

Association of systemic inflammatory biomarkers with the clinical forms of acute cholecystitis

Novruz Hajiyev¹, Jabbar Hajiyev¹, Najiba Eynullayeva², Vidadi Allahverdiyev¹, Elman Tagisoy¹, Ismayil Gafarov³

¹Department of General Surgery, Azerbaijan Medical University, Baku - Azerbaijan

²Department of Radiology, Azerbaijan Medical University, Baku - Azerbaijan

³Department of Medical Statistics, Azerbaijan Medical University, Baku - Azerbaijan

ABSTRACT

Introduction: The objective of this study was to conduct a comparative evaluation of systemic inflammatory markers in various forms of gallbladder inflammation in patients with acute calculous cholecystitis (ACC).

Methods: The article presents information about a scientific study conducted to study the content of peripheral blood leukocytes, taking into account the form of ACC in 116 patients. The patients were divided into two groups: Group I consisted of 53 patients with the catarrhal form of ACC, and Group II included 63 patients with the destructive forms (phlegmonous and gangrenous). Dynamic studies conducted before and after cholecystectomy in 116 patients showed that the level of leukocytes depended on the form of ACC.

Results: The cell indices evaluated in this study, such as lymphocyte neutrophil ratio (LNR), lymphocyte monocyte ratio (LMR), neutrophil lymphocyte ratio (NLR), monocyte lymphocyte ratio (MLR), and systemic inflammation response index (SIRI), present a more accessible and efficient alternative to assess systemic inflammation in clinical practice, especially in the context of acute cholecystitis.

Conclusion: Systemic inflammatory cell biomarkers, such as the LNR, LMR, NLR, MLR, LER, and SIRI, are significantly associated with the clinical forms of ACC and provide useful insights into the intensity of the inflammatory process in the gallbladder.

Keywords: Acute cholecystitis, Inflammation, Systemic inflammation response index (SIRI)

Introduction

Despite the success achieved in the surgical treatment of acute calculous cholecystitis (ACC) and its complications in contemporary clinical practice, the results obtained still do not fully satisfy surgeons (1,2). ACC often manifests with a widespread clinical picture in approximately 35% of cases (3), particularly in patients over 60 years of age with severe comorbidities, where destructive processes rapidly develop in 26-60.2% of cases (4,5), resulting in complications such as systemic inflammatory response syndrome (SIRS). Late diagnosis and delayed hospitalization are critical factors that significantly impact the outcomes of surgical treatment.

Modern diagnostic methods currently available do not allow for the early detection of destructive processes in the gallbladder. While elevated leukocyte counts and changes in the leukogram are considered classical markers of

inflammation, recent studies have demonstrated the importance of peripheral blood indices, such as the lymphocyte neutrophil ratio (LNR), lymphocyte monocyte ratio (LMR), neutrophil lymphocyte ratio (NLR), neutrophil monocyte ratio (NMR), monocyte lymphocyte ratio (MLR), lymphocyte eosinophil ratio (LER), and the systemic inflammation response index (SIRI). These biomarkers have been successfully used in clinical practice for the diagnosis of various diseases, including localized purulent-inflammatory processes, evaluation of clinical progression, and prediction of outcomes (6-14). Recent studies have focused on the active investigation of SIRI as a novel biomarker in various pathological conditions, reflecting the dynamic interactions between innate and adaptive immune responses (15-18). These indices are being continuously studied as potential, simple, and accessible indicators in everyday clinical practice.

Objective

The objective of this study was to conduct a comparative evaluation of systemic inflammatory markers in various forms of gallbladder inflammation in patients with ACC.

Methods

The study included 116 patients aged 19-87 years, diagnosed with ACC, who underwent cholecystectomy at the

Received: August 11, 2025

Accepted: December 23, 2025

Published online: January 23, 2026

Corresponding author:

Hajiyev Novruz

email: novruz.gadjiyev@rambler.ru



Journal of Circulating Biomarkers - ISSN 1849-4544 - www.aboutscience.eu/jcb

© 2026 The Authors. This article is published by AboutScience and licensed under Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0).

Commercial use is not permitted and is subject to Publisher's permissions. Full information is available at www.aboutscience.eu

Educational-Surgical Clinic of Azerbaijan Medical University. Of these patients, 19 (16.4%) were male, and 97 (83.6%) were female. The patients underwent either laparoscopic cholecystectomy (105 patients) or open cholecystectomy (11 patients). Morphological examination of the excised specimen was performed, and no fatalities were observed. Histological examination revealed no cases of gallbladder cancer.

The research was conducted in accordance with international standards accepted in clinical practice, and the protocol was approved by the Ethics Committee of Azerbaijan Medical University. The results were collected, reviewed, and analyzed by all authors at Azerbaijan Medical University.

According to the TG 13 protocol, patients diagnosed with acute cholecystitis were divided into 2 groups: Group I consisted of 53 patients with the catarrhal form of ACC, and Group II included 63 patients with the destructive forms (phlegmonous and gangrenous).

Exclusion criteria included patients under the age of 19, individuals with diseases of the gastrointestinal tract or biliary system, as well as those with oncological conditions.

All patients underwent ultrasonography (USG), and peripheral blood analysis was conducted at the time of admission. Various components of the leukocyte formula were studied, and systemic inflammatory biomarkers were calculated, both in absolute (#) and relative (%) values:

LNR (Lymphocytes Neutrophils Ratio)

$$LNR\# = \frac{lymph.\#}{neut.\#} \text{ and } LNR\% = \frac{lymph.\%}{neut.\%}$$

LMR (Lymphocytes Monocytes Ratio)

$$LMR\# = \frac{lymph.\#}{mon.\#} \text{ and } LMR\% = \frac{lymph.\%}{mon.\%}$$

NLR (Neutrophil Lymphocytes Ratio)

$$NLR\# = \frac{neut.\#}{lymph.\#} \text{ and } NLR\% = \frac{neut.\%}{lymph.\%}$$

NMR (Neutrophil Monocytes Ratio)

$$NMR\# = \frac{neut.\#}{mon.\#} \text{ and } NMR\% = \frac{neut.\%}{mon.\%}$$

MLR (Monocytes Lymphocytes Ratio)

$$MLR\# = \frac{mon.\#}{lymph.\#} \text{ and } MLR\% = \frac{mon.\%}{lymph.\%}$$

LER (Lymphocytes Eosinophils Ratio)

$$LER\# = \frac{lymph.\#}{eos.\#} \text{ and } LER\% = \frac{lymph.\%}{eos.\%}$$

SIRI (Systemic Inflammation Response Index)

$$SIRI\# = \frac{neut.\# \times mon\#}{lymph.\#} \text{ and } SIRI\% = \frac{neut.\% \times mon\%}{lymph.\%}$$

The cell composition of the blood was analyzed using the MINDRAY BC-6200 (China) hematology analyzer.

The results of 20 healthy control individuals were used for the comparison group (Table 1).

TABLE 1 - Peripheral blood components in the control group

	M	Me	Q1	Q3
Leuk ($10^9/l$)	7.65	7.55	6.58	9.40
ESR (mm/h)	10.4	9.0	6.5	13.5
Neut #	4.70	4.77	3.70	5.80
Neut %	58.8	57.7	54.6	62.7
Lym #	2.23	2.24	1.82	2.70
Lym. %	31.6	32.2	28.3	35.2
Mon #	0.57	0.63	0.48	0.67
Mon %	7.81	7.85	6.45	9.10
EOS #	0.15	0.15	0.10	0.20
EOS %	1.74	2.00	1.30	2.00
BAS #	0.02	0.02	0.00	0.03
BAS %	0.18	0.10	0.10	0.30
LNR #	0.494	0.457	0.380	0.555
LNR %	0.546	0.558	0.454	0.651
LMR #	3.98	4.00	3.43	4.55
LMR %	4.17	4.12	3.83	4.56
NLR #	2.16	2.19	1.82	2.63
NLR %	1.92	1.82	1.54	2.20
NMR #	8.39	9.14	6.98	9.70
NMR %	7.79	7.53	6.35	9.24
LER #	15.5	14.8	13.0	18.8
LER %	21.0	17.9	14.4	21.3
SIRI #	1.25	1.20	0.90	1.65
SIRI %	14.97	13.80	12.95	15.85
MLR #	0.262	0.250	0.220	0.290
MLR %	0.252	0.240	0.220	0.260

Statistical Analysis

The statistical analysis of the data obtained was performed using the IBM SPSS Statistics version 26 software package. Variation analysis was conducted using the U-Mann-Whitney method, and ROC (Receiver Operating Characteristic) analysis was performed. The null hypothesis was rejected when $p < 0.05$ (19).

Results

The leukocyte formula and other peripheral blood components were analyzed in both groups of patients at the time of admission to the clinic. Table 2 provides a summary of the peripheral blood leukocyte formula for both groups of patients.

Table 2 clearly demonstrates that in both clinical forms of ACC, the leukocyte count, a classical biomarker of inflammation, was elevated compared to healthy individuals upon patient admission. Furthermore, the degree of leukocytosis in these patients was directly correlated with the type of inflammation present in the gallbladder. Specifically, in patients exhibiting destructive changes in the gallbladder, the leukocyte count significantly exceeded the reference levels, with a marked increase compared to the catarrhal form. It is important to note that the elevation in leukocyte count across all forms of gallbladder inflammation was primarily attributed to an increase in both the absolute and relative counts of neutrophils,



monocytes, and basophils, when compared to similar parameters in healthy individuals. While both groups demonstrated an elevation in neutrophils, the highest absolute and relative levels were observed in the destructive form (Table 2).

Additionally, absolute and relative lymphopenia were observed in both groups. However, the depth of lymphopenia was dependent on the form of inflammation. Compared to healthy individuals, the destructive form of ACC showed a statistically significant greater reduction in both absolute and relative lymphocyte counts.

Upon patient admission to the clinic, notable alterations in systemic inflammatory response markers, specifically cell indices, were observed in relation to the intensity of gallbladder

inflammation. These changes were compared to the reference values in healthy individuals, as outlined in Table 3.

As seen in Table 3, the interactions between T- and B-cells and the balancing of the immune response, reflected by the LNR, were significantly reduced in all forms of gallbladder inflammation compared to the control group ($p < 0.001$). However, the level of reduction was dependent on the clinical form of ACC. In the catarrhal form, the LNR (#) and LNR (%) were reduced 1.6 times ($p < 0.001$) and 1.7 times ($p < 0.001$), respectively, whereas in the destructive form, these values were reduced by 3.4 times ($p < 0.001$) and 3.1 times ($p < 0.001$), respectively. The reduction in LNR in ACC patients, especially in the context of destructive processes,

TABLE 2 - Comparative analysis of leukocyte formula and peripheral blood components between patients with different clinical forms of ACC

	Acute calculous cholecystitis								P_u	
	Catarrhal				Destuctive					
	M	Me	Q1	Q3	M	Me	Q1	Q3		
Leuk, $10^9/l$	8.87	8.57	7.70	9.50	13.09	12.60	9.70	15.90	<0.001*	
Neut., $10^9/l$ (#)	6.00	5.60	5.00	6.54	10.44	9.70	7.10	12.40	<0.001*	
Neut %	66.9	65.3	63.7	69.5	75.0	74.0	72.6	76.6	<0.001*	
Lym., $10^9/l$ (#)	1.79	1.82	1.70	2.00	1.35	1.30	1.20	1.50	<0.001*	
Lym. %	21.8	22.6	19.6	24.4	13.0	13.0	11.6	14.3	<0.001*	
Mon., $10^9/l$ (#)	0.84	0.80	0.60	0.90	1.15	1.00	0.90	1.31	<0.001*	
Mon %	9.43	9.20	8.60	10.50	10.67	10.70	9.70	11.60	<0.001*	
EOS., $10^9/l$ (#)	0.17	0.12	0.10	0.21	0.20	0.15	0.10	0.21	0.791	
EOS %	1.68	1.40	0.80	2.40	1.64	1.30	0.70	2.00	0.327	
BAS., $10^9/l$ (#)	0.03	0.01	0.00	0.03	0.03	0.00	0.00	0.04	0.725	
BAS %	0.32	0.20	0.10	0.30	0.25	0.20	0.10	0.30	0.854	

Note: M – Mean; Me – Median; Q1, Q3 – Quartiles;

P_u – Statistical accuracy of the difference according to the Mann–Whitney U test;

*- “Null” hypothesis is rejected

TABLE 3 - Indicators of systemic inflammatory cell indices based on the nature of Inflammation in the gallbladder wall

	Acute calculous cholecystitis								P_u	
	Catarrhal				Destuctive					
	M	Me	Q1	Q3	M	Me	Q1	Q3		
LNR #	0.313	0.333	0.241	0.365	0.146	0.140	0.094	0.188	<0.001*	
LNR %	0.330	0.342	0.278	0.381	0.175	0.178	0.153	0.195	<0.001*	
LMR #	2.32	2.22	1.90	2.77	1.28	1.33	0.91	1.58	<0.001*	
LMR %	2.37	2.22	1.98	2.76	1.24	1.18	1.04	1.42	<0.001*	
NLR #	3.43	3.00	2.74	4.15	7.96	7.17	5.33	10.68	<0.001*	
NLR %	3.18	2.93	2.63	3.59	6.16	5.63	5.13	6.55	<0.001*	
NMR #	7.75	7.43	6.15	8.77	9.36	8.83	7.22	10.93	<0.001*	
NMR %	7.28	7.01	6.32	8.07	7.20	6.92	6.38	7.81	0.581	
MLR #	0.474	0.450	0.360	0.530	0.875	0.750	0.630	1.090	<0.001*	
MLR %	0.444	0.450	0.360	0.510	0.864	0.850	0.700	0.970	<0.001*	
LER #	13.6	13.7	8.2	18.8	10.5	8.0	5.2	15.0	0.003*	
LER %	20.0	14.8	9.7	25.4	15.3	10.3	6.2	19.8	0.004*	
SIRI #	2.92	2.60	1.92	3.25	9.77	6.93	5.14	14.65	<0.001*	
SIRI %	29.9	29.4	23.0	34.2	65.2	63.1	52.8	71.5	<0.001*	

Note: M – Mean; Me – Median; Q1, Q3 – Quartiles;

P_u – Statistical accuracy of the difference according to the U-Mann-Whitney method;

*- “Null” hypothesis is rejected



indicates an imbalance in the immune response, insufficient adaptation, and dysfunction in immune reactions.

The LMR decreased in both clinical forms of ACC, with a more significant reduction in the destructive forms (Table 3). It is worth noting that the reduction in LMR (#) and LMR (%) was accompanied by an increase in the absolute and relative values of monocytes. This suggests that the immune system's effector chain (T-helper cells and cytotoxic T-cells) interactions were more disrupted in the destructive form of inflammation in the gallbladder.

Neutrophil lymphocyte ratio (NLR) increased in both groups of patients compared to the control group. In the catarrhal form, NLR (#) and NLR (%) were increased by 1.6 times ($p < 0.001$) and 1.7 times ($p < 0.001$), respectively, while in the destructive form, NLR was increased by 3.7 times ($p < 0.001$) and 3.2 times ($p < 0.001$). This increase indicates a change in the interactions between regulatory T-cells and effector cells (cytotoxic T-cells and neutrophils), reflecting the dynamic and acute inflammatory response (20). The significant increase in NLR levels, which characterize both innate and acquired immune responses during inflammation, confirms the intensification of the inflammatory process in the body and the increase in the amount of segmented neutrophils, the major population of leukocytes in peripheral blood. The rise in NLR reflects the deepening of inflammation in the gallbladder and the unfavorable progression of the inflammatory process.

The study of NMR levels showed that NMR (#) and NMR (%) changed in all forms of ACC. Compared to the control group, in the catarrhal form, NMR (#) was increased by 7.6% ($p = 0.038$), while NMR (%) decreased by 6.5% ($p = 0.186$). In the destructive form, NMR (#) increased by 11.6% ($p = 0.424$), and NMR (%) decreased by 7.6% ($p = 0.178$) compared to the catarrhal form. The mosaic change in NMR, which reflects cell-phagocytic activity, is attributed to the increased absolute and relative levels of neutrophils and monocytes, depending on the intensity of inflammation in the gallbladder.

The MLR, which reflects the ratio of monocytes to lymphocytes, increases in both forms of ACC compared to healthy individuals. This increase in MLR (#) and MLR (%) is dependent on the form of inflammation in the gallbladder: in the catarrhal form, MLR (#) and MLR (%) increased 1.8 times ($p < 0.001$) and 1.8 times ($p < 0.001$), respectively, while in the destructive form, MLR (#) and MLR (%) increased 3.3 times ($p < 0.001$) and 3.4 times ($p < 0.001$). The increase in MLR reflects the disruption of immune mechanisms in the gallbladder in the presence of inflammation.

In both clinical forms of ACC, the LER values decreased compared to the control group (Table 3), with a greater decrease observed in the destructive form. LER (#) and LER (%) were reduced by 22.8% ($p_{u1} = 0.003$) and 23.5% ($p_{u1} = 0.004$), respectively, compared to the catarrhal form.

The level of the new systemic inflammation biomarker, SIRI (#) and SIRI (%), increased significantly in patients with both forms of gallbladder inflammation compared to the control group. As the intensity of inflammation in the gallbladder increased, SIRI (#) and SIRI (%) also increased in parallel: in the catarrhal form, compared to the control group, SIRI (#) increased 2.4 times ($p < 0.001$) and SIRI (%) increased 2.0 times ($p < 0.001$), while in the destructive form, SIRI (#)

increased 7.8 times ($p < 0.001$) and SIRI (%) increased 4.4 times ($p < 0.001$) (Table 3).

The results of the ROC analysis of leukocyte and leukogram indicators and ESR show a statistically significant association between the relative (%) count of neutrophils (AUC = 0.926 ± 0.025 ; 95% CI: 0.877-0.975; $p < 0.001$), the absolute (#) count (AUC = 0.891 ± 0.029 ; 95% CI: 0.833-0.948; $p < 0.001$), the leukocyte count (AUC = 0.848 ± 0.036 ; 95% CI: 0.777-0.918; $p < 0.001$), ESR (AUC = 0.826 ± 0.038 ; 95% CI: 0.751-0.901; $p < 0.001$), the absolute (#) count of monocytes (AUC = 0.779 ± 0.044 ; 95% CI: 0.692-0.865; $p < 0.001$), and the relative (%) monocyte levels (AUC = 0.746 ± 0.046 ; 95% CI: 0.656-0.835; $p < 0.001$) with the destructive form of acute cholecystitis (Fig. 1, Table 4).

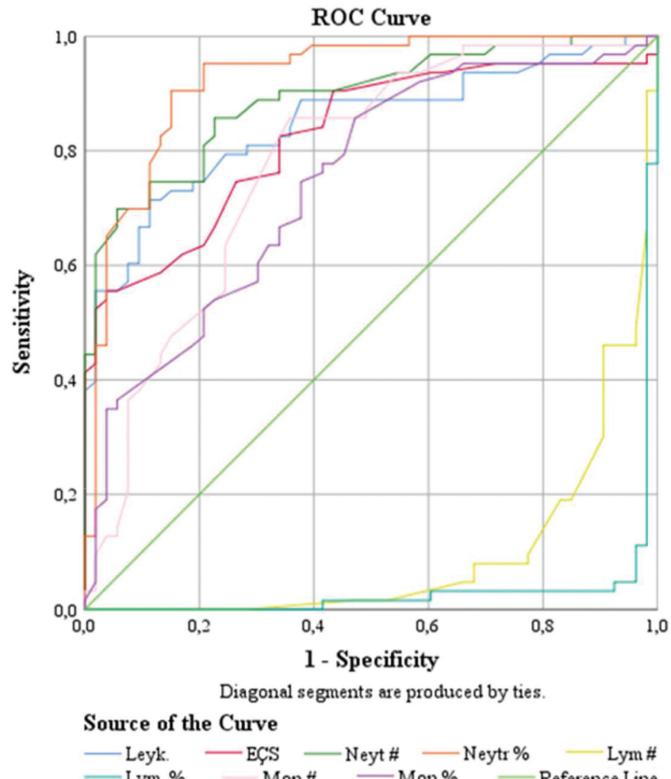


FIGURE 1 - ROC Analysis of Peripheral Blood Indicators.

TABLE 4 - ROC analysis of peripheral blood indicators

Indica- tors	Area	St. error	p-value	Area under the curve (AUC)	
				95% Confidence interval (CI) Lower bound	Upper bound
Leuk.	0.848	0.036	0.000*	0.777	0.918
ESR	0.826	0.038	0.000*	0.751	0.901
Neut #	0.891	0.029	0.000*	0.833	0.948
Neut %	0.926	0.025	0.000*	0.877	0.975
Lym #	0.095	0.029	0.000*	0.039	0.151
Lym. %	0.032	0.018	0.000*	0.000	0.067
Mon #	0.779	0.044	0.000*	0.692	0.865
Mon %	0.746	0.046	0.000*	0.656	0.835

Note: * - «Null» hypothesis is rejected

As a result of ROC analysis, threshold values were determined for the systemic inflammatory markers we investigated: For LNR, the area under the curve (AUC) = 0.951 ± 0.018; 95% confidence interval (CI): 0.917-0.986, $p < 0.001$; For SIRI, AUC = 0.943 ± 0.021, 95% CI: 0.903-0.984, $p < 0.001$; For MLR, AUC = 0.925 ± 0.026, 95% CI: 0.874-0.976, $p < 0.001$; For NMR, AUC = 0.675 ± 0.050, 95% CI: 0.577-0.773, $p < 0.001$; For LER, AUC = 0.339 ± 0.050, 95% CI: 0.241-0.437, $p = 0.003$; For LMR, AUC = 0.073 ± 0.026, 95% CI: 0.023-0.123, $p < 0.001$; For NLR, AUC = 0.049 ± 0.018, 95% CI: 0.014-0.083, $p < 0.001$ (Fig. 2, Table 5).

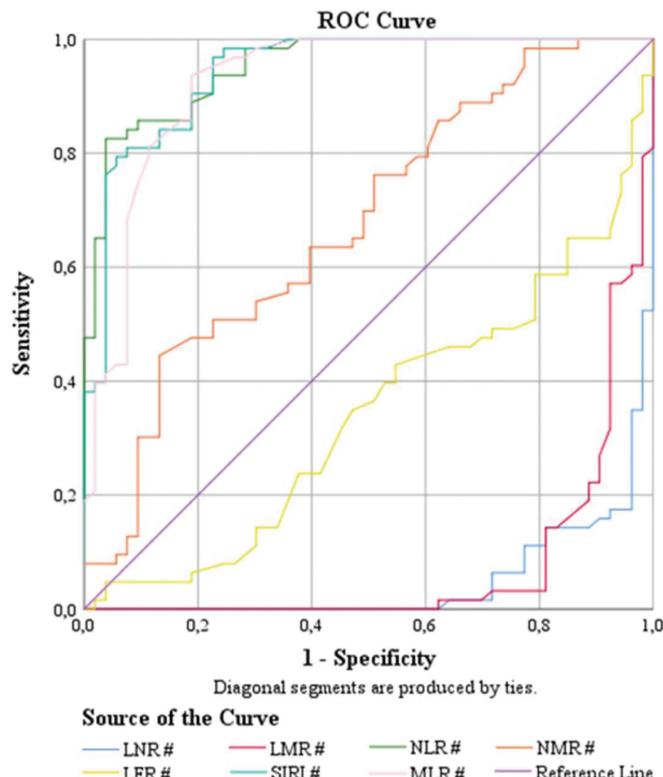


FIGURE 2 - ROC curves for LNR, LMR, NLR, NMR, MLR, LER, and SIRI.

TABLE 5 - ROC curves for LNR, LMR, NLR, NMR, MLR, LER, and SIRI

Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.	Area Under the Curve	
				Lower Bound	Upper Bound
LNR #	0.049	0.018	0.000	0.014	0.083
LMR #	0.075	0.026	0.000	0.024	0.126
NLR #	0.952	0.017	0.000	0.917	0.986
NMR #	0.677	0.050	0.001	0.579	0.775
LER #	0.342	0.050	0.003	0.243	0.440
SIRI #	0.943	0.021	0.000	0.903	0.984
MLR #	0.925	0.026	0.000	0.874	0.976

The comparison of all significant ROC curves for LNR, LMR, NLR, NMR, MLR, LER, and SIRI showed that the largest AUC was for NLR, and slightly smaller for SIRI and MLR (Fig. 2).

A comparative evaluation of ROC analysis with NLR (#) and SIRI (#) as a marker of CRP, which is recommended for use in the diagnosis of ACC, is given in Table 6.

TABLE 6 - Results of ROC curve analysis

	AUC (95%)	Cut-off	P	Sensitivity (%)	Specificity (%)
NLR #	0.951	>5.12	0.000*	82.5	96.2
SIRI #	0.943	>3.45	0.000*	96.8	77.7
CRP	0.886	>8.8	0.000*	88.9	84.9

The overall diagnostic value was 88.8% for NLR #, 87.9% for SIRI #, and 87.1% for CRP.

The results of evaluating the diagnostic power of these comparable factors using ANOVA analysis of variance (FS-Fisher Snedekor) were as follows: For NLR # 95% CI = 61,9; LB₉₅ = 60,6; UB₉₅ = 63,2; $p=0.000$; sing.***; For SIRI # 95% CI = 58,5%; LB₉₅ = 57,1; UB₉₅ = 60,0; $p = 0.000$; sing.***; For CRP 95% CI = 54,6; LB₉₅ = 53,1; UB₉₅ = 56,2; $p=0.000$; sing.***.

Although strong positive correlations were found between all three markers compared, these relationships are stronger between NLR and SIRI.

Discussion

Our study highlights that the peripheral blood leukocytes and their subtypes – neutrophils, monocytes, and lymphocytes do not always adequately reflect the inflammatory processes at the local and systemic levels. In our comparative analysis, we observed that the absolute and relative values of neutrophils, monocytes, and the total leukocyte count were significantly associated with the destructive form of acute cholecystitis. The study confirms that these markers can serve as reliable indicators for distinguishing between the clinical forms of the disease, particularly in cases with severe systemic involvement.

After removing of gallbladder, its color was examined macroscopically, both externally and in cross-sectionally. The contents of the gallbladder, the condition of its mucous membrane, and the presence of ulcers are identified. A histological examination of the removed specimens was also performed. The association of external gallbladder examination data, histological examination results, and systemic inflammatory biomarkers are presented in Table 7.

For instance, the NLR, MLR, and SIRI showed significant elevations in patients with the destructive forms of acute cholecystitis compared to those with the catarrhal form. These elevated indices correlate with the intensity of the inflammatory response and indicate a more severe disease progression. Specifically, NLR and SIRI demonstrated the most substantial changes, which could be considered effective biomarkers for predicting the severity and prognosis of acute cholecystitis.

In our study, the cut-off point reflecting the inflammatory process in the gallbladder was >5.12 for NLR# and > 3.45 for SIRI#.

In two patients (3.2%) with destructive changes in early postoperative period was a complication developed in the form of partial wound suppuration, which resulted in high MLR and SIRI values. We did not observe a relationship between the length of hospital stay and the studied biomarkers of systemic inflammation.

TABLE 7 - Association of clinical forms of acute cholecystitis with the results of histological examination and biomarkers of systemic inflammation

Clinical form	External examination data	Histological examination results	Studied biomarkers
Catarrhal form	The inflamed serous membrane of the bladder is grayish in color, shiny and smooth. The mucous membrane has a velvety appearance, bright red or dirty green in color, with areas of dark red hemorrhage and erosion.	The histological picture was characterized by hyperemia of the mucous membrane, desquamation of the epithelium and erosions. The gallbladder wall was thickened, the presence of subepithelial lymphoid infiltrates and, in places, Aschoff-Rokitansky intussusception was determined.	Moderate decrease in LNR, LMR, NLR, and LER, and, conversely, a moderate decrease in SIRI and MLR compared to the control.
Destructive form	The gallbladder wall is thickened, the mucous membrane is dull, and the color is dirty gray or gray-green in most cases, with filmy grayish-yellow deposits of fibrin. The gallbladder wall is stratified, sometimes with mucosal detachment. In a gangrenous gallbladder, the serous membrane is purple-black or a menacing brownish color. In most cases, the thickened wall was easily deformed and destroyed.	Histological examination of the removed gallbladders in this category of patients revealed lymphocytic-leukocyte infiltrates of the wall, excessive filling and dilation of blood vessels, partial destruction of the mucous membrane, in some places, micro abscesses with involvement of the serous membrane or fibrin deposition is observed on the serous membrane of the gallbladder wall, foci of necrosis in the wall and extensive leukocyte infiltrates, mainly of neutrophilic leukocytes.	A more significant decrease in the LNR, LMR, NLR and LER values, on the contrary, an abrupt increase in the MLR and SIRI values compared to the control and the values in the catarrhal form



FIGURE 3 - Gangrenous cholecystitis (endofoto).

Moreover, while other markers such as presepsin and procalcitonin are informative, they are not always readily available in emergency settings, and their use may require more specialized equipment and expertise. The cell indices evaluated in this study, such as LNR, LMR, NLR, MLR, and SIRI, present a more accessible and efficient alternative to assess systemic inflammation in clinical practice, especially in the context of acute cholecystitis.

These biomarkers of systemic inflammation can also be used not only in patients with ACC, but also in patients with acute acalculous cholecystitis.

Conclusion

Systemic inflammatory cell biomarkers, such as the LNR, LMR, NLR, MLR, LER, and SIRI, are significantly associated with the clinical forms of ACC and provide useful insights into the intensity of the inflammatory process in the gallbladder. These markers, due to their simplicity and accessibility, have the potential to aid in the early diagnosis and management of acute cholecystitis, particularly in older patients and those with severe disease presentations. Furthermore, these

biomarkers can be used alongside clinical and instrumental examination methods for a more accurate assessment of disease severity and prognosis.

Disclosures

Conflict of interest: The authors declare no conflict of interest.

Financial support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Gutt C, Schläfer S, Lammert F. The treatment of gallstone disease. *Dtsch Arztebl Int.* 2020;117(9):148-158. [CrossRef](#) [PubMed](#)
2. Hajiyev NJ, Sultanova MJ, Eynullayeva NA, et al. Peripheral blood leukocyte content in acute calculous cholecystitis: dependence on the clinical form of the disease. *Azerbaijan Medical Journal.* 2024;4:11-16. [CrossRef](#)
3. Eynullayeva NA, Hajiyev NJ, Sultanova MJ. The role of ultrasound scan in the diagnosis of destructive forms of acute cholecystitis. Abstract of the 20th International Euroasian Congress of Surgery and Hepatogastroenterology. 2024;65.
4. Pyfrom DP, Ali MZ, Ghose F, et al. The use of systemic inflammatory response syndrome (SIRS) and elevated liver enzymes as predictive factors of gangrenous cholecystitis: a case report. *Cureus.* 2023;15(2):e34727. [CrossRef](#) [PubMed](#)
5. Hamdamov BZ, Musoev TY, Khaydarov FN, et al. Dynamics of cytokine blood profile at destructive forms of acute calculus cholecystitis. *Eur J Psychol.* 2021;17(3):93-101.
6. Li Q, Ma X, Shao Q, et al. Prognostic impact of multiple lymphocyte-based inflammatory indices in acute coronary syndrome patients. *Front Cardiovasc Med.* 2022;9:811790. [CrossRef](#) [PubMed](#)
7. Varman A, Alkan S. Evaluation of neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, mean platelet volume, and neutrophil/monocyte ratio in patients with benign breast lesions. *Bratisl Lek Listy.* 2021;122(7):489-492. [CrossRef](#) [PubMed](#)
8. Xu X, Cai L, Chen T, et al. Predictive value of inflammation-based Glasgow prognostic score, platelet-lymphocyte ratio, and global registry of acute coronary events score for major



cardiovascular and cerebrovascular events during hospitalization in patients with acute myocardial infarction. *Aging (Albany, NY)*. 2021;13(14):18274-18286. [CrossRef](#) [PubMed](#)

9. Kahraman S, Agus HZ, Avci Y, et al. The neutrophil to lymphocyte ratio (NLR) is associated with residual syntax score in patients with ST-segment elevation myocardial infarction. *Angiology*. 2021;72(2):166-173. [CrossRef](#) [PubMed](#)

10. Dziedzic EA, Gąsior JS, Tuzimek A, et al. Investigation of the associations of novel inflammatory biomarkers – Systemic Inflammatory Index (SII) and Systemic Inflammatory Response Index (SIRI) – with the severity of coronary artery disease and acute coronary syndrome occurrence. *Int J Mol Sci*. 2022;23(17):9553. [CrossRef](#) [PubMed](#)

11. Han K, Shi D, Yang L, et al. Prognostic value of systemic inflammatory response index in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Ann Med*. 2022;54(1):1667-1677. [CrossRef](#) [PubMed](#)

12. Erdogan M, Erdöl MA, Öztürk S, et al. Systemic immune-inflammation index is a novel marker to predict functionally significant coronary artery stenosis. *Biomark Med*. 2020;14(16):1553-1561. [CrossRef](#) [PubMed](#)

13. Sayın MR, Özderya A, Konuş AH, et al. The use of systemic immune-inflammation index to predict new onset atrial fibrillation in the context of acute coronary syndrome. *Kardiologiya*. 2022;62(8):59-64. [CrossRef](#) [PubMed](#)

14. Lin KB, Fan FH, Cai MQ, et al. Systemic immune inflammation index and system inflammation response index are potential biomarkers of atrial fibrillation among the patients presenting with ischemic stroke. *Eur J Med Res*. 2022;27(1):106. [CrossRef](#) [PubMed](#)

15. Sharts VA, Talibova SM, Sokolskaya MA, et al. Association of novel biomarkers of systemic inflammation with atherosclerosis and its severity. *Ross Kardiol Z*. 2024;29(8):6025. [CrossRef](#)

16. Li J, He D, Yu J, et al. Dynamic status of SII and SIRI alters the risk of cardiovascular diseases: evidence from Kailuan Cohort Study. *J Inflamm Res*. 2022;15:5945-5957. [CrossRef](#) [PubMed](#)

17. Çirakoğlu ÖF, Yılmaz AS. Systemic immune-inflammation index is associated with increased carotid intima-media thickness in hypertensive patients. *Clin Exp Hypertens*. 2021;43(6):565-571. [CrossRef](#) [PubMed](#)

18. Huang R, Yue J. Predictive value of absolute lymphocyte count and systemic immune-inflammation index in advanced hepatocellular carcinoma patients treated with anti-PD-1 therapy. *Int J Radiat Oncol Biol Phys*. 2021;111(3):e45-e46. [CrossRef](#)

19. Gafarov, Ismayil. Biostatistika. 2022

20. Zulfic Z, Weickert CS, Weickert TW, et al. Neutrophil-lymphocyte ratio – a simple, accessible measure of inflammation, morbidity and prognosis in psychiatric disorders? *Australas Psychiatry*. 2020;28(4):454-458. [CrossRef](#) [PubMed](#)

