Research Article

Prognostic Performance of the Admission C-Reactive Protein to Lymphocyte Ratio in Acute Pancreatitis

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Abstract: Background: Early risk stratification in acute pancreatitis (AP) is important, but many prognostic scores are complex or require serial measurements. We evaluated the admission C-reactive protein-to-lymphocyte ratio (CLR) as a predictor of moderately severe/severe AP.

Objective: To assess the diagnostic performance of admission CLR for predicting moderately severe or severe AP (MSAP/SAP) and to derive an optimal admission cut-off for early risk stratification.

Materials and Methods: The Prospective, exploratory diagnostic accuracy study was conducted during January 1st 2024 to 30th June 2025. It was done in collaboration with the Department of Medicine and the Department of Pathology, Quaid-e-Azam Medical College and Bahawal Victoria Hospital, Bahawalpur bearing Ethical approval no. (IRB QAMC 1585, Dated 15 December 2023). Out of 72 AP patients screened, 12 were excluded (including missing admission CRP or absolute lymphocyte count), leaving 60 for complete-case analysis (40 mild AP, 20 MSAP/SAP). Labs were obtained within 24 hours. Discrimination was assessed by ROC analysis and association with MSAP/SAP used Firth-penalized logistic regression limited to pre-specified predictors (CLR per 10 units and age) to reduce overfitting.

Result: Patients who developed MSAP/SAP had higher admission CRP and CLR values, with no significant differences in age or sex between groups. Median CLR increased from 33.6 (IQR 23.7–52.4) in mild AP to 236.5 (IQR 163.2–288.1) in MSAP/SAP ($p<0.001$). Each 10-unit CLR increase was independently associated with MSAP/SAP (adjusted OR 1.63, 95% CI 1.22–2.37; $p=0.001$). CLR showed good discrimination (AUC 0.818, 95% CI 0.693–0.942). A Youden-derived cut-off of 67.7 yielded 85.0% sensitivity and 72.5% specificity. Length of stay was longer in MSAP/SAP (10.1±1.9 vs 5.8±2.4 days; $p<0.001$).

Conclusion: Admission CLR ≥67.7 was associated with MSAP/SAP and may aid risk assessment. Because CRP alone showed higher discrimination, CLR should be viewed as an adjunct, not a substitute for established CRP strategies (including 48-hour CRP). Larger multicenter studies should validate the threshold and assess whether serial CLR adds prognostic value.

Keywords: Acute pancreatitis, C reactive protein, Lymphocyte count, Severity prediction, Biomarker.

INTRODUCTION

Acute pancreatitis (AP) is one of the most frequent gastrointestinal emergencies worldwide. Around one in four patients develops moderately severe or severe disease, which is defined by persistent organ failure and is linked to high early mortality [1, 2]. National epidemiologic data from Pakistan remain limited, but reports from tertiary hospitals suggest that gallstone disease (about 45%) and hypertriglyceridemia (about 25%) are major causes. These audits also describe case fatality rates of roughly 6–8% in settings where early risk stratification is not routinely performed [3, 4].

Several prognostic tools are used to estimate severity, including the Ranson score [5], the Bedside Index of Severity in Acute Pancreatitis (BISAP) [6], the Acute Physiology and Chronic Health Examination (APACHE-II) [7], and the computed tomography severity index (CTSI) [8, 9]. Although these approaches can be reasonably accurate, they rely on multiple clinical, biochemical, and radiologic inputs and often require repeated measurements. This limits their practicality in high-volume, resource-limited emergency departments across South Asia. A low-cost biomarker available from a single blood draw that reflects the early inflammatory and immune response could therefore be clinically useful.

Recent work supports the role of serum markers in predicting local and systemic complications in AP and in estimating severity and mortality risk [10, 11]. Attention has also shifted toward composite indices, including ratios such as CRP-to-calcium and CRP-to-albumin, which further highlight the potential value of CRP-based measures for early triage [12, 13].

Within this group, the C-reactive protein to lymphocyte ratio (CLR) has gained interest across several conditions, including pancreatic cancer, colorectal cancer, and COVID-19 [14-16].

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CRP alone is already known to correlate with pancreatic necrosis and more severe disease in AP, but its prognostic performance varies by timing (often improving at 48 hours rather than at admission), which contributes to conflicting findings across studies [17]. In a 2024 Chinese study of 476 patients, an admission CLR ≥45 predicted moderate-to-severe AP with strong discrimination (AUC 0.88), and the association appeared to plateau beyond this level [18]. However, CLR has not been assessed in a South Asian population. Differences in etiology of the disease, metabolic co-morbidity and delay in presentation may affect the performance and threshold of this marker in our setting.

The objective of the present study was to assess the predictive value of admission CLR for identifying MSAP/SAP (primary outcome) as per the 2012 Revised Atlanta Classification among the patients presenting to Quaid-e-Azam Medical College & Allied Hospital, Bahawalpur. Because South Asian populations have a high burden of metabolic risk (e.g. insulin resistance, dyslipidemia, and diabetes) that can affect the underlying inflammatory tone and lymphocyte response. It may be necessary to have a local calibration of CLR, as opposed to transporting one cut-off across settings. A locally validated cut-off could be used for rapid patient triage and more efficient use of limited resources, with the potential for downstream benefits such as patient outcomes. Because CRP may not be at peak at the time of admission, the use of an admission-time inflammatory-immune ratio might aid in the risk assessment at admission and to wait for the results of later markers (e.g., 48-hour CRP) and imaging, if indicated.

MATERIALS AND METHODS

A prospective single center exploratory study for diagnostic accuracy was done in collaboration with the Department of Medicine and the Department of Pathology, Quaid-e-Azam Medical College and Bahawal Victoria Hospital, Bahawalpur. Ethical approval was obtained from the Quaid e Azam Medical College Institutional Review Board (IRB QAMC 1585, dated 15th December 2023), and written informed consent was secured from all participants or their legal guardians.

This is a 1,600-bed tertiary care referral hospital that serves Southern Punjab and nearby areas of Sindh. The study was conducted for 18 months from 1st January 2024 to 30th June 2025 and patients were followed till discharge or death in a hospital setting for in-hospital outcomes. The sample size was estimated using the method of Hanley and McNeil for ROC studies. Null AUC was set at 0.60 and expected AUC for C-reactive protein to lymphocyte ratio was set at 0.80 (based on pilot observations), CLR. Using a two-sided alpha equal to 0.05, 80% power and an assumed rank correlation of 0.50 between paired test results, the minimum sample needed was 54 patients, including the expected 18 cases of moderately severe or severe acute pancreatitis. This also fulfilled the rule of at least 10 outcome events for every variable for a logistic model with two predictors. Allowing for a projected 10% attrition, the goal was 60. However, to enhance precision and generalizability, the goal was made to enroll all 72 consecutive patients presenting with acute pancreatitis during the study period. 18 years old adults or older were eligible if they had a first episode of acute pancreatitis as diagnosed by two or more of the following: characteristic epigastric pain, serum amylase or lipase more than three times the upper limit of normal or imaging with ultrasound or computed tomography consistent with acute pancreatitis. Patients had to present within 24 h of the onset of symptoms and had to give written informed consent, either themselves or by a next of kin. Patients were excluded if they were readmitted with recurrent acute pancreatitis during the study window, had known chronic pancreatitis or pancreatic malignancies, were immunosuppressed due to HIV infection, post-transplant status, systemic steroids or biologics, had active hematological malignancy or received chemotherapy in the previous 6 weeks, had severe hepatic failure, defined as Child Pugh class C or estimated glomerular filtration rate less than 30 mL/min/1.73 m^2 or could not provide consent or were unwilling to consent.

Within six hours of admission, data were recorded using a structured proforma. The proforma included demographic details. It also captured the time since the onset of pain. Etiological factors were documented. These included gallstones, alcohol use, and triglyceride levels. Vital signs were recorded. Bedside severity scores were calculated. These included BISAP and APACHE II. One venous blood sample was obtained. Routine laboratory tests were performed. These included a complete blood count with absolute lymphocyte count. Serum C-reactive protein (CRP) was measured. Calcium and albumin were assessed. Creatinine and triglyceride levels were also tested. The CRP to lymphocyte ratio was then calculated. C-reactive protein was measured using a high-sensitivity immunoturbidimetric method on the Cobas e411 platform (Roche Diagnostics) with an inter-assay coefficient of variation of 4.2%. Complete blood counts were performed on a Swelab Alfa Plus automated hematology analyzer (Boule Diagnostics, Sweden), with daily calibration and two-level internal quality control in line with CLSI H26 A3 guidance. Contrast-enhanced computed tomography was performed when clinically indicated, and the computed tomography severity index was documented. Patients were assessed daily until discharge or death for organ failure parameters, local complications, need for ICU transfer, length of stay, and in-hospital mortality, and final severity grading was assigned using the 2012 Revised Atlanta Classification [19].

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 29 and R version 4. Missing data were assessed for all candidate variables. The primary analysis used complete cases. Patients missing admission CRP or absolute lymphocyte count were excluded because CLR could not be calculated. Continuous variables were assessed for normality using Shapiro-Wilk testing and Q-Q plots. Normally distributed variables were reported as mean with standard deviation and compared using the Welch t test, while skewed variables were reported as median with interquartile range and compared using the Mann-Whitney U test. Categorical variables were summarized as counts with percent-

ages and compared using the chi-square test or Fisher's exact test, as appropriate. Diagnostic accuracy of admission markers, including CLR, CRP, and APACHE II, for moderately severe or severe acute pancreatitis was evaluated using the area under the ROC curve with 1,000 sample bootstrap confidence intervals, and differences between AUCs were tested with the DeLong method. The Youden index was used to select an optimal CLR cut-off, and sensitivity, specificity, and likelihood ratios were then calculated. Because the number of severe events was limited, a Firth penalized logistic regression model including CLR expressed per 10 unit increase and age was used to reduce small sample bias. Model calibration was evaluated using bootstrap corrected calibration intercept and slope, with ideal values of 0 and 1, respectively, along with an optimism adjusted AUC, all based on 1,000 bootstrap resamples. A two-tailed p-value below 0.05 was considered statistically significant.

RESULT

Out of 72 screened patients, 12 were excluded for predefined reasons: chronic pancreatitis (n = 4), pancreatic tumor (n = 2), immunosuppression (n = 2), severe renal/hepatic failure (n = 1), or incomplete baseline laboratory data (n = 3), yielding 60 eligible participants (Fig. **1**). According to the Revised Atlanta Classification, 40 (66.7 %) had mild acute pancreatitis (AP) and 20 (33.3 %) had moderate to severe AP (MSAP + SAP).

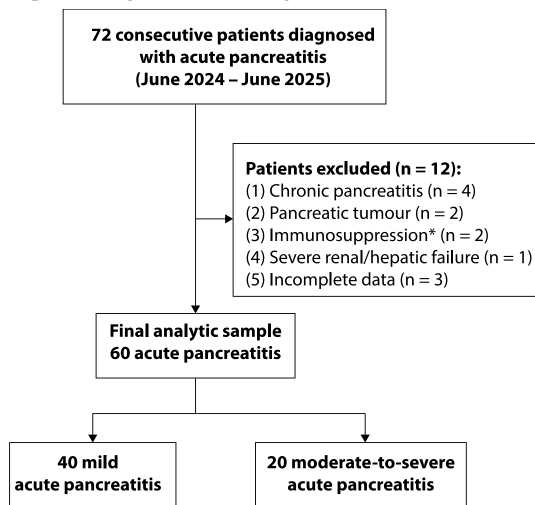

Fig. (1). Flow diagram of patient selection and analysis.

Table **1** summarizes the baseline characteristics of the 60 patients. Median CRP was markedly higher in the MSAP/SAP group at 167 mg/L (IQR 150–186) versus 47 mg/L (36–56) in mild AP ($p < 0.001$). CLR showed a more pronounced separation: 237 (163–288) in MSAP/SAP vs 34 (24–52) in mild cases ($p < 0.001$). Median symptom-to-door time did not significantly differ (14.1 h vs 13.8 h, p = 0.556), but patients with MSAP/SAP had significantly higher APACHE II scores (10.2 ± 2.4 vs 5.7 ± 2.3, $p < 0.001$), more frequent SIRS (90 % vs 30 %, $p < 0.001$), and longer hospital stay (10.1 ± 1.9 vs 5.8 ± 2.4 days, $p < 0.001$). Age, sex, BMI, and hematocrit were not significantly different between groups.

Table 1. Baseline Characteristics of Patients with Acute Pancreatitis (n=60).

Variable	Mild AP (n = 40)	Moderate + Severe AP (n = 20)	p-value
Age, years, median (IQR)	43.5 (36.5–49.9)	42.7 (39.2–47.8)	1.000
Male sex, n (%)	29 (72%)	11 (55%)	0.246
BMI, kg/m², mean ± SD	25.9 ± 4.3	25.8 ± 4.7	0.960
Symptom-to-door time, h, median	13.8 (11.6–18.2)	14.1 (13.1–15.0)	0.556
Gallstone etiology, n (%)	20 (50%)	9 (45%)	0.788
Hypertriglyceridemia, n (%)	10 (25%)	9 (45%)	0.138
Triglycerides, mmol/L, median	2.7 (1.9–3.9)	4.7 (3.2–7.0)	<0.001
CRP, mg/L, median (IQR)	47.2 (36.3–55.6)	167.3 (149.8–185.7)	<0.001
ALC, ×10⁹/L, median	1.4 (1.1–1.7)	0.7 (0.5–0.9)	<0.001
CLR, median (IQR)	33.6 (23.7–52.4)	236.5 (163.2–288.1)	<0.001
Serum creatinine, µmol/L, median	84.7 (78.3–89.9)	130.2 (112.4–148.5)	<0.001
Hematocrit, %, mean ± SD	39.2 ± 5.4	42.1 ± 6.2	0.058
SIRS, n (%)	12 (30%)	18 (90%)	<0.001
APACHE-II score, mean ± SD	5.7 ± 2.3	10.2 ± 2.4	<0.001
Length of stay, days, mean ± SD	5.8 ± 2.4	10.1 ± 1.9	<0.001

ROC analysis confirmed good discrimination for all three admission markers. CLR yielded an AUC = 0.818 (95 % CI 0.693–0.942). CRP showed the numerically best performance (AUC = 0.860, 95 % CI 0.749–0.971), but the advantage over CLR was not statistically significant (ΔAUC = +0.042, p = 0.617). After correcting the coding direction, APACHE II displayed similar accuracy (AUC = 0.812, 95 % CI 0.700–0.924); its difference from CLR was likewise non significant (ΔAUC = 0.006, p = 0.912). At the Youden-based CLR cut off of 67.7, sensitivity was 85.0 % and specificity 72.5 % ($LR^+ = 3.1$; $LR^- = 0.21$) (Fig. **2**, Table **2**).

Table 2. Diagnostic Performance (AUC) of Admission Biomarkers for Predicting MSAP/SAP.

Marker	AUC (95 % CI)	ΔAUC vs CLR (p)
CRP	0.860 (0.749 – 0.971)	+0.042 (p = 0.617)
APACHE II	0.812 (0.700 – 0.924)	−0.006 (p = 0.912)
CLR	0.818 (0.693 – 0.942)	—

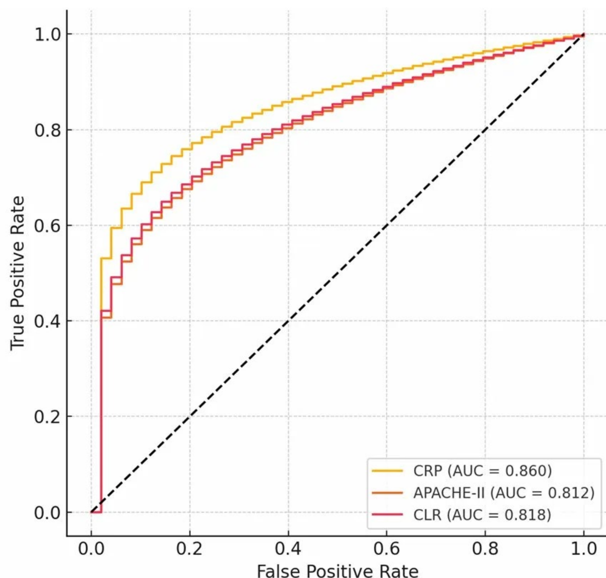

Fig. (2). Receiver Operating Characteristic Curves for CLR, CRP, and APACHE II.

In the Firth penalized logistic model, every 10-point rise in CLR (CLR10) independently increased the odds of MSAP/SAP by 63 % (adjusted OR = 1.63, 95 % CI 1.22–2.37; p = 0.001). Age exerted a modest but significant effect (adjusted OR = 1.06 per year, 95 % CI 1.00–1.12; p = 0.046) (Table **3**). Bootstrap internal validation confirmed satisfactory calibration (intercept = 0.12, slope = 0.85) and preserved discrimination (optimism corrected AUC = 0.818).

Table 3. Multivariable Logistic Regression Model for Severity of Acute Pancreatitis.

Predictor	β (log OR)	Adjusted OR	95 % CI	p value
CLR (per 10 unit rise)	0.49	1.63	1.22 – 2.37	0.001
Age (per year)	0.06	1.06	1.00 – 1.12	0.046

OR = odds ratio; CI = confidence interval; CLR = C-reactive protein to lymphocyte ratio; MSAP/SAP = moderately severe or severe acute pancreatitis.

When CLR was stratified into quartiles, the prevalence of MSAP/SAP climbed progressively, from 7 % in Q1 (≤ 34) to 13 % in Q2 (35–50), 47 % in Q3 (51–67), and 67 % in Q4 (≥ 68). The upward trend was significant (p for trend = 0.003); prevalence rose steeply once CLR exceeded ~60 and continued upward through the highest quartile (Fig. **3**).

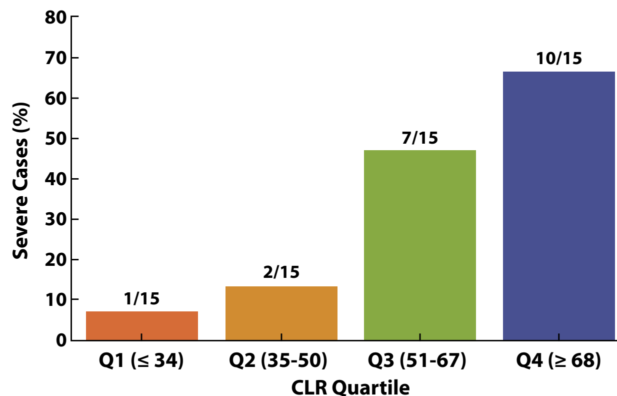

Fig. (3). Dose–Response Relationship between CLR and Risk of Moderate to Severe Acute Pancreatitis.

Patients with MSAP + SAP had significantly longer hospital stays than those with mild AP (10.2 ± 1.7 vs 5.8 ± 2.2 days, p < 0.001).

DISCUSSION

The admission CLR was confirmed as a practical and easily available early marker for severity stratification in acute pancreatitis. Good discriminatory performance was seen for predicting moderately severe and severe acute pancreatitis with an AUC of 0.818 (95% CI 0.693 to 0.942). An optimal cut-off of 67.7 was found using Youden analysis and this cut-off offered 85.0% sensitivity and 72.5% specificity. These findings support the use of CLR as an early rule in tool in emergency care. It may be of particular use where decisions need to be reached in a short amount of time.

Our CLR has shown that she can discriminate well and overlaps the previous work, although published thresholds differ from one cohort to the next. In a large cross-sectional Chinese study, (n=476), Chen *et al.* found an area under the plasma concentration-time curve (AUC) of 0.88 and a proposed threshold of a CLR of 45 for severe acute pancreatitis.18 The cut-off in our cohort (approximately 68) is plausible in a South Asian referral setting. Differences in etiology and comorbidity may alter early behavior of biomarkers, especially in the setting of increased incidence of hypertriglyceridemia-related pancreatitis and metabolic risk. These things can affect CRP kinetics and suppression of lymphocytes. Timing also matters. Even within a 24-hour admission window, there can be variation both in symptom duration and sampling to influence performance. Our small sample size provides even more uncertainty in our estimate of the threshold.

Evidence from other settings supports the general concept of early inflammatory–immune ratios, while underscoring heterogeneity. A 2024 Chinese multicenter study (n=217) found that an admission lymphocyte-to-CRP ratio cut-off of 56.5 predicted progression to severe disease (AUC 0.845) [20]. Jemaa *et al.* similarly reported that admission CLR was associated with moderate-to-severe disease (AUC 0.83) [16]. These results suggest

that combining CRP with lymphocyte count captures complementary biology beyond either marker alone. In our dataset, CRP alone showed slightly higher discrimination than CLR. We therefore interpret CLR as an admission-time adjunct for early risk assessment, not a superior substitute for established CRP-based strategies.

Turkey's nationwide multicenter cohort (n=2144) highlights how AP case-mix and severity can vary by setting. Biliary disease predominated (67.1%), hypertriglyceridemia was uncommon (6%), severe AP occurred in 2.6%, and mortality was 1.6% [21]. In contrast, our cohort had a higher MSAP/SAP proportion and a relatively greater burden of hypertriglyceridemia-related disease, which may plausibly shift early CRP kinetics and lymphocyte suppression and, in turn, raise CLR distributions and the optimal cut-off. Differences in referral patterns may also contribute, as single-center referral samples can be enriched for more complicated presentations.

Similarly, the Spain-wide prospective cohort across 23 hospitals (n=1655) reported mortality of 4.2% and showed that persistent organ failure was the dominant determinant of severity, with local complications and comorbidity exacerbation also contributing [22]. These multicenter data emphasize spectrum effects: when etiology mix, baseline comorbidity, severity prevalence, and timing of sampling differ, biomarker AUCs and cut-offs will also vary. This supports regional calibration and multicenter validation of CLR rather than direct transport of thresholds across populations.

CLR may be operationally attractive because it uses routinely available admission tests and captures both inflammatory burden (CRP) and immune response (lymphocyte count). Composite models that add clinical variables and multiple biomarkers can perform well (e.g., BISAP+CRP+NLR), but they require more inputs and may be harder to apply consistently in high-volume settings [23]. Regarding CRP alone, evidence syntheses generally support prognostic value, but reported accuracy varies and is strongly influenced by timing (admission vs 48–72 hours) and severity definitions, which limits direct comparability across studies [24]. In our dataset, CRP alone showed slightly higher discrimination than CLR. Therefore, CLR should be viewed as a ratio-based adjunct for early admission-time risk enrichment rather than a replacement for established CRP strategies, particularly 48-hour CRP.

Other markers are being studied. A recent Chinese study reported an AUC of 0.82 for the CRP to calcium ratio [13]. The systemic inflammatory grade is another option. It contributed to a nomogram with an AUC of 0.85 in an international validation dataset [25]. These approaches are promising. Yet they often rely on non-standard tests or dedicated scoring systems. CLR remains easier to apply. It uses routine measures such as complete blood count and CRP [26]. It also has low analytic cost.

From a biological perspective, CLR captures both inflammatory burden and immune reserve. CRP reflects the hepatic acute phase response. Lymphopenia reflects stress-related immune suppression [27]. In our cohort, the proportion of moderate to severe cases increased across CLR quartiles. The trend did not plateau. This implies that increasing inflammation was clinically meaningful up to CLR >120 [18].

STRENGTHS AND LIMITATIONS

The prospective nature of this study and consecutive enrollment helped strengthen it. It also used a single early venous sample, which is a routine practice in emergency care. Severity classification was done using the Revised Atlanta criteria, and outcome assessment was done without access to CLR results, reducing the possibility of observer bias. Multivariable adjustment was applied, Firth penalization was applied to overcome small sample bias and internal validation was conducted through bootstrapping, then internal validation was acceptable (slope 0.85; optimism-corrected: 0.818 (AUC)). The work was also an early South Asian evaluation using CLR in acute pancreatitis and helps address an evidence gap for the region. At the same time, interpretation should consider that a single center design and a relatively small sample size, as well as a male predominant study cohort and a relatively high proportion of hypertriglyceridemic cases, may restrict the generalizability. Only admission values were analyzed, and therefore the possible added value of serial CLR trends was not evaluated. Outcomes were only collected to discharge so delayed complications and 30-day mortality were not accounted for. Restricting inclusion to patients presenting within 24 hours may have introduced spectrum bias, as they may have excluded late or atypical presentations, and residual confounding from unmeasured factors such as intercurrent infections or cytokine profile could not be totally excluded.

IMPLICATIONS AND FUTURE RESEARCH

CLR is a quick and cheap measure that can be used to supplement early risk stratification in acute pancreatitis. It is most helpful in situations where imaging or complicated scoring means are not available. Studies to validate the 67.7 cut-off in larger South Asian populations are required in the future. They should determine if serial CLR measurements are of predictive value. They also should compare CLR directly with more state-of-the-art markers like CCR and SIG. Health economic studies are required to define the role of CLR in improving cost-effective care in different health systems.

CONCLUSION

An admission CLR of 67.7 or greater is a cheap and widely available marker of inflammatory status. After age adjustment it remained linked to an increased risk of MSAP or SAP. Its AUC was slightly lower than CRP and similar to APache II. CLR showed good calibration. It does not require any testing other than a routine complete blood count and CRP. This makes it appropriate for early triage, especially in resource-limited settings. Larger multicenter studies should validate the threshold and investigate the usefulness of repeated measurements.

ABBREVIATIONS

ALC: Absolute Lymphocyte Count.

AP: Acute Pancreatitis

Apache-II: Acute Physiology and Chronic Health Examination.

BISAP: Bedside Index of Severity in Acute Pancreatitis.

BMI: Body Mass Index.

CLR: C-reactive Protein to Lymphocyte Ratio.

CRP: C-reactive Protein.

CTSI: Computed tomography severity index.

IRB: Institutional Review Board.

MSAP/SAP: Moderately Severe and Severe Acute Pancreatitis.

SIRS: Systemic Inflammatory Response Syndrome.

AUTHORS' CONTRIBUTION

Sara Reza: Conceptualization, Study design, Methodology, Data analysis and interpretation, Writing Draft, Critical review and revision the manuscript, Final approval, final proof to be published.

Lubna Sarfraz: Study design, Methodology, Data analysis and interpretation, Critical review and revision the manuscript.

Fahad Qaiser and Muhammad Ehsan Sukhera: Methodology, Data analysis and interpretation, Critical review and revision the manuscript, Final approval, final proof to be published.

Saira Saleem: Conceptualization, Study design, Writing Draft, Critical review and revision the manuscript, Final approval, final proof to be published.

All authors approved the final manuscript and take responsibility for the integrity of the work.

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Declared none.

ETHICAL DECLARATIONS

Data Availability Statement

The dataset analyzed during the current study is available from the corresponding author on reasonable request.

Ethical Approval

Ethical approval was obtained from the Quaid-e-Azam Medical College Institutional Review Board (IRB QAMC 1585, dated 15 December 2023).

Consent to Participate

Written informed consent was secured from all participants or their legal guardians.

Consent for Publication

Consent for publication was obtained from all individual participants included in the study.

Conflict of Interest

Declared none.

Competing Interest/Funding

No funding was received for this study.

Use of AI-Assisted Technologies

The authors declare that ChatGPT was used solely for language refinement. The final content was reviewed and verified by the authors, who take full responsibility for the content of the article.

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