

Neutrophil-to-lymphocyte ratio, platelets-to-lymphocyte ratio, and red cell distribution width as prognostic indicators for length of hospital stay in pediatric asthma

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ABSTRACT

الأهداف: دراسة العلاقة بين نسبة العدلات إلى الخلايا اللمفاوية (NLR)، ونسبة الصفائح الدموية إلى الخلايا اللمفاوية (PLR)، وعرض توزيع الخلايا الحمراء (RDW) وطول مدة الإقامة في المستشفى (LOS) عند الأطفال المصابين بالربو القصبي.

المنهجية: قامت هذه الدراسة المرتكزة على المستشفى بفحص سجلات الأطفال المصابين بالربو الذين تم إدخالهم إلى مستشفيات جازان، جازان، المملكة العربية السعودية. تم استخراج البيانات في وقت القبول. وكذلك الحصول على مدة الإقامة في المستشفى والمعلومات المختبرية من الدم.

النتائج: شملت هذه الدراسة 489 طفلاً، بمتوسط عمر 5.8 ± 3.5 عام، منهم 59.7% ذكور. والجدير بالذكر أن 77.7% من المرضى يقيمون في المناطق الريفية بجازان. كان متوسط LOS هو 3.38 ± 0.35 يوماً، مع إقامة قصيرة لـ 2.9% (أقل من 24 ساعة) وتصنيف 64.2% على أنها إقامة متوسطة (1-3 أيام). وكان متوسط 5.33 ± 1.20 NLR، مع وقوع 46.8% ضمن المعدل الطبيعي. وبالمثل، كان متوسط 184.84 ± 16.55 PLR، مع تصنيف 42.7% على أنها طبيعية. تبين أن PLR وLOS مرتبطين بشكل كبير ($p=0.021$)، في حين لا يوجد مثل هذا الارتباط لـ NLR أو RDW مع LOS. من بين المؤشرات الحيوية للدم التي تم تقييمها، أظهر PLR أعلى قيمة تنبؤية لـ LOS عند الأطفال المصابين بالربو، مما أدى إلى منطقة تحت منحنى 0.664 (فاصل الثقة: 0.606-0.723؛ $p=0.000$).

الخلاصة: أظهرت النتائج عدم وجود علاقة ذات دلالة إحصائية بين NLR و RDW مع LOS. على العكس من ذلك، لوحظ وجود علاقة ملحوظة بين PLR وLOS، مما يشير إلى أن PLR قد يكون بمثابة علامة تنبؤية قيمة لـ LOS في مرضى الأطفال المصابين بالربو.

Objectives: To examine the relationship between neutrophil-to-lymphocyte ratio (NLR), platelets-to-lymphocyte ratio (PLR), and red cell distribution width (RDW) and the length of hospital stay (LOS) in children with bronchial asthma

Methods: This hospital-based study examined the records of children with asthma admitted to Jazan Hospitals, Jazan, Kingdom of Saudi Arabia. Data were extracted at the time of admission. Length of hospital stay and laboratory parameters were acquired from blood.

Results: This study involved 489 children, with a mean age of 5.8 ± 3.5 years, of which 59.7% were male. Notably, 77.7% of the patients resided in rural areas of Jazan. The mean LOS was 3.38 ± 0.35 days, with 2.9% having a short stay (<24 hours) and 64.2% categorized as having a medium stay (1-3 days). The mean NLR was 5.33 ± 1.20 , with 46.8% falling within the normal range. Similarly, the mean PLR was 184.84 ± 16.55 , with 42.7% classified as normal. The PLR and LOS were shown to be significantly correlated ($p=0.021$), while no such association existed for NLR or RDW with LOS. Among the blood biomarkers assessed, PLR demonstrated the highest predictive value for LOS in children with asthma, yielding an area under the curve of 0.664 (confidence interval: 0.606-0.723; $p=0.000$).

Conclusion: The findings showed no significant association between NLR and RDW with LOS. Conversely, a notable correlation was observed between PLR and LOS, suggesting that PLR may serve as a valuable predictive marker for LOS in pediatric patients with asthma.

Keywords: asthma, length of hospital stay, NLR, PLR, RDW

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Bronchial asthma is a prevalent allergic disease associated with morbidity and frequent hospitalizations.¹ Characterized by recurrent episodes of severe dyspnea, typically occurring at night or in the early morning, bronchial asthma is also marked by coughing, wheezing, and chest tightness, which often intensify after physical activity or stress.² The prevalence of bronchial asthma varies globally, affecting 10.6% of children and adolescents in Eastern Mediterranean Regional Office (EMRO) countries.³ These variations are attributed to varied epidemiological definitions of asthma, measurement techniques, and environmental factors across communities.³ Asthma prevalence among Saudi children has reached 31.5% in certain industrialized cities, exceeding the national range of 8% to 25% reported in other regions.⁴

The hallmarks of chronic inflammation in asthma are reversible airway obstruction, bronchial hyperreactivity, and excessive mucus production brought on by immune system stimulation following allergen exposure.² The underlying etiology involves multiple pro-inflammatory mechanisms, including inflammatory and physiological reactions mediated by both innate and adaptive immune pathways.⁵ Numerous cell types are responsible for chronic inflammation, including B cells, mast cells, eosinophils, neutrophils, and T-helper cells, alongside structural bronchial cells like smooth muscle cells. Inflammation is a critical feature of asthma, frequently presenting with altered morphology and function of blood tissues in the peripheral blood and airways, particularly within neutrophil, eosinophil, lymphocyte, and platelet populations.^{6,7}

Asthma phenotypes can be identified using various biomarkers; however, given the heterogeneous nature of severe asthma, determining the most accurate and definitive biomarkers remains challenging.⁷ The platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) have emerged as promising biomarkers for assessing acute asthma risk. These indicators, accessible through standard laboratory investigations, offer key insights into systemic inflammation.⁸⁻¹⁰ Another potential biomarker, red cell distribution width (RDW), has shown prognostic value in patients admitted with acute conditions, such as pneumonia.¹¹

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Frequent visits to emergency departments and inpatient facilities impose substantial economic pressure on the healthcare system, with costs for children with asthma considerably exceeding those for children without the condition.¹² Hospitalizations for asthma typically involve an average length of stay of 2.52 days, with a higher predominance among male patients than females.¹³ Certain predictors, such as heart rate, respiratory rate, and oxygen saturation levels assessed using percentile-based cutoffs, have been identified as independent predictors of hospital stay in children with asthma. However, studies correlating the length of hospital stay (LOS) with hematological biomarkers are scarce.^{14,15} This study aims to assess the predictive value of NLR, PLR, and RDW among pediatric asthma patients in the Jazan region of Saudi Arabia and to explore their correlation with the LOS.

Methods. This retrospective hospital-based study focused on children diagnosed with bronchial asthma admitted to pediatric hospitals in the Jazan region of Saudi Arabia. The Jazan region, located in the southwestern part of the country, covers an area of 13,457 square kilometers.¹⁶ The study included 5 pediatric hospitals—Prince Mohamed Bin Nassir, Jazan, King Fahad, Abuarish, and Sabya—representing the plains, coastal, and mountainous regions.

Data was collected during May and June 2024, including records of pediatric patients up to 18 years of age admitted to the selected hospitals in the Jazan region with a diagnosis of bronchial asthma between June 2020 and June 2024. Records that did not meet the inclusion criteria lacked important data, or pertained to patients with comorbid chronic illnesses necessitating admission alongside asthma were excluded.

Data were gathered using specially prepared extract sheets that included information available immediately upon patient admission. The variables encompassed age, sex, asthma symptom history, other chronic conditions, long-term asthma medications, prior hospitalizations, clinical signs at presentation, and LOS. The length of inpatient care during a single admission is referred to as LOS. To present descriptive analysis, LOS was classified into 4 categories based on previous research: short stay (less than 24 h), medium stay (1–3 days), long stay (4–7 days), and very long stay (more than 7 days).¹⁷

The laboratory parameters were acquired from blood tests performed the day following the child's admission. The NLR was computed by either comparing the percentage of neutrophils to lymphocytes in the complete blood count (CBC) or by dividing the absolute number of neutrophils by the absolute number of lymphocytes.

While a precise NLR cutoff for children has yet to be established, values in the range of 1–3 are generally considered normal, with values exceeding three deemed abnormal.¹⁸⁻²⁰ Similarly, the PLR was counted as the number of platelets divided by the lymphocyte count. Based on prior research, a PLR of less than 120 was considered normal, while a value of 120 or above was regarded as abnormal for pediatric patients, with normal ranges typically falling between 111 and 120.²¹⁻²³

Statistical analysis. The complete dataset was reviewed and coded, and data analysis was carried out utilizing the Statistical Package for the Social Sciences (SPSS) software for windows version 23 (IBM Corp., Armonk, N.Y., USA). Frequency distributions of patient characteristics and descriptive statistics were calculated. The chi-square tests and one-way analysis of variance (ANOVA) were used to compare hematological biomarkers and LOS. All parameter values are represented as mean±standard deviation (SD). Correlations among study parameters were assessed using Pearson's r correlation analysis. Statistical significance was determined based on a set threshold. Further analysis evaluated the predictive values of NLR, PLR, and RDW for LOS, using a receiver operating characteristic (ROC) curve to calculate the area under the curve (AUC), with values ranging from 0 to 1.

This study was conducted in accordance with the principles of the Declaration of Helsinki, and ethical approval was obtained from the Jazan Ethics Committee of Jazan Health Group, Kingdom of Saudi Arabia. All data remained confidential, with no names or identities recorded. Written consent was not required since the study relied on patient records without direct interviews.

Results. A total of 489 asthmatic children records were studied following their admission to the emergency departments of 5 pediatric hospitals. The mean age was 5.8±3.5 years, and 59.7% were male. Most patients, 380 (77.7%), were from rural areas in Jazan, while 44 (9%) resided in Jazan city, and 65 (13.3%) were from other cities within the Jazan region. Additionally, 4.6% of the patients had other allergies, such as food allergies and eczema, and 28.8% had a positive family history of bronchial asthma (Table 1).

Upon admission, 90.6% of patients entered through the emergency department to a regular ward, while 8.2% were admitted to the pediatric intensive care unit. Of these patients, 6.8% were considered unstable, and 1.6% required resuscitation. The most common initial diagnosis was asthma exacerbation, noted in 365 patients (74.6%), followed by asthma with other diseases in 100

Table 1 - The characteristics of the involved asthmatic children.

Characteristic	n	(%)
Gender		
Male	292	(59.7)
Female	197	(40.3)
Age (years)		
<1	2	(0.4)
1-5	253	(51.7)
6-10	175	(35.8)
11-15	54	(11.6)
>15	1	(0.2)
Residence		
Jazan town	44	(9)
Other town in Jazan Region	65	(13.3)
Jazan rural area	380	(77.7)
If patient has other type of allergy		
Yes	23	(4.7)
No	338	(69.1)
Not recorded	128	(26.2)
Long term medications		
No medications	339	(69.3)
Short acting beta agonist±inhaled corticosteroid (ICS)	133	(27.2)
Leukotriene receptor antagonist±ICS	3	(0.6)
Long acting beta agonist ±ICS	12	(2.5)
Family history of bronchial asthma		
Yes	142	(29)
No	214	(43.8)
Not recorded	133	(27.2)
Area of admission		
Regular ward	443	(90.6)
Pediatrics intensive care unit	40	(8.2)
Isolation	6	(1.2)
Patient condition when admitted		
Stable	254	(51.9)
Non-Stable	32	(6.5)
Not recorded	203	(41.5)
The need of resuscitation on admission		
Yes	8	(1.6)
No	287	(58.7)
Not recorded	194	(39.7)
Provisional diagnosis		
Exacerbation of bronchial asthma alone	365	(74.6)
Exacerbation of bronchial asthma with pneumonia	24	(4.9)
Exacerbation of bronchial asthma with other cause	100	(20.4)
If chest x-ray was done		
Yes	419	(83.1)
No	84	(16.9)

patients (20.4%), and asthma with pneumonia in 24 patients (4.9%). All patients underwent CBC during admission, and 83.1% received chest radiography, though only 1% underwent a C-reactive protein test. Regarding long-term medication use, 339 patients

(69.3%) were not receiving any medications, whereas 133 patients (27.2%) were on short-acting beta-agonists with or without inhaled corticosteroids.

Table 2 presents laboratory investigations of a study sample, showing the mean and SD for various hematological parameters. Hemoglobin levels averaged 11.82 g/dL \pm 4.85, while the Total White Blood Cell Count (TWBC) was 11.41 \times 10⁹/L \pm 5.38. Neutrophil and lymphocyte levels are observed at 18.44% \pm 24.30 and 43.85% \pm 8.00, respectively, with eosinophil levels at 0.79% \pm 1.86. The platelet count was recorded as 371.44 \times 10⁹/L \pm 116.17. Additionally, the NLR averaged 5.33 \pm 5.54, the PLR was 184.84 \pm 167.15, and RDW averaged 15.15 \pm 2.7.

The mean LOS was 3.38 \pm 0.35 days, with 14 patients (2.9%) having a short stay (<24 hours), 314 (64.2%) experiencing a medium stay (1-3 days), 135 (27.6%) a long stay (4-7 days), and 26 patients (5.3%) as having a very long stay (>7 days).

The mean NLR was 5.33 \pm 1.20, with 229 patients (46.8%) falling within the normal range (1-3) and 260 patients (53.2%) classified as abnormal (>3). Mean while, the mean PLR was noted to be 184.84 \pm 16.55, with 209 patients (42.7%) classified as normal (<120) and 280 patients (57.3%) as abnormal (>120).

Table 3 presents a cross-tabulation of the distribution of patients across various PLR and NLR categories relative to different LOS. A Chi-squared test highlights a significant association between PLR categories and LOS, yielding a Chi-squared statistic of 9.779 and a low *p*-value of 0.021. In contrast, the association between NLR categories and LOS was not statistically significant, as indicated by a chi-squared value of 0.542 and a *p*-value of 0.910. These results suggest that PLR plays a more substantial role than NLR in influencing the duration of hospital stay. Furthermore, to compare the RDW values across different LOS categories, a one-way ANOVA was conducted to test the hypothesis of significant mean differences among these groups. The results indicated no significant difference in RDW among these categories (*p*=0.405), as shown in **Table 4**.

A ROC curve was applied to analyze the predictive performance of each blood biomarker for LOS in children with asthma. The AUC was calculated to summarize the overall effectiveness of the model. In the ROC curve presented in **Figure 1**, the y-axis represents the actual positive rate (sensitivity), while the x-axis denotes the false positive rate (1-specificity). The analysis revealed that PLR was the closest biomarker to the sensitivity axis, yielding an AUC of 0.664 (confidence interval: 0.606-0.723; *p*=0.000), as detailed in **Table 5**. This result indicates that PLR is a more effective predictor

Table 2 - Blood test that performed on admission for involved patients.

Variables	Mean \pm Standard deviation
Hemoglobin	11.82 \pm 4.85
Total white blood cells	11.41 \pm 5.38
Neutrophil	18.44 \pm 24.30
Lymphocyte	43.85 \pm 8.00
Eosinophil	0.79 \pm 1.86
Red cell distribution width	15.15 \pm 2.7
Platelet	371.44 \pm 116.17
Neutrophil to lymphocyte ratio	5.33 \pm 5.54
Platelets to lymphocyte ratio	184.84 \pm 167.15

of LOS than NLR and RDW. However, the AUC for PLR suggests fair discrimination, as it falls below the threshold of 0.8.

Discussion. The Jazan Region comprises coastal, mountainous, and plane terrains, with numerous towns and villages. The study revealed that approximately 77.7% of the admitted patients were from rural areas of Jazan, indicating the impact of specific triggers contributing to asthma exacerbation. Research has demonstrated an inverse relationship between temperature, humidity, altitude changes, and the occurrence of asthma symptoms.²⁴ Consequently, these variables might have played a role in the disparities in asthma prevalence in various areas of Jazan. This finding were in line with previous studies conducted in the region, which showed a higher prevalence of asthma in rural settings.^{25,26}

Approximately half of the patients in this study were aged between 1 and 5 years, with a predominance of males. No data linking asthma prevalence to different age groups in Saudi Arabia were identified. Most existing studies relied on questionnaires for data collection, primarily focusing on school-aged children while neglecting preschoolers. Additionally, around 69% of patients involved in this study were not receiving any medication, suggesting either recent diagnoses or milder disease presentations.

Bronchial asthma is a systemic inflammation that typically increases inflammatory markers, such as neutrophils and platelets, which can be measured through basic blood count tests. Under stressful circumstances, lymphocyte counts tend to decline, whereas neutrophil levels increase. The NLR offers a more sensitive metric for stress diagnosis compared to individual cell counts, as it considers both cell types.²⁷ Another emerging indicator of systemic inflammation in pediatric patients is the PLR, with elevated platelet activity often linked to increased inflammation.⁸ Given its association with

Table 3 - Cross tabulation for the distribution of patients across various PLR and NLR categories concerning different lengths of stay.

Variables	Length of Stay				Total	P-value
	Short stay <24 hours	Medium stay: 1-3 days	Long stay: 4-7 days	Very long stay: > 7 days		
PLR						
Normal : <120	6 (1.2%)	144 (29.4%)	66 (13.5%)	13 (2.7%)	229 (46.8%)	9.779 (0.021)
Abnormal : ≥ 120	8 (1.6%)	170 (34.8%)	69 (14.1%)	13 (2.7%)	260 (53.2%)	
NLR						
Normal : 1 - 3	6 (1.2%)	144 (29.4%)	66 (13.5%)	13 (2.7%)	229 (46.8%)	0.542 (0.910)
Abnormal: > 3	8 (1.6%)	170 (34.8%)	69 (14.1%)	13 (2.7%)	260 (53.2%)	

p-value significant<0.05

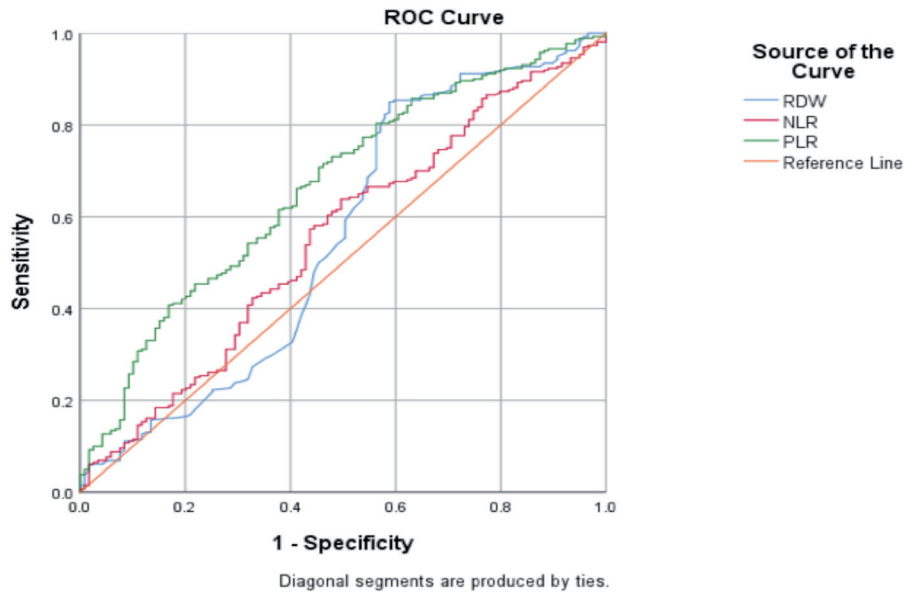


Figure 1 - A receiver operating characteristic curve (ROC curve) to analyze the predictive value of each blood biomarker for length of hospital stay in asthma children. X-axis: 1-specificity, Y-axis: sensitivity, RDW: red cell distribution width, NLR: neutrophil-to-lymphocyte ratio, PLR: platelets-to-lymphocyte ratio

the inflammatory response, the RDW may serve as a prognostic measure for inflammatory disease activity. Numerous studies have established a correlation between RDW and disease activity, demonstrating elevated levels in various inflammatory conditions.^{11,28}

In this study, CBC was obtained for all patients, while C-reactive protein levels were assessed in only 1% of patients at admission. The TWBC exhibited elevated values, with a mean of 11.4±5.38. The NLR was calculated, revealing a high mean level (5.33±5.54) compared to the established cutoff point. Additionally, the PLR and RDW were elevated, with means of 184.84±167.15 and 15.15±2.7, respectively. These outcomes are consistent with previous studies linking these 3 biomarkers with asthma exacerbation.⁸⁻¹⁰

Healthcare planning and prognosis in bronchial asthma are directly affected by LOS, which indirectly measures hospital resource utilization and operational efficiency. Moreover, LOS is a reliable predictor of clinical outcomes and patient recovery trajectories.^{12,29} In this study, the mean LOS was observed to be 3.38±0.35 days, with two-thirds of patients experiencing a medium stay duration (1–3 days). These findings align with prior studies documenting LOS in asthma patients.^{29,30}

The predictive performance of each blood biomarker in this study for LOS indicated a notable correlation between the PLR and LOS, suggesting that PLR is a potential marker in assessing pediatric asthma cases. Growing evidence highlights a strong correlation between elevated PLR levels and increased systemic

Table 4 - One-way ANOVA analysis to compare the RDW based on different lengths of stay.

Length of stay	N	Mean±SD	F-statistics (p-value)
Short stay:< 24 hours	12	15.1583± 2.29801	0.974 (0.405)
Medium stay: 1-3 days	245	15.0706± 2.81536	
Long stay: 4-7 days	100	15.1311± 2.33441	
Very long stay: >7 days	20	16.1450± 3.22873	

P-value significant<0.05, RDW: Red cell distribution width, ANOVA: Analysis of variance

Table 5 - Area under the curve (AUC) for diagnostic differentiation between RDW,NLR,PLR in relation to length of hospital stay.

Variables	Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
				Lower bound	Upper bound
RDW	0.555	0.035	0.087	0.487	0.623
NLR	0.553	0.032	0.099	0.490	0.616
PLR	0.664	0.030	0.000	0.606	0.723

RDW: red cell distribution width, NLR: neutrophil to lymphocyte ratio, PLR: platelets to lymphocyte ratio, Std: standard deviation, ^aUnder the nonparametric assumption, ^bNull hypothesis: true area=0.5

inflammation, which may influence the course and prognosis of numerous conditions, including bronchial asthma.^{31,32} Our results are in agreement with earlier studies identifying PLR as a predictor of hospitalization risk and asthma exacerbation. Analysis of the predictive performance of PLR for LOS in asthmatic children revealed that PLR most closely aligns with the actual positive rate compared to the NLR and RDW.

In the current cohort of asthma cases, a non-significant association was observed between elevated NLR and RDW with LOS. The connection between high NLR and asthma exacerbation has been extensively documented in several studies.⁸⁻¹⁰ Despite significantly higher NLR levels indicative of increased inflammation, LOS remained unaffected, displaying a lower sensitivity index as indicated by the ROC curve. Similarly, RDW demonstrated a high yet non-significant predictive value for LOS. Generally, T helper 2 cells and eosinophils are crucial in mediating airway inflammation in pediatric asthma.³³ In a subset of severe adult asthma characterized by the presence of neutrophils in the airway, their role in asthma pathogenesis remains uncertain, potentially due to bacterial lung infections and high neuro-steroid use.^{34,35} This uncertainty may account for the lack of significance of NLR in our pediatric cohort.

Study limitations. This study aims to identify the most effective markers among PLR, NLR, and RDW as predictors of hospital stay duration in children with bronchial asthma, providing practical insights. Additionally, it highlights areas for further research to establish reliable predictive biomarkers for bronchial asthma, guiding future investigation in this direction. However, certain limitations and confounders should be considered, including the effects of immunological

factors and drugs on biomarkers, such as assessing the possible influence of systemic steroid use on the studied biomarkers. Due to the retrospective nature of this analysis, these variables cannot be accurately recognized in the current dataset. Furthermore, reliance on PLR and NLR cutoff points derived from previous studies with potentially different settings from our study necessitates caution in interpreting these conclusions.

In conclusion, a high PLR was significantly associated with prolonged hospital stay in asthma patients, while no significant association was observed with NLR and RDW. Further studies are required to confirm this hypothesis.

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