ORIGINAL ARTICLE

Can a test as simple as Complete Blood Count predict Surgeon's night mares of Calot's triangle in Laparoscopic Cholecystectomies?

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Abstract:

Introduction: The degree of adhesions around gall bladder is something that always comes as a surprise to the operating surgeon. If surrogate markers are found, specially the ones easily available and cost-effective, surgeons can get great help in predicting difficulty of dissection before hand.

Objectives: To find predictive value of complete blood count parameters and derivatives for intra-operative adhesions in early laparoscopic cholecystectomies in patients with acute cholecystitis.

Materials and Methods: Reterospective cohort study was done on patients presenting with acute cholecystitis to Surayya Azeem Hospital from year 2020 to 2023. Data was collected from hospital record on a predesigned proforma. Patients presenting with acute cholecystitis who were diagnosed on the basis of Tokyo criteria and underwent early cholecystectomies were included in the research. Patients with chronic cholecystitis, gall bladder pathologies other than acute calculous/acalculous cholecystitis, comorbidities like diabetes mellitus, hypertension and those who underwent interval cholecystectomies were excluded from the research. Data was entered in IBM SPSS statistics version 23 software. Chi square test was used to find association of categorical variables with adhesions around gall bladder. Continuous variables were analysed using Mann-Whitney U test. ROC analysis was done to find predictive ability and optimal cut-off values. Logistic regression analysis was done to minimize the interference of confounders and find the strength of predictive ability. P-value of less than 0.05 was considered significant.

Results: Out of a total of 450 patients, 87(19.3%) were males and 363(80.7%) were females. Highest number of clustering of the patients {113(29%)} was seen in the age bracket of 40 years to 49 years. WBC count (p-value=0.00), ANC (p-value=0.00), NLR(p-value=0.00), PLR (p-value=0.00), SIRI (p-value=0.00), SII (p-value=0.00) and ESR were found to be significantly higher in the patients with extensive adhesions. ALC (p-value=0.00) and MLR (p-value=0.00) were found to be lower. NLR (AUC=0.88), PLR (AUC=0.74), MLR (AUC=0.73), SIRI (AUC=0.81) and SII (AUC=0.84) were found to be useful markers for discrimination between two groups. ESR showed poor discrimination (AUC=0.64). However, only NLR emerged as a reliable predictive factor for intra-operative adhesions in multivariate analysis (p-value= 0.00). On analysing colinear variables separately, SIRI (p-value=0.00), SII (p-value=0.00) and PLR (p-value=0.00) were also found to be predictors.

Conclusion: Neutrophil to lymphocyte ratio (NLR) is a reliable predictor of surgeon's difficulty in early laparoscopic cholecystectomies for acute cholecystitis. A cut-off of > 4.54 predicts extensive adhesions with 71% sensitivity and 97% specificity. SIRI, SII and PLR were also found to be independent predictors with cut offs of 1.46, 1169.6 and 169.9 respectively.

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Keywords: Acute cholecystitis; early laparoscopic cholecystectomy; Neutrophil to lymphocyte ratio (NLR); Monocyte to lymphocyte ratio (MLR); Platelet to lymphocyte ratio (PLR); Systemic Inflammatory Response Index (SIRI); Systemic Immune Inflammation index (SII); adhesions.

Introduction:

Laparoscopic cholecystectomy has been the procedure of choice for gallbladder related pathologies for many years.[1] The main reason for its wide acceptability lies in many advantages it has over open cholecystectomies. These include

more comfortable post-operative phase, shorter hospital stay and improved cosmesis.[2] These benefits are particularly pronounced if it is performed within 72 to 96 hours of symptom onset of acute cholecystitis.[3] Despite clear benefits of the procedure, it has been attached to some horrors for the surgeon as well; the conversion of laparoscopic cholecystectomy to open cholecystectomy. This difficulty is commonly encountered by laparoscopic surgeons.[4] Anatomic variations that cause difficult operation and resulting conversion include abnormal Calot's anatomy and intrahepatic gallbladder.[4] However, leading cause of conversion remains adhesions and difficult dissection in Calot's triangle. Dense pericholecystic adhesions have been a cause of conversion for many surgeons that lowers its feasibility as a procedure of choice in case of acute cholecystitis.[5] However, for some, the degree of gallbladder adhesions has poor correlation with conversion.[6] Pre-operative ultrasound is used to risk stratify patients. Utrasonography as a screening tool has eased prediction through detection of gallbladder wall thickness.[7] However, its sensitivity and specificity is low in complicated cases.[8,9]

Neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and monocyte to lymphocyte ratio (MLR), Systemic Immune Inflammation index (SII) and Systemic Inflammatory Response Index (SIRI) are derived hematological parameters that have been widely studied in cases of acute inflammation. They have been shown to be increased in rheumatoid arthritis, brucellosis, gastrointestinal disorders, autoimmune disorders and many more.[10-13]

In this study, we aim to evaluate NLR, PLR, MLR, SIRI, SII and ESR as predictors of operative difficulty in terms of pericholecystic adhesions. This will help reduce intra-operative surprises for surgeons and better counselling of patients pre-operatively. Together with radiology these markers can improve efficacy of prediction of dense adhesions and operator's difficulty.

Materials and Methods:

Ethical approval was taken from Ethical Review Board. Reterospective cohort analysis was done on 450 patients presenting with acute cholecystitis to Surayya Azeem hospital from year 2020 to 2024. Data was collected from hospital record. Adult patients who had been diagnosed with acute cholecystitis on the basis of Tokyo criteria and underwent early laparoscopic cholecystectomies were included in the research. Patients with chronic cholecystitis, comorbidities, gall bladder pathologies other than acute cholecystitis and those who underwent interval cholecystectomies were excluded from the research. Demographic data, history (fever, pain abdomen) and examination (Murphy's sign, right upper quadrant tenderness/mass) points were noted on a predesigned proforma. Complete blood count was done on Sysmex XN-1000 and ultrasound abdomen findings were noted. Due to easy availability and cost effectiveness for the patients, ESR was done in place of CRP. Data was entered in IBM SPSS statistics version 23.

Ratios and indices from CBC were calculated manually using following formulas:

- Neutrophil to lymphocyte ratio (NLR) = Absolute neutrophil count (ANC) / Absolute lymphocyte count (ALC)
- Platelet to lymphocyte ratio (PLR) = Platelet count / Absolute lymphocyte count (ALC)
- Monocyte to lymphocyte ratio (MLR) = Absolute monocyte count (AMC) / Absolute lymphocyte count (ALC)
- Systemic Inflammatory Response Index (SIRI) = (ANC x AMC) / ALC
- Systemic Immune Inflammation index = (ANC x platelet count) / ALC

Patients were categorized into two groups based on intra-operative findings; those with few adhesions and those with dense/extensive adhesions in Calot's triangle. Association between categorical variables like age and gender and adhesions was found by Chi-square test. For continuous variables, test of normality was car-

Table 1: CBC characteristics of study population

Parameter	Median	Inter-quartile range	Minimum	Maximum	Mean±SD
Hemoglobin (g/dL)	12.2	11.2–13.1	7.0	16.8	12.2±1.6
WBC count (x10^9/L)	8.5	7.1– 10.8	3.0	25.4	9.2±3.1
Platelet count (x10^9/L)	284.5	223.75–349	33	835	296.5±103.3
Absolute neutrophil count (x10^9/L)	5.3	4.2– 7.2	1.7	23.1	6.2±3.0
Absolute lymphocyte count (x10^9/L)	2.4	1.8– 2.9	0.3	4.9	2.4±0.9
Absolute monocyte count (x10^9/L)	0.3	0.2– 0.5	0.1	6.4	0.4±0.4
ESR(mm in first hour)	34	22– 54	2.0	132	39.8±23

Table 2: Comparison of CBC parameter medians in both study groups

Parameters	Few adhesions	Dense adhesions
Hemogobin (g/dL)	12.2	12.3
WB Ccount (x10^9/L)	8.3	11.9
Platelet count (x10^9/L)	285.5	279.0
Absolute neutrophil count (x10^9/L)	5.0	9.9
Absolute lymphocyte count(x10^9/L)	2.5	1.5
Absolute monocyte count (x10^9/L)	0.3	0.4

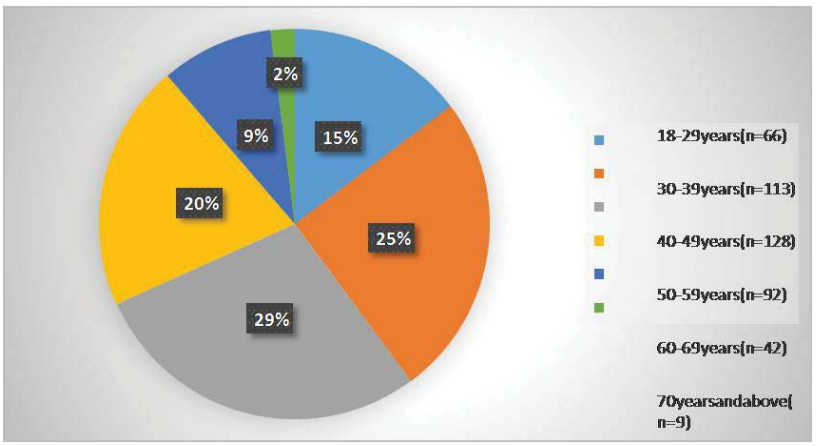

Figure 1: Age distribution

Table 4: ROC analysis summary

Parameter	ROC analysis				Logistic Regression	
	AUC*	Cut-off	Sensitivity	Specificity	OR**	P-value
Neutrophil to lymphocyte ratio (NLR)	0.88	4.54	71%	97%	2.61	0.00
Monocyte to lymphocyte ratio (MLR)	0.73	0.18	70%	70%	0.84	0.96
Platelet to lymphocyte ratio (PLR)	0.74	169.9	54%	85%	0.99	0.36
Systemic Inflammatory Response Index (SIRI)	0.81	1.46	70%	87%	0.87	0.78
Systemic Immune Inflammation Index (SII)	0.84	1169.6	69%	90%	1.00	0.41
ESR (mm in first hour)	0.64	44.5	51%	71%	1.00	0.88

**Area under curve, **Odds ratio*

ried out using Kolmogorov-Smirnov test and association was checked using Mann-Whitney U test. P-values were noted.

ROC analysis was done for NLR, PLR, MLR, SIRI, SII and ESR. Area under curve (AUC), sensitivity, specificity and cut-off values were noted. AUC was interpreted according to following descriptions.

- 0.5 = No discrimination
- 0.5-0.6 = Very poor discrimination
- 0.6-0.7 = Poor / limited discrimination
- 0.7-0.8 = Acceptable discrimination but not highly accurate
- 0.8-0.9 = Excellent discrimination
- > 0.9 = Outstanding discrimination
- 1.0 = Perfect discrimination

Logistic regression analysis was done to find effect of confounders and strength of predictive model. Colinear variables were sought and analysed separately through Logistic regression analysis to get rid of falsely inflated p-values. P-values and odds ratio were calculated. P-values less than 0.05 were considered statistically significant.

Results:

A total of 450 patients were included in the study. 87(19.3%) were male and 363(80.7%) females. Male to female ratio was 0.2:1. Age distribution in our study population is shown in figure 1. Complete blood count characteristics of whole population are summarized in table1.

In our study, 370 patients (82.2%) had few adhesions and 80 patients (17.8%) had dense adhesions.

Association of different parameters with adhesions was analysed and results are shown in table-3.

Table 3: Association of CBC parameters with intra-operative adhesions

Parameter	p-value
Age	0.12
Gender	0.00
Hemoglobin	0.96
WBC count	0.00
Platelet count	0.96
ESR	0.00
Absolute neutrophil count (x10^9/L)	0.00
Absolute lymphocyte count (x10^9/L)	0.00
Absolute monocyte count (x10^9/L)	0.11
Neutrophil tolymphocyte ratio	0.00
Monocyte tolymphocyte ratio	0.00
Platelet tolymphocyte ratio	0.00
Systemic immune inflammation index	0.00
Systemic inflammatory response index	0.00

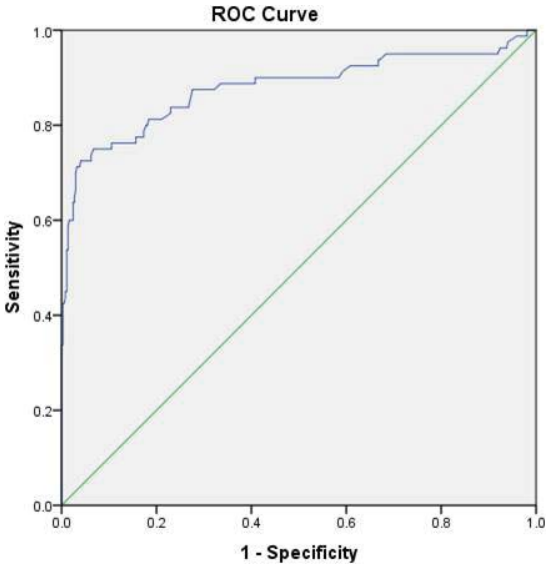

Figure 2: ROC curve for neutrophil to lymphocyte ratio (NLR)

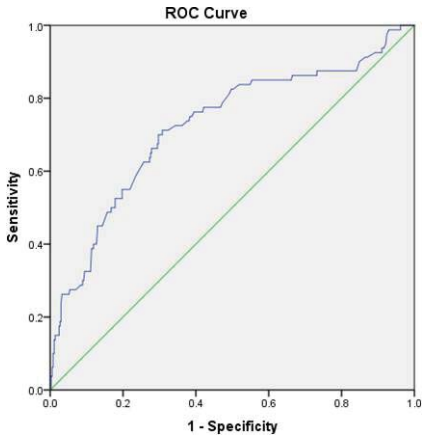

Figure 3: ROC curve for monocyte to lymphocyte ratio (MLR)

The ROC curves for NLR, MLR, PLR, SIRI and SII are shown in Figures 2, 3, 4, 5 and 6 respectively. Summary of ROC analysis is given in table-4.

Discussion:

Inflammatory indices have been widely studied in the recent years by different research groups. Durak D et al. studied WBC count, MLR and CRP in patients undergoing cholecystectomies. They found CRP to be the best predictor of intensity of adhesions and the cut off of 0.269 for MLR was given for this purpose with a sensitivity and specificity of 81% and 63% respectively.[14] Ahmed SE et al concluded that higher NLR was significantly associated with difficult early cholecystectomies and gave a cut off of 5.0 at admission as a predictor.[15] Serban D et al evaluated SII in addition to NLR and PLR and found NLR to be the best among fore- mentioned predictors with a cut off of 4.19 for predicting operator's difficulty and conversion with a sensitivity 85.5% of and specificity of 66.9%.[16] Stoica PL gave NLR cut off of 6.2 for difficult laproscopic cholecystectomies.[17] Micic D gave a NLR cut off 4.18 for severe acute cholecystitis and intraoperative and perioperative complications.[18] Gunes Y et al also found SII as a useful preoperative marker for severity of acute cholecystitis.[19]

In our study, we had a total of 450 patients with majority of females. 29% of our cases clustered in the age bracket of 40 to 49 years. 370 patients had few adhesion and 80 had dense adhesions. Simple association analysis revealed positive association with gender, WBC count, absolute neutrophil count, absolute lymphocyte count, NLR, PLR, MLR, SIRI and SII. Males were found to have more extensive adhesions. High WBC count, ANC, NLR, PLR, SIRI, SII and low absolute lymphocyte count was seen in patients with dense adhesions. In ROC analysis, we found NLR to be the best predictor of extensive adhesions (AUC=0.88), followed by SII (AUC=0.84), SIRI (AUC=0.81), PLR (AUC=0.74) and MLR (AUC=0.73). However, when multivariate analysis was performed and adjustments were done for confounders including age, gender and hemoglobin concentration,

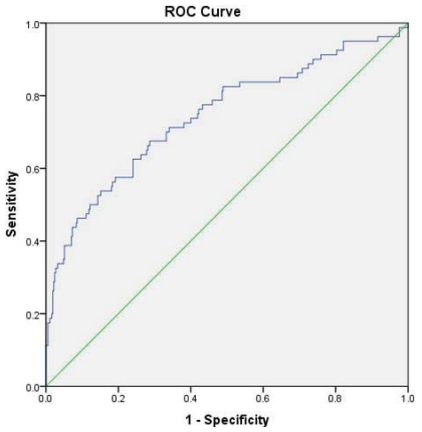

Figure 4: ROC curve for platelet to lymphocyte ratio (PLR)

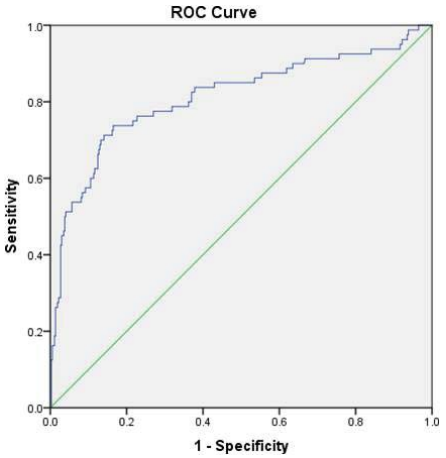

Figure 5: ROC curve for Systemic Inflammatory Response Index (SIRI)

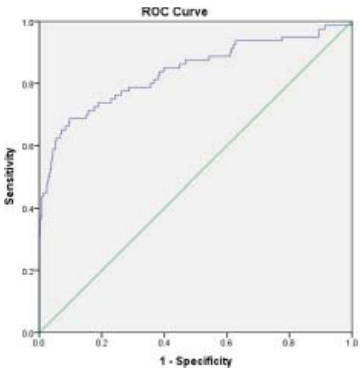

Figure 6: ROC curve for Systemic Immune Inflammation index (SII)

Table 5: Discussion summary

	NLR	MLR	PLR	SIRI	SII
Statistically significant difference in two groups	Yes	Yes	Yes	Yes	Yes
Discriminatory ability	Excellent discrimination	Limited discrimination; not very accurate	Limited discrimination; not very accurate	Excellent discrimination	Excellent discrimination
Association with dense adhesions	Yes	Yes	Yes	Yes	Yes
Independent predictive value	Yes	No	No	No	No
Inference	Cut-off for NLR of 4.54 reliably predicts extensive adhesions. Each unit rise in NLR predicts more than two-fold rise in density of adhesions.				

only NLR emerged as an independent predictor of extensive adhesions with each unit rise in NLR being associated with more than two-fold rise in difficulty of dissection. We checked the variables for collinearity and when collinear variables were assessed separately, we found SIRI, SII and PLR to be important predictors as well. We found that males were at 22.9% more risk of extensive adhesions as compared to females but the difference was not statistically significant (p-value=0.68). No significant predictive value of age or hemoglobin was seen. MLR, PLR, SII and SIRI although useful markers as per univariate analysis, were not found to be independent predictors of surgeon's difficulty after adjusting for confounding variables. High ESR was shown to be associated with dense adhesions in univariate analysis but it showed marginal predictive value on ROC analysis and after adjusting for confounders it was shown that with each unit rise in ESR, the risk of adhesions increases by 0.1% and this difference was statistically not significant. Inferences are summarized in Table 5.

In this research, we could not evaluate CRP as a predictor. In the past, researchers have shown high predictive value of CRP. Therefore, researches should be conducted for evaluation of CRP as an indicator as well.

Conclusions:
Systemic inflammatory indices are useful predictors of operative difficulty is Calot's triangle. NLR, MLR, PLR, SIRI and SII are all useful markers with individual discriminatory ability. In our study however, we found NLR as the only independent predictor of extensive adhesions with a cut off of >4.54. SIRI, SII and PLR were also found to be independent predictors when further assessment was done with cut offs of 1.46, 1169.6 and 169.9 respectively.

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Role and contribution of authors:
Maryam Afzal, collected the data, references and wrote the article.

Mehmood-ul-Haq Farooqi, collected the data, referenecs and helped in introduction and discussion writing.

Sobia Ashraf, critically review the article and give useful suggestion.

Muhammad Afzal, critically review the article and made final changes.

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