cholecystectomy and NLR.

Table 7: Distribution of cases according Intraoperative Complications

Intraoperative Complications	No. of Patients	Percentage
Inflammation	20	19.04
Empyema	14	13.33
Gangrene	4	3.809524
Perforation of gall bladder	4	3.809524
Adhesion and difficult Calot's triangle	27	25.71429

In this study total 5 types of complications were noted. adhesions and difficult calot's triangle anatomy The maximum number of patients were suffered with comprising 27 patients followed by 20 patients with

cholecystitis ( inflammation),14 patients with empyema of gall bladder, 4 patients with perforation of gall bladder

and equal number of patients with gangrene of gall bladder.

Table 8: Correlation of NLR Ratio with Intraoperative Complication

Intraoperative Complications	NLR <3 (n=75)		NLR ≥3 (n=30)		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Inflammation	5	6.666667	15	50	<0.0001
Empyema	2	2.666667	12	40	<0.0001
Gangrene	0	0	4	13.33333	0.001
Perforation of gall bladder	2	2.666667	2	6.666667	0.33
Adhesion and difficult Calot's triangle	6	8	21	70	<0.0001

The commonest complication was adhesion and difficult calot's triangle anatomy. There were 6 patients in group NLR <3 and 21 patients in group NLR ≥3. The p value was <0.0001 suggestive of statistically significant association between above mentioned complication and NLR.

The second commonest complication encountered was cholecystitis. There were 5 patients in group NLR <3 and 15 patients in group NLR ≥3. The p value was <0.0001 suggestive of statistically significant association between above mentioned complication and NLR.

The next commonest complication encountered was empyema of gall bladder. There were 2 patients in group NLR <3 and 12 patients in group NLR ≥3. The p value was <0.0001 suggestive of statistically significant association between above mentioned complication and NLR.

The least commonest complication found in our study was gangrene of gall bladder. There was no case in group NLR <3 and 4 cases in group NLR ≥3. The p value was 0.001 suggestive of strong statistically association between gangrene of gall bladder and NLR.

The last complication found in our study was perforation of gall bladder. There were 2 patients in group NLR <3 and 2 patients in group NLR ≥3. The p value was <0.33 suggestive of not statistically significant association between above mentioned complication and NLR.

Table 9: Correlation of NLR with the Mean length of hospitalization

NLR	Mean LOH
<3	1.50±0.57
≥3	2.3±0.57
p-value	<0.0001

In group NLR <3, the mean length of hospitalization was 1.5 days and in group NLR ≥3 was 2.3 days. p-value was <0.0001 suggestive of significant association between NLR and LOH.

Table 10: Correlation of NLR Ratio with amount of blood loss.

Blood loss	NLR <3 (n=75)		NLR ≥3 (n=30)		P-Value
	Mean	SD	Mean	SD	
	43.43	23.78	59.42	31.37	
	53.3±28.37				

In our study, the mean blood loss in group NLR <3 was 43.43 ml and in group NLR ≥3 The mean blood loss was 59.42 ml. The p value was 0.005 suggestive of strong statistical association between blood loss and NLR.

Table 11: Corelation of NLR Ratio with duration of surgery

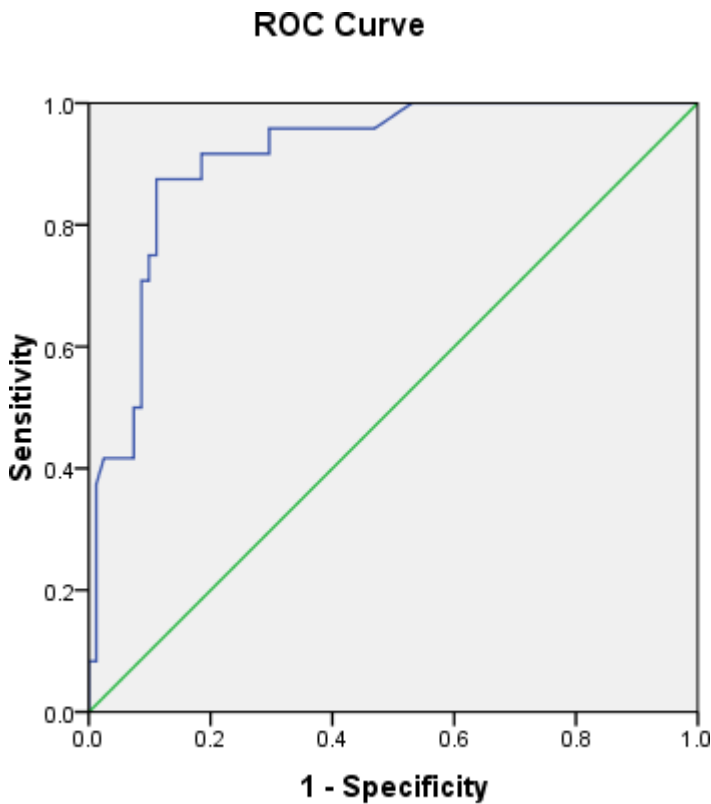
Duration of Surgery	NLR <3 (n=75)		NLR ≥3 (n=30)		P-Value
	Mean	SD	Mean	SD	
	32.5	9.54	52.6	20.9	

In our study, the mean duration of surgery in group NLR <3 was 32.5 minutes and in group NLR ≥3 The mean duration of surgery was 52.60 min .the p value was <0.0001 suggestive of strong statistical association between duration of surgery and NLR.

Table 12: ROC Curve.

For NLR	For severity
Area	0.913
p-value	<0.0001
95CI	0.854-0.971
Cut off	3.0
Sensitivity	95.8
Specificity	66.7

The receiver operating curve (ROC) analysis was done to study the NLR values and the presence of severe cholecystitis.



Diagonal segments are produced by ties.

Area under the ROC curve was 0.913. with an NLR of  $>3.0$  associated with a sensitivity of 95.8 % and a specificity of 66.7 %. An NLR value of 3.0 was taken as cut off and data allocation to two groups, depends on whether NLR is greater than or less than 3.

### Discussion

The ROC analysis gave an area under the ROC curve similar to that found in earlier studies with an NLR of 3 associated with sensitivity of 95.8 % and a specificity of 66.7 % which is similar to the values of around 70 % each as found by researchers in earlier studies with more number of subjects.<sup>4</sup>

The raised NLR values were found significantly associated with presence of severe cholecystitis, increased operating time and a lengthier post-operative hospital stay. This is similar to what has been described earlier by Lee et al, Karthik Hareen et al and Ahmed et al.<sup>4,5,6</sup>

The elevated NLR values were associated significantly with severe cholecystitis explains the association of

increased operating time with elevated NLR as more severe cholecystitis presents a more difficult surgical scenario to deal with gangrenous gall bladder, abscess formation, presence of pus and frank perforation are all associated with increased difficulty in surgery requiring more skill and patience from the surgeon.

Similarly, more severe the cholecystitis, severe and intense is the overall inflammatory response mounted by the body. This may be reason for a relatively delayed convalescence and a longer hospital stay.

Higher NLR has been found associated with increased age in earlier studies by lee et al, Karthik Hareen et al and Ahmed et al.<sup>4,5,6</sup> In our study the  $\text{NLR}>3$  group had a higher mean age as compared to the  $\text{NLR}<3$  group. However, this difference was not found statistically



significant. The reason for this can be the lesser number of subjects in our study as compared to the number of subjects in earlier studies.

Lee et al and Karthik Hareen et al<sup>4,5</sup>, they have found male gender significantly associated with raised NLR values at admission. Our study did not show male gender associated with higher NLR values. The reason can be that our study had a smaller number of male subjects which was not reflective of population at large.

In our study, raised NLR value group had a higher mean total leucocyte count as compared to the lower NLR value group. This is similar to what has been described by researchers earlier.<sup>4,7,8</sup>

However, this difference was not found statistically significant. The reason for this lack of statistical significance may be the smaller number of subjects studied.

The study had several limitations, most important of which was a smaller number of cases studied. A larger study group tends to be more representative of the population at large. Another limitation was that this study was an observational study and prospective trials are required to further validate its results.

### Summary and conclusion:

On the basis of the analysis of the data, the following conclusions can be made:-

1. As per the study group data cholecystitis has been more commonly seen in women as compared to men. (male: female=1.2.75 )
2. Similarly, cholecystitis was more commonly seen in the 4<sup>th</sup> decade of age.(mean age 43.19)
3. An NLR at admission >3 has been found to be significantly associated with :
  - Difficulty in cholecystectomy
  - Intra-operative complications (inflammation,

empyema, gangrene, adhesions and difficult calot's triangle anatomy)

- Length of hospitalization
- Blood loss
- Operative time

The result substantiate the view that NLR can be used as an adjunct in assessing, managing and prioritizing patients as far as acute cholecystitis is concerned. However more research is needed to find out more details and develop patterns of management based on NLR values at the time of admission.

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