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Hematological and inflammatory indicators as diagnostic tools in community-acquired pneumonia, Ecuador

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Keywords:
community-acquired pneumonia; C-reactive protein; neutrophils; lymphocytes; platelets; differential diagnosis; inflammation (source: MeSH-NLM).

ABSTRACT

Objective. To evaluate the discriminative ability of C-reactive protein (CRP), the neutrophil-to-lymphocyte ratio (NLR), and the platelet-to-lymphocyte ratio (PLR) to differentiate bacterial and viral etiologies of community-acquired pneumonia (CAP). **Methods.** A retrospective observational study was conducted at the General Hospital of the Instituto Ecuatoriano de Seguridad Social in Riobamba, Ecuador, between January 2023 and July 2025. A total of 100 patients with CAP and microbiologically confirmed diagnoses were included (50 bacterial and 50 viral cases). Complete blood count parameters and CRP levels were analyzed at admission. Receiver operating characteristic (ROC) curves were constructed for each biomarker, optimal cutoff points were determined, and multivariable logistic regression analysis was performed. **Results.** The CURB-65 severity score and length of hospital stay were higher in the bacterial CAP group ($p < 0.001$). NLR, CRP, and PLR values were significantly higher in bacterial pneumonia ($p < 0.001$). Diagnostic performance was as follows: NLR, AUC = 0.99 (cutoff > 5.85); CRP, AUC = 0.94 (cutoff > 65.55 mg/L); and PLR, AUC = 0.83 (cutoff > 181.7). In multivariable analysis, an NLR > 5.85 was identified as an independent predictor of bacterial etiology (adjusted OR 14.8, 95% CI: 4.20–52.10), along with age (adjusted OR 1.04, 95% CI: 1.01–1.07) and a CURB-65 score ≥ 3 (adjusted OR 5.60, 95% CI: 1.60–19.50). **Conclusions.** NLR demonstrated the best diagnostic performance, followed by CRP and PLR. These accessible biomarkers may support clinical decision-making and the rational use of antibiotics; however, prospective multicenter validation is required.

Indicadores hematológicos e inflamatorios como herramientas diagnósticas en la neumonía adquirida en una comunidad, Ecuador

Palabras clave:
neumonía adquirida en la comunidad; proteína C reactiva; neutrófilos; linfocitos; plaquetas; diagnóstico diferencial; inflamación (fuente: DeCs-BIREME).

RESUMEN

Objetivo. Evaluar la capacidad discriminativa de la proteína C reactiva (PCR), el índice neutrófilo/linfocito (INL) y el índice plaquetas/linfocitos (IPL) para diferenciar la etiología bacteriana y viral de la neumonía adquirida en la comunidad (NAC). **Métodos.** Estudio observacional retrospectivo realizado en el Hospital General del Instituto Ecuatoriano de Seguridad Social de Riobamba, en Ecuador, entre enero de 2023 y julio de 2025. Fueron incluidos 100 pacientes con NAC y diagnóstico microbiológico confirmado (50 de origen bacteriano y 50 de origen viral). Al ingreso se analizaron hemograma y los niveles de PCR. Se construyeron curvas ROC para cada biomarcador, se determinaron puntos de corte óptimos y se realizó análisis de regresión logística multivariable. **Resultados.** El puntaje de evaluación de severidad CURB-65 y la estancia hospitalaria fueron mayores en el grupo con NAC bacteriana ($p < 0,001$). Los valores de INL, PCR e IPL fueron más elevados en la neumonía bacteriana ($p < 0,001$). El rendimiento diagnóstico fue: INL, AUC = 0,99 (punto de corte > 5,85); PCR, AUC = 0,94 (punto de corte > 65,55 mg/L); e IPL, AUC = 0,83 (punto de corte > 181,7). En el análisis multivariable, un INL > 5,85 se identificó como predictor independiente de etiología bacteriana (ORa 14,8, IC 95 %: 4,20-52,10), junto con la edad (ORa 1,04, IC 95 %: 1,01-1,07) y un CURB-65 ≥ 3 (ORa 5,60, IC 95 %: 1,60-19,50). **Conclusiones.** El INL mostró el mejor desempeño diagnóstico, seguido de la PCR y el IPL. Estos biomarcadores accesibles podrían apoyar la toma de decisiones clínicas y el uso racional de antibióticos; sin embargo, se requiere validación prospectiva multicéntrica.

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INTRODUCTION

Community-acquired pneumonia (CAP) continues to be one of the leading causes of hospitalization and mortality worldwide, especially among older adults and people with chronic comorbidities [1]. Despite advances in microbiological diagnosis and antimicrobial therapy, clinically distinguishing bacterial pneumonia from viral pneumonia remains a considerable challenge. This difficulty frequently leads to the empirical use of antibiotics, which contributes to the increase in antimicrobial resistance [2,3].

According to the Pan American Health Organization (PAHO) [4], in Latin America the burden of CAP is substantial, with an estimated incidence of 3-5 cases per 1,000 adults and in-hospital case fatality rates that may exceed 10%. In Ecuador, lower respiratory tract infections remain among the five leading causes of morbidity and mortality, especially in Andean regions such as Riobamba, where climatic and altitude-related conditions favor the recurrence of acute respiratory illnesses [5].

Conventional microbiological diagnostic methods, such as bacterial cultures or molecular tests for respiratory viruses, have limitations related to availability, cost, and processing time, especially in second-level general hospitals. In this context, low-cost inflammatory and hematological biomarkers emerge as useful alternatives for guiding etiologic differentiation and supporting clinical decision-making [6].

Among the most studied biomarkers are C-reactive protein (CRP) and the neutrophil-to-lymphocyte ratio (NLR). CRP, synthesized by the liver in response to proinflammatory cytokines, tends to rise to a greater extent in bacterial infections than in viral infections [7]. In turn, the NLR reflects the balance between neutrophilic activation and stress-induced lymphopenia, and it has been associated with the severity and prognosis of CAP [8].

In a complementary manner, the platelet-to-lymphocyte ratio (PLR) has emerged as an additional indicator of systemic inflammation and tissue damage, with prognostic value in respiratory infections and sepsis [9,10]. The combined use of CRP, NLR, and PLR could enhance the etiologic discrimination of CAP by integrating the acute-phase response (CRP) with the cellular components of inflammation (neutrophils, lymphocytes, and platelets). This pathophysiological synergy reinforces their potential as a simple, reproducible, and accessible diagnostic panel, particularly useful in settings where microbiological tests are not routinely available.

In Ecuador, evidence on the combined usefulness of these biomarkers is limited. Evaluating their diagnostic performance in the local context would make it possible to optimize the rational use of antibiotics and improve the clinical management of CAP in regional hospitals. Therefore, the aim of this study was to evaluate the diagnostic capacity of CRP, NLR, and PLR, individually and in combination, to discriminate between the bacterial and viral etiologies of community-acquired pneumonia in hospitalized patients in Riobamba, Ecuador, by means of ROC curve analysis for the determination of optimal cutoff points and the application of logistic regression models to identify independent predictors of bacterial etiology.

METHODS

Study type and area

An observational, retrospective, analytical study was conducted through a review of the medical records of hospitalized patients diagnosed with CAP at the Instituto Ecuatoriano de la Seguridad Social (IESS) General Hospital in Riobamba, Ecuador, during the period from January 2023 to July 2025. The study was conducted and reported in accordance with the recommendations of the STARD guideline (Standards for Reporting Diagnostic Accuracy Studies), in order to ensure adequate reporting of the diagnostic performance of the biomarkers evaluated.

Population and sample

A total of 334 hospitalized patients with a clinical and radiological diagnosis of CAP at the IESS General Hospital of Riobamba were assessed. Two hundred twenty-nine patients were excluded for the following reasons: nosocomial pneumonia or pneumonia associated with mechanical ventilation (n = 48), bacterial-viral coinfection (n = 62), the presence of hematological diseases, immunosuppression, or corticosteroid treatment (n = 29), and the absence of microbiological confirmation of the diagnosis (n = 90).

Of the 105 patients with microbiologically, clinically, and radiologically confirmed CAP, 5 additional cases were excluded because complete blood count or CRP results were not available. Finally, the sample

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consisted of 100 patients, equally distributed into two etiologic groups: 50 with bacterial pneumonia and 50 with viral pneumonia. This distribution was a consequence of the process of consecutive inclusion and the refinement of eligible cases, and was not the result of deliberate selection or prior matching of participants.

The final sample size was calculated and verified using Epidat 4.2 software for the comparison of independent means between both groups, considering the expected values of the neutrophil-to-lymphocyte ratio (NLR) reported in previous studies. A 95% confidence level and 80% statistical power were assumed, yielding a minimum required sample size of 45 patients per group (90 in total). To compensate for possible missing data, the final number was increased to 100 patients, who constituted the definitive study sample.

Inclusion and exclusion criteria

Patients older than 18 years were included if they had a clinical and radiological diagnosis compatible with CAP, with bacterial or viral etiologic confirmation by sputum culture, tracheal aspirate, or blood culture, rapid antigen tests, or reverse transcription polymerase chain reaction (RT-PCR), according to diagnostic availability in hospital and private laboratories in the city of Riobamba, and if complete blood count and C-reactive protein results were available at hospital admission.

Conversely, patients with nosocomial pneumonia or pneumonia associated with mechanical ventilation, as well as those with bacterial-viral coinfection, were excluded from the study. Likewise, patients presenting hematological diseases, immunosuppression, or treatment with corticosteroids or anti-inflammatory drugs in the two weeks prior to diagnosis were excluded because of their possible influence on the inflammatory response and on NLR and PLR values.

Variables and data collection instruments

The analyzed variables were grouped into three categories:

Clinical variables: the main comorbidities reported in the medical record were documented, including type 2 diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and ischemic heart disease. The etiology of pneumonia (bacterial or viral) was established according to the clinical, radiological, and microbiological findings recorded in the medical record. In addition, the CURB-65 score, used as an indicator of severity at hospital admission, and the length of hospital stay in days were recorded.

Laboratory variables: the absolute neutrophil, lymphocyte, and platelet counts were obtained from the automated complete blood count performed in the hospital's clinical laboratory using a Sysmex XN-1000 automated analyzer. Based on these values, the derived hematological indices were calculated.

The neutrophil-to-lymphocyte ratio (NLR) was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. The platelet-to-lymphocyte ratio (PLR), in turn, was determined by dividing the platelet count by the absolute lymphocyte count.

CRP concentration was determined by automated immunoturbidimetry on a Roche Cobas c311 analyzer (Roche Diagnostics, Germany). Reference values: < 5 mg/L. This value was used exclusively for descriptive purposes, whereas the diagnostic cutoff points were derived from the ROC analysis.

Demographic variables: age and sex were recorded for each participant, based on information obtained from the institutional medical records. Age was expressed in years and analyzed as a continuous variable.

Data collection techniques and procedures

Data were collected through documentary review of the medical records of hospitalized patients with a confirmed diagnosis of CAP. A structured data collection form designed by the research team was used as the instrument, allowing the collection of demographic information (age, sex), clinical information (comorbidities, type of etiologic agent, CURB-65 score, and length of hospital stay), and laboratory data (absolute neutrophil, lymphocyte, and platelet counts), as well as the derived hematological indices and serum CRP concentration. All laboratory parameters corresponded to samples obtained at hospital admission, with a maximum accepted interval of ≤ 24 hours from admission.

The data were transcribed and verified in an electronic database prepared in Microsoft Excel, assigning a numerical code to each record to preserve confidentiality. The information was subsequently exported to GraphPad Prism version 9.0 and R version 4.3.2 for statistical analysis. Data validation included cross-checking against the original clinical

laboratory records and institutional medical reports, thereby ensuring consistency and accuracy in the final analytical database.

Severity assessment: CURB-65

The clinical severity of CAP was assessed using the CURB-65 scale. This tool assigns one point for the presence of each of the following criteria: mental confusion, serum urea > 7 mmol/L, respiratory rate ≥ 30/min, systolic blood pressure < 90 mm Hg or diastolic blood pressure ≤ 60 mmHg, and age ≥ 65 years. According to international guidelines, CAP was considered mild when the score was 0-1, moderate with 2 points, for which hospitalization is recommended, and severe with ≥ 3 points, suggesting the need for management in an intensive care unit [12]. All CURB-65 components were available at the time of admission for all included patients.

Data analysis

Statistical analysis was performed using GraphPad Prism v 9.0 and R v 4.3.2, using the pROC package for ROC curves. The normality of continuous variables was verified with the Shapiro-Wilk test. As the normality criteria were not met, comparisons between the bacterial and viral groups were performed using the Mann-Whitney U test, with results expressed as median and interquartile range. Categorical variables were analyzed using the chi-square or Fisher's exact test, as appropriate.

The diagnostic performance of the biomarkers was evaluated using ROC curves, calculating the area under the curve (AUC), the 95% confidence interval, and the optimal cutoff point using the Youden index. Differences between AUCs were determined with the DeLong test. Likewise, sensitivity, specificity, and positive and negative likelihood ratios were calculated. Finally, binary and multivariable logistic regression was applied to identify independent predictors of bacterial pneumonia, adjusting for age, sex, CURB-65 score, chronic obstructive pulmonary disease, and type 2 diabetes mellitus. Prior to construction of the multivariable logistic regression model, possible collinearity among the inflammatory variables included was evaluated by calculating the variance inflation factor (VIF). A VIF value ≥ 5 was considered indicative of relevant collinearity. In the present study, all variables incorporated into the model showed VIF values below 2, which allowed the presence of significant collinearity to be ruled out and justified their simultaneous inclusion in the multivariable analysis. Values of $p < 0.05$ were considered significant.

Ethical considerations

The protocol was approved by the Research Directorate of the IESS General Hospital of Riobamba, approval number 10-2023. Given its retrospective nature and the exclusive use of clinical records without direct contact with patients, the study did not require individual informed consent, in accordance with national ethical regulations and the guidelines of the Declaration of Helsinki. Data confidentiality was guaranteed by coding the records without including personally identifiable information.

RESULTS

A total of 100 hospitalized patients at the IESS General Hospital of Riobamba, Ecuador, diagnosed with CAP were analyzed, of whom 50 had a bacterial etiology and 50 a viral etiology.

The median age was 64 years (IQR: 52-75), significantly higher in bacterial pneumonia than in viral pneumonia ($p = 0.041$). No differences were observed in sex distribution. The most frequent comorbidities were hypertension (46%) and type 2 diabetes mellitus (30%), with no significant differences between groups.

CURB-65 score and length of hospital stay were higher in bacterial pneumonia ($p < 0.001$), whereas in-hospital mortality was 8%, with no significant differences between etiologies (see Table 1).

Hematological and acute-phase analyses showed significant differences between the two etiologies. Patients with bacterial pneumonia had higher leukocyte and neutrophil counts, together with a relative reduction in lymphocytes, which translated into a marked increase in the neutrophil-to-lymphocyte ratio (NLR). Consistently, CRP and the platelet-to-lymphocyte ratio (PLR) were significantly higher in the bacterial group, reflecting a more intense systemic inflammatory response (see Table 2).

Inflammatory biomarkers

Figure 1 (A-C) shows the boxplots corresponding to the three biomarkers analyzed. In all cases, patients with bacterial pneumonia exhibited a significantly more intense systemic inflammatory response than those with viral etiology. CRP

Table 1. Clinical and demographic characteristics of patients with community-acquired pneumonia

Variable		Total (n = 100)	Bacterial pneumonia (n = 50)	Viral pneumonia (n = 50)	*p*-value*
Age (years), median (IQR)		64 (52-75)	68 (55-78)	60 (50-70)	0.041
Sex	Male n (%)	58 (58)	32 (64)	26 (52)	0.23
	Female n (%)	42 (42)	18 (36)	24 (48)	
Comorbidities, n (%)					
Type 2 diabetes mellitus		30 (30)	18 (36)	12 (24)	0.19
Hypertension		46 (46)	25 (50)	21 (42)	0.43
COPD		18 (18)	12 (24)	6 (12)	0.11
Ischemic heart disease		10 (10)	6 (12)	4 (8)	0.51
CURB-65, median (IQR)		2 (1-3)	3 (2-4)	2 (1-2)	<0.001
CURB-65 ≥ 3, n (%)		36 (36)	28 (56)	8 (16)	<0.001
Length of hospital stay (days), median (IQR)		8 (6-11)	10 (8-13)	6 (5-8)	<0.001
In-hospital mortality, n (%)		8 (8)	6 (12)	2 (4)	0.14

*p values were obtained using the Mann–Whitney U test for continuous variables and the chi-square (χ^2) test for categorical variables. IQR: interquartile range; COPD: chronic obstructive pulmonary disease.

reached a median of 117.1 mg/L in the bacterial group compared with 34.75 mg/L in the viral group (median difference = 82.35 mg/L; $p < 0.0001$). The NLR showed a median of 8.650 in bacterial pneumonia versus 3.450 in viral pneumonia (median difference = 5.200; $p < 0.0001$). Likewise, the PLR showed medians of 232.0 and 175.0, respectively (median difference = 57.0; $p < 0.001$).

Diagnostic performance of the biomarkers evaluated

In the diagnostic performance analysis, the three biomarkers evaluated showed variable discriminatory ability for differentiating bacterial from viral pneumonia. NLR showed the best performance, with an area under the ROC curve (AUC) of 0.999, an optimal cutoff point > 5.850, 100% sensitivity,

Table 2. Hematological and inflammatory parameters according to the etiology of community-acquired pneumonia

Variable	Total (n = 100)	Bacterial pneumonia (n = 50)	Viral pneumonia (n = 50)	*p*-value*
Leukocytes x mm³	9,200 (6,800-12,600)	12,000 (9,800-14,500)	6,750 (5,200-8,200)	<0.001
Neutrophils x mm³	7,400 (5,100-10,800)	10,216 (8,100-12,900)	4,771 (3,500-6,200)	<0.001
Lymphocytes x mm³	1,180 (900-1,700)	1,181 (800-1,600)	1,383 (1,000-1,800)	<0.01
Platelets x mm³	258,000 (210,000-280,000)	232,000 (192,000-269,000)	175,000 (145,000-191,000)	<0.01
CRP (mg/L)	102.5 (95-152.6)	117.1 (97.98-139.6)	34.75 (28-44.85)	<0.0001
NLR	6.1 (3.2-9.4)	8.65 (6.2-10.1)	3.45 (2.1-4.7)	<0.0001
PLR	208 (162-270)	232 (190-280)	175 (150-189)	<0.0001

*Data are expressed as median (interquartile range). Mann-Whitney U test.
CRP: C-reactive protein; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio.

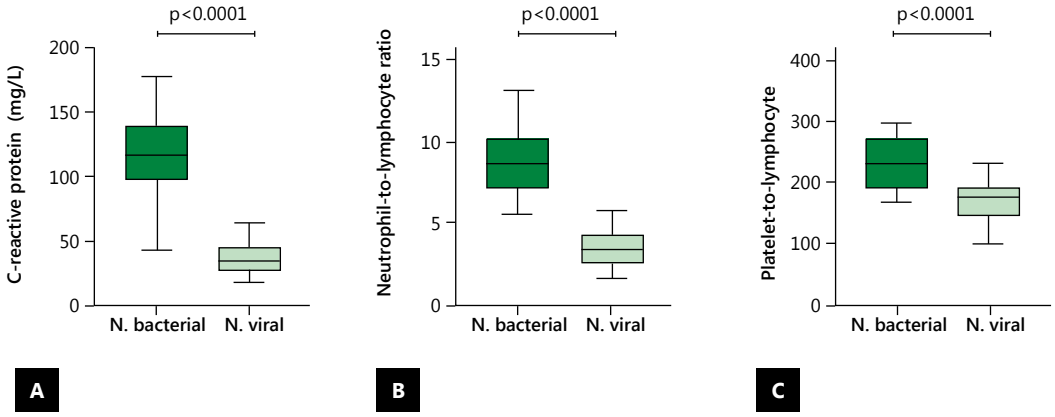

Figure 1. Distribution of inflammatory biomarkers according to the etiology of CAP (n = 50 per group)

*(A) C-reactive protein (CRP); (B) neutrophil-to-lymphocyte ratio; (C) platelet-to-lymphocyte ratio.
** The boxes represent the interquartile range (IQR), the central line indicates the median, and the whiskers represent the minimum and maximum range. Significant differences were observed for all three biomarkers (p < 0.001, Mann-Whitney U test); n = 50 per group.

and 96% specificity, which translated into a Youden index of 0.96, a positive likelihood ratio (+LR) of 25.0, and a negative likelihood ratio (−LR) close to zero, reflecting excellent ability both to confirm and to rule out bacterial etiology. CRP also showed high performance (AUC = 0.948; cutoff point > 65.55 mg/L; sensitivity = 100%; specificity = 94%; Youden = 0.94; +LR = 16.7; − LR = 0), although with slightly lower specificity. In contrast, PLR showed moderate diagnostic ability (AUC = 0.833; cutoff point > 181.7; sensitivity = 64%; specificity = 80%; Youden = 0.44; +LR = 3.2; − LR = 0.45), limiting its standalone clinical utility. Comparison of the ROC curves using the DeLong test confirmed statistically significant differences among the biomarkers, establishing a hierarchical order of performance of NLR > CRP > PLR ($p < 0.05$), positioning NLR as the most robust parameter for etiologic discrimination in community-acquired pneumonia (see Figure 2 and Table 3).

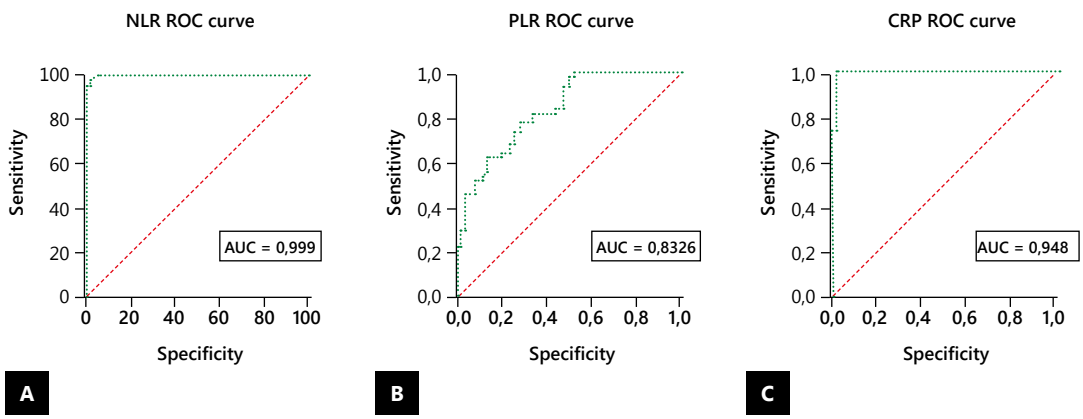

Figure 2. Receiver operating characteristic (ROC) curves of inflammatory biomarkers for differentiating bacterial pneumonia (n = 50) from viral pneumonia (n = 50)

*(A) Neutrophil-to-lymphocyte ratio (NLR); (B) platelet-to-lymphocyte ratio (PLR); (C) C-reactive protein (CRP).
**All differences were statistically significant ($p < 0.0001$). The diagonal line represents the line of chance (AUC = 0.5). NLR showed the best diagnostic performance (DeLong test: NLR > CRP > PLR; $p < 0.05$).

Table 3. Diagnostic performance of NLR, PLR, and CRP for differentiating bacterial pneumonia from viral pneumonia

Biomarker	Optimal cutoff point	Sensitivity (%)	Specificity (%)	+LR	−LR	(J)	Clinical interpretation
NLR	> 5.850	100	96	25.0	0.00	0.96	NLR > 5.850: high probability of bacterial pneumonia; start antibiotics. NLR ≤ 5.850: viral etiology is highly likely; antibiotic therapy may be avoided.
CRP	> 65.55 mg/L	100	94	16.7	0.00	0.94	CRP > 65.55: moderate diagnostic support for bacterial infection; CRP ≤ 65.55: limited usefulness as a rule-out test.
IPL	> 181.7	64	80	3.20	0.45	0.44	PLR > 181.7: moderate probability of bacterial etiology; PLR ≤ 181.7 does not rule out bacterial infection (limited diagnostic value).

*NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; CRP: C-reactive protein.
**Cutoff points were determined by ROC curve analysis to discriminate between bacterial and viral pneumonia. +LR: positive likelihood ratio; −LR: negative likelihood ratio; J: Youden index. A higher J value indicates a better balance between sensitivity and specificity.

The multivariable model showed that an NLR > 5.850 was independently associated with bacterial etiology, even after adjustment for other inflammatory biomarkers, age, sex, severity, and comorbidities. In contrast, neither a PLR > 181.7 nor a CRP > 65.55 mg/L reached statistical significance, suggesting that the diagnostic component of systemic inflammation is concentrated mainly in the neutrophilic response. Older age and a CURB-65 score ≥ 3 also behaved as independent predictors of bacterial infection, in agreement with the reviewed literature, which points to a higher risk in older patients or in those with severe pneumonia. Inflammatory biomarkers were included simultaneously together with the clinical adjustment variables. Prior assessment of collinearity by means of the variance inflation factor showed values below 2 for all variables, confirming the absence of relevant collinearity and the stability of the model. Consequently, the estimated odds ratios reflect independent associations with the probability of bacterial pneumonia (see Table 4).

DISCUSSION

This study evaluated the usefulness of accessible biomarkers—CRP, NLR, and PLR—for distinguishing between bacterial and viral etiologies of community-acquired pneumonia in a hospital setting in Riobamba, Ecuador. Cases of bacterial pneumonia were characterized by a more severe clinical presentation and a more prolonged course than those of viral origin, which is consistent with the more intense systemic inflammatory response that usually accompanies bacterial infections. This pattern has been documented previously, as higher severity scores and longer hospital stays are associated with the magnitude of the neutrophilic

Table 4. Independent predictors of bacterial etiology in community-acquired pneumonia: multivariable logistic regression analysis

Predictor	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
NLR > 5.85	22.40 (7.80-64.30)	<0.001	14.80 (4.20-52.10)	<0.001
PLR > 181.7	2.30 (0.80-6.40)	0.121	1.90 (0.60-6.10)	0.270
CRP > 65.55 mg/L	3.10 (1.10-8.60)	0.032	1.40 (0.50-4.00)	0.120
Age (years)	1.05 (1.02-1.08)	0.002	1.04 (1.01-1.07)	0.012
Male sex	1.50 (0.70-3.30)	0.290	1.30 (0.50-3.40)	0.580
CURB-65 ≥ 3	7.80 (2.80-21.90)	<0.001	5.60 (1.60-19.50)	0.007
COPD	2.60 (0.90-7.40)	0.076	2.10 (0.70-6.30)	0.180
Type 2 diabetes mellitus	1.90 (0.70-5.10)	0.207	1.60 (0.60-4.30)	0.350

*OR = odds ratio; 95% CI = 95% confidence interval; CURB-65 = community-acquired pneumonia severity scale; COPD = chronic obstructive pulmonary disease.
**Biomarker cutoff values (NLR > 5.850, PLR > 181.7, and CRP > 65.55 mg/L) were determined using the Youden index derived from ROC curves. The model was adjusted for age, sex, comorbidities (COPD and type 2 diabetes mellitus), and clinical severity (CURB-65 ≥ 3). The dependent variable was bacterial etiology (1 = bacterial, 0 = viral). A p value < 0.05 was considered statistically significant.

response and the inflammatory burden [13]. Consistent with this, several studies have shown that patients with severe pneumonia present neutrophilia, relative lymphopenia, and marked activation of the acute-phase response, findings reflected in an increased NLR, which has been linked to both clinical severity and mortality [14].

From a pathophysiological standpoint, bacterial CAP tends to trigger an early and vigorous innate immune response characterized by activation and massive release of neutrophils from the bone marrow, driven by the recognition of pathogen-associated molecular patterns (PAMPs) through Toll-like receptors and the activation of proinflammatory pathways. This cascade leads to increased levels of proinflammatory cytokines, particularly IL-1β, IL-6, and TNF-α, which promote neutrophilia, effector-cell mobilization, and microbicidal processes such as phagocytosis, degranulation, and NETosis, while also stimulating the production of acute-phase proteins such as CRP [15].

In contrast, viral infections usually trigger early interferon-mediated responses and greater involvement of lymphocyte-mediated immunity, including CD8+ T cells and NK cells, with less sustained neutrophil mobilization, which explains the tendency toward lower NLR values in viral etiologies. At the same time, inflammatory stress signals and certain soluble mediators promote lymphopenia through lymphocyte apoptosis, redistribution to tissues, or sequestration in lymph nodes, resulting in the characteristic rise in NLR observed in acute bacterial conditions [16]. This difference in immunological profiles provides a solid pathophysiological basis for NLR to serve as a discriminatory marker between etiologies [17].

In this study, NLR was the biomarker with the best discriminatory ability between bacterial and viral etiologies. CRP also showed good performance, whereas PLR showed only moderate performance. In the multivariable analysis, only NLR > 5.85 emerged as an independent predictor of bacterial etiology. These findings are relevant because most previous studies have focused on the prognostic value of NLR (mortality or ICU admission) rather than on its diagnostic capacity. For example, although previous studies have reported higher CRP concentrations in bacterial than in viral pneumonia, its discriminatory power was lower than that observed here, with cutoff values ranging from 40 to 60 mg/L [18].

In the literature, the findings regarding the ability of CRP to distinguish bacterial from viral etiologies are heterogeneous. Some authors found significantly higher concentrations in bacterial CAP [19,20], whereas others observed substantial overlap in values between the two etiologies: up to 25% of viral cases had CRP > 80 mg/L and nearly 23% of bacterial cases showed values < 20 mg/L [21]. This variability precludes the establishment of a universal cutoff point and explains the reported differences in sensitivity and specificity. Overall, the evidence suggests that although CRP reflects the magnitude of systemic inflammation, its standalone diagnostic value is limited and may be improved by combining it with other immunological markers or clinical parameters.

The excellent performance of NLR compared with CRP may be explained by its dual nature, as it integrates two dynamic components of the immune response: the innate arm (neutrophils) and the adaptive arm (lymphocytes) [22]. By contrast, CRP is an acute-phase reactant whose hepatic synthesis can also be triggered by noninfectious inflammatory stimuli [23,24].

Moreover, although PLR was significantly higher in the bacterial group, it showed only moderate performance and was not an independent predictor. This is consistent with the literature, in which PLR has been studied mainly as a prognostic marker in sepsis, cancer, or COPD, rather than as an etiologic marker. Some studies have demonstrated its association with mortality or ICU admission, but not with the type of causal agent [25]. From a pathophysiological perspective, platelets play key immunologic roles, but their count may vary according to comorbidities, altitude, or prior treatments, which could limit their discriminatory value [26].

This study has several limitations. Its retrospective, single-center design limits the generalizability of the findings and increases the risk of selection and information bias. The exclusion of a high percentage of patients, mainly those without microbiological confirmation, may have introduced selection bias; however, this decision was necessary to ensure etiologic classification. Widely used biomarkers such as procalcitonin were not included because of limitations in availability and cost in the hospital setting studied. Likewise, the proposed cutoff points were not validated through internal validation techniques or in external cohorts and should therefore be interpreted as exploratory. Finally, the results correspond to a hospital in the Andean region, which may limit their extrapolation to other epidemiological settings.

Conclusions

The neutrophil-to-lymphocyte ratio showed the best diagnostic performance for differentiating bacterial from viral pneumonia in hospitalized patients with CAP, outperforming CRP and PLR. These accessible, low-cost biomarkers may support clinical decision-making and antibiotic stewardship, particularly in settings with limited access to microbiological testing. However, their clinical implementation requires prospective multicenter validation before routine adoption.

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DTS: formal analysis, discussion, supervision, funding acquisition, investigation, project administration, material resources, software, conceptualization, methodology, data curation, writing – original draft, and writing – review & editing.

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