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# Diagnostic potential of neutrophil-to-lymphocyte ratio in pediatric acute appendicitis: A multi-centric study

Warda Tahir[1] - Muhammad Usama Aziz[1] - Rigman Darius Gabriel[2] - Carlo Sturz[3] - Arun Quadros Darian[4] – Luisa Alejandra Morales Argueta[5]

1. Department of Pediatric Surgery University of Child Health Sciences, The Children Hospital Lahore, Pakistan
2. George Emil Palade University of Medicine, Pharmacy, Sciences and Technology, Târgu Mureș, Romania
3. Albert Ludiwgs Universität Freiburg, Faculty of Medicine, Freiburg, Germany
4. Universidade de São Caetano do Sul, Brasil
5. Department of Pediatrics, Nombre Clínica Morales Argueta, Guatemala

**Correspondence**
Warda Tahir, Department of Pediatric Surgery University of Child Health Sciences, The Children Hospital Lahore, Pakistan.

**e-mail**
tahir.warda123@gmail.com

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**ORCID ID of the author(s):**
WT: 0000-0002-3420-2036
MUA: 0000-0001-6445-4704
RDG: 0000-0001-5278-2946
CS: 0009-0009-0683-0770
AQD: 0000-0002-1842-6240
LAMA: 0009-0002-1909-998X

## Abstract

**Objective:** In this study, we aimed to investigate the diagnostic value of NLR in pediatric appendicitis.

**Materials and methods:** This retrospective cohort study was undertaken in the pediatric emergency department of our hospital from January 2019 to December 2022. We enrolled patients aged between 5 and 18 years presenting with suspicions of acute appendicitis. Based on their final diagnoses, these patients were divided into two primary groups: Negative appendectomy (Group 1) and positive appendectomy (Group 2).

**Results:** In a comparative study of 290 pediatric patients divided into Group 1 (n=40) and Group 2 (n=250), we explored differences in demographics, presenting symptoms, and blood test results. Both groups had a similar age range (2-18 years) and gender distribution ($p>0.05$ for both age and gender). Abdominal pain, nausea, and vomiting were prevalent symptoms in both groups; however, statistical analysis revealed no significant differences in their presentation ($p>0.05$ for all symptoms). The duration of symptoms and past medical histories were also comparable between the groups ($p>0.05$). Blood test results indicated that Group 2 had significantly higher WBC ($p=0.005$) and neutrophil counts ($p=0.003$), while other parameters like CRP, platelet count, and lymphocyte count showed no significant differences ($p>0.05$ for all). The NLR was identified as a significant discriminator, with Group 2 having a higher value ($p=0.002$). Using an optimal NLR cut-off of 4.1, we achieved a sensitivity of 77% and a specificity of 52% for predicting the diagnosis. The diagnostic utility of NLR was further affirmed by an AUC value of 0.642 in the ROC curve analysis.

**Conclusions:** This study underscores the potential diagnostic value of the NLR in pediatric acute appendicitis. With its cost-effectiveness and easy availability as part of routine blood tests, the NLR could be an invaluable tool in assisting clinical decisions in pediatric acute appendicitis.

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## Abbreviations

- AA: Acute appendicitis
- AUC: Area under curve
- CBC: Complete blood count
- CRP: C-reactive protein
- LYM: Lymphocyte
- NEU: Neutrophil
- NLR: Neutrophil-to-Lymphocyte ratio
- NOM: Non-operative management
- NPV: Negative predictive value
- PLT: Platelet
- PLR: Platelet-to-Lymphocyte ratio
- PPV: Positive predictive value
- ROC: Receiver operating characteristic
- SD: Standard deviation
- US: Ultrasonography
- WBC: White blood count

## Introduction

Acute appendicitis (AA) stands as the leading abdominal surgical emergency encountered in pediatric emergency rooms. Early diagnosis is pivotal, as delays can escalate the chances of advanced appendicitis and even mortality (1,2). Yet, diagnosing AA promptly and accurately can be complex, especially due to challenges in patient communication and the lack of characteristic symptoms. Non-invasive diagnostic criteria often involve various laboratory parameters or evaluation scales for those suspected of AA. Recent studies have highlighted the potential of hematological ratios, such as the NLR or the mean platelet volume-to-lymphocyte ratio, as effective tools for diagnosing appendicitis in children (3-5).

The NLR is a simple laboratory marker that has been explored in various clinical scenarios, ranging from malignancies to cardiovascular diseases, as an indicator of systemic inflammation and stress. The NLR is derived from a routine CBC test – thus making it cost-effective and readily available in most healthcare settings. Its potential role in adult appendicitis has already sparked interest among researchers. Still, its applicability and relevance in the pediatric population remain relatively unexplored (6-8).

In this study, we aimed to investigate the diagnostic value of NLR in pediatric appendicitis.

## Materials and methods

### Patients and group

This retrospective cohort study was undertaken in the pediatric emergency department of our hospital from January 2019 to December 2022. We enrolled patients aged between 5 and 18 years presenting with suspicions of acute appendicitis. Based on their final diagnoses, these patients were divided into two primary groups: Negative appendectomy (Group 1) and positive appendectomy (Group 2). Data collection involved extracting relevant information from electronic medical records. This encompassed demographics, clinical presentations, findings from physical examinations, and notably, laboratory results, with a particular emphasis on the CBC with differential. From this, the NLR was computed by determining the ratio of neutrophils to lymphocytes. Ethical considerations were paramount; the study protocol received approval from the our hospital Ethical Committee.

### Eligibility criteria

The inclusion criteria comprised an age range of 5 to 18 years, clinical suspicion of acute appendicitis anchored in symptoms such as abdominal pain, nausea, vomiting, or right lower quadrant tenderness, and having undergone a CBC test during their hospital visit. We excluded patients with known hematological disorders potentially affecting neutrophil or lymphocyte counts, those with a history of immunosuppressive treatment, those diagnosed with chronic inflammatory conditions like inflammatory bowel disease, those who had undergone prior abdominal surgeries, and instances where medical records were either unavailable or incomplete.

### Statistical analysis

For the statistical analysis phase, we employed SPSS software (version 26). Continuous variables were characterized using mean and SD, while categorical ones were described through frequencies and percentages. We utilized the independent t-test to juxtapose the mean NLR values of the Appendicitis Group against the Non-Appendicitis Group. The diagnostic potency of the NLR in pinpointing pediatric appendicitis was ascertained via ROC curves. The ideal cutoff value for NLR was derived from the maximum Youden's index, and we computed the sensitivity, specificity, PPV, NPV. A p-value below 0.05 was established as the threshold for statistical significance.

## Results

In our study encompassing 290 pediatric patients, 40 were categorized into Group 1 and 250 into Group 2. Delving into the age parameter, both groups presented a patient age range from 2 to 18 years. The mean age for Group 1 was 10.1±3.9, while for Group 2, it was 10.4±4.3 (p>0.05). Group 1 consisted of 55% males (n=22) and 45% females (n=18). On the other hand, Group 2 comprised 55.2% males (n=138) and 44.8% females (n=112) (p>0.05). Abdominal pain was predominant in Group 1, with 95% (n=38), as opposed to 83% (n=207) in Group 2. Nausea was reported by 70% (n=28) of Group 1 and 58% (n=145) of Group 2. Vomiting was experienced by 65% (n=26) in Group 1, while 50% (n=125) of Group 2 reported the same. Notwithstanding these observed variations, statistical analysis conveyed no significant differences in the presenting symptoms between the two groups (p>0.05). In terms of symptom duration, Group 1's patients experienced symptoms for an average of 36 hours (ranging from 12 to 72 hours). In comparison, Group 2's average was marginally more extended at 40 hours, with a range between 8 to 80 hours (p>0.05). Fifteen percent of Group 1 (n=6) had experienced prior similar episodes, while this was true for 10% of Group 2 (n=25). Familial history of appendicitis was reported by 5% in Group 1 (n=2) and 3% in Group 2 (n=7) (p>0.05) (Table 1).

Group 1 exhibited a mean CRP level of 8.11±6.14, whereas Group 2 had a mean value of 14.29±12.93 (p>0.05). The mean WBC count for Group 1 was 11.10±2.97 compared to 14.54±2.54 for Group 2. The difference was statistically significant with a p-value of 0.005. Group 1 demonstrated a mean neutrophil count of 6.81±2.41, while Group 2 showed a mean of 10.38±3.17 (p=0.003). The platelet count averaged at 341±68 for Group 1 and 300±78 for Group 2 (p>0.05). Group 1 had a mean lymphocyte count of 2.11±1.21, in contrast to Group 2, which had a mean count of

**Table 1:** Patients demographic

| | Group 1 (n=40) | Group 2 (n=50) | p-value |
|---|---|---|---|
| **Total patients** | 40 | 250 | |
| **Age** | | | |
| - Range | 2 to 18 years | 2 to 18 years | |
| - Mean±SD | 10.1±3.9 | 10.4±4.3 | >0.05 |
| **Gender distribution** | | | >0.05 |
| - Male (%) | 22 (55%) | 138 (55.2%) | |
| - Female (%) | 18 (45%) | 112 (44.8%) | |
| **Presenting symptoms (%)** | | | >0.05 |
| - Abdominal pain | 38 (95%) | 207 (83%) | |
| - Nausea | 28 (70%) | 145 (58%) | |
| - Vomiting | 26 (65%) | 125 (50%) | |
| **Duration of symptoms** | | | >0.05 |
| - Mean (hours) | 36 | 40 | |
| - Range (hours) | 12-72 | 8-80 | |
| **Past medical history (%)** | | | >0.05 |
| - Prior similar episodes | 6 (15%) | 25 (10%) | |
| - Familial history of appendicitis | 2 (5%) | 7 (3%) | |
| - Other significant histories | 2 (5%) | 12 (5%) | |

* SD: Standart deviation

**Table 2:** Comparison of the blood test results

| | Group 1 (n=40) | Group 2 (n=250) | p-value |
|---|---|---|---|
| CRP | 8.11±6.14 | 14.29±12.93 | >0.05 |
| WBC | 11.10±2.97 | 14.54±2.54 | **0.005** |
| NEU | 6.81±2.41 | 10.38±3.17 | 0.003 |
| PLT | 341±68 | 300±78 | >0.05 |
| LYM | 2.11±1.21 | 3.79±3.51 | >0.05 |
| NLR | 2.26±0.74 | 5.14±1.45 | **0.002** |
| PLR | 107±43 | 135±78 | >0.05 |

* CRP: C-reactive protein; WBC: White blood count; NEU: Neutrophil; LYM: Lymphocyte; PLT: Platelet; NLR: Neutrophil-to-Lymphocyte ratio; PLR: Platelet-to-Lymphocyte ratio.

**Table 3:** Cut-off value and test result

| | NLR |
|---|---|
| **Cut-off** | 4.1 |
| **Sensitivity (%)** | 77% |
| **Spesificity (%)** | 52% |
| **PPV (%)** | 75% |
| **NPV (%)** | 56% |
| **AUC** | 0.642 |

* PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area under curve

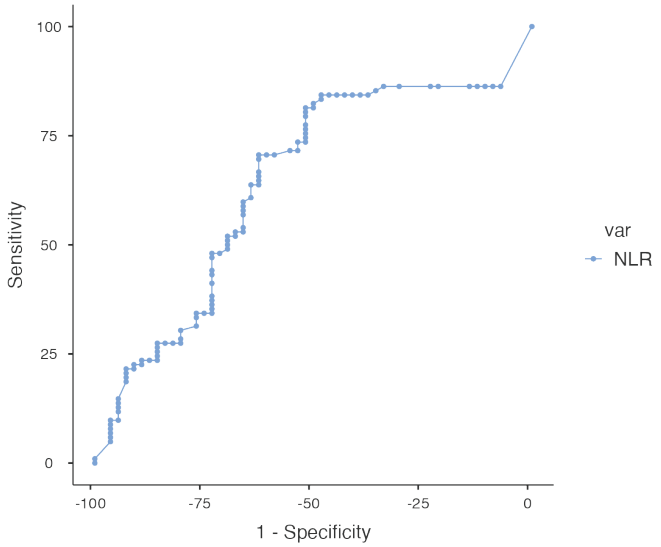


*Figure 1: ROC curve of NLR*

3.79±3.51. The difference between the two groups was not statistically significant (p>0.05). The NLR for Group 1 was 2.26±0.74, whereas for Group 2, it was 5.14±1.45. The observed difference was statistically significant with a p-value of 0.002. Group 1 presented with a mean PLR of 107±43, while Group 2 exhibited a mean of 135±78 (p>0.05) (Table 2).

The optimal cut-off value for NLR, determined to maximize both sensitivity and specificity, was identified as 4.1. At this cut-off: The sensitivity of the NLR in predicting the diagnosis was 77%. The specificity stood at 52%. The PPV, which represents the probability that subjects with a positive screening test truly have the condition, was calculated to be 75%. The NPV, illustrating the probability that subjects with a negative screening test genuinely do not have the condition, was noted at 56%. Furthermore, the ROC curve, a tool that assesses the diagnostic ability of a binary classifier, yielded an AUC value of 0.642 (Table 3 and Figure 1).

## Discussion

Acute appendicitis remains a significant diagnostic challenge, especially in the pediatric population where symptom presentation can be ambiguous. Although numerous non-invasive diagnostic tools are currently in place to assist in identifying AA, there is an ongoing quest for a readily accessible and reliable marker. In this context, our study explored the diagnostic potential of NLR in pediatric AA (1-5).

Our study provided evidence that the NLR might serve as an essential diagnostic indicator in distinguishing between negative and positive appendectomy cases in children. Although both groups in our study had comparable demographics, clinical presentations, and duration of symptoms, we found a statistically significant difference in their NLR values. This distinction supports the notion of NLR as an indicator of systemic inflammation and stress, as elucidated in the literature for other clinical conditions, ranging from malignancies to cardiovascular diseases (6,7).

Ultrasonography (US) is a quick and safe method that doesn't necessitate IV access, contrast use, or radiation exposure (8,9). A comprehensive review by Doria et al. (10) encompassing 7,448 patients, revealed US's accuracy at 88% sensitivity and 94% specificity. However, it's widely understood that the efficacy of US varies with the operator. While some reports state an appendiceal diameter of 9 cm using US, others suggest that non-operative management (NOM) might be feasible even in complex appendicitis cases when the physical check-up doesn't show complications. A review by Fugazzola et al. (11) indicated that NOM had a success rate of about 90%. The dilemma remains regarding the appropriate treatment for patients with concerning physical findings but inconclusive US results.

For many years, the hallmark diagnostic criterion for acute appendicitis has been an elevated WBC count dominated by neutrophils. However, recently, easily obtainable and inexpensive indicators like NLR and PLR have gained prominence. Zouari et al. (12) assessed 102 consecutive pediatric patients post-appendectomy, differentiating between those with acute appendicitis and those without. They found that a CRP level of ≥ 10 mg/L upon admission and a leukocyte count of ≥ 16,100/mL were indicators of pediatric acute appendicitis. In another study, Çelik and colleagues identified threshold values for NLR and PLR when distinguishing between simple and complex acute appendicitis (13). A Korean meta-analysis, involving 19 studies and 5,974 pediatric patients, found the NLR had 82% sensitivity and 86% specificity, with an AUC of 0.86 (14).

In the realm of clinical diagnosis, the quest to determine benchmark values for key indicators remains one of the most pivotal endeavors. This study, in line with several predecessors, dives into the depths of evaluating markers such as WBC, neutrophil counts, CRP, NLR, and PLR, specifically focusing on pediatric appendicitis. The imperative nature of this task emerges from the very inconsistency it seeks to address. Numerous research works have indeed reported varying benchmark values, a variability that can be primarily attributed to the different patient populations being studied (13). Such findings prompt a pivotal discourse on the implications of these discrepancies and the way forward.

First and foremost, it is vital to appreciate the inherent heterogeneity among patient populations. Factors like genetic predispositions, environmental exposures, dietary habits, and even sociocultural practices can significantly influence health indicators (14-16). When these factors differ across populations, it is almost a given that the readings of indicators such as NLR or WBC might vary. This means that a benchmark value determined from one population might not be universally applicable, underscoring the need for context-specific evaluations.

Our study revealed that the optimal cut-off value for NLR, which balances both sensitivity and specificity, stands at 4.1. At this juncture, the sensitivity and specificity were 77% and 52%, respectively. The PPV was 75%, emphasizing that a significant majority of those testing positive would genuinely have the condition. The NPV was 56%, indicating a somewhat balanced probability for those with a negative test. However, the ROC curve's AUC value of 0.642 presents a modest predictive power.

While our study provides a valuable insight into the diagnostic potential of NLR in pediatric acute appendicitis, there are limitations that need acknowledgment. Primarily, this was a retrospective analysis, thus inherently predisposed to biases related to data recording and selection. Although we ensured stringent eligibility criteria to minimize inconsistencies, there's an unavoidable margin of error, especially in a retrospective design. The sample size, though substantial, might not entirely capture the nuances of a larger, more varied pediatric population. Also, our study did not investigate the potential effects of other inflammatory markers concurrently with NLR, which might offer a more comprehensive diagnostic picture. Lastly, it's paramount to note that the NLR, while indicative, cannot and should not override clinical acumen; the ultimate diagnosis should encompass a holistic evaluation combining laboratory results, clinical signs, and imaging findings.

## Conclusions

Our retrospective cohort study underscores the potential diagnostic value of the NLR in pediatric acute appendicitis. With its cost-effectiveness and easy availability as part of routine blood tests, the NLR could be an invaluable tool in assisting clinical decisions in pediatric acute appendicitis. Further prospective studies are warranted to confirm its utility.

## Conflict of interest

The authors report no conflict of interest.


## Funding source

No funding was required.


## Ethical approval

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki). The authors declare that they have followed the protocols of their work center on the publication of patient data.

## Informed consent

Written informed consent was obtained from all individual participants and/or their gaurdians.


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No


## Peer-review

Externally. Evaluated by independent reviewers working in at least two different institutions appointed by the field editor.

## Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Contributions

Research concept and design: **RDG, CS, AQD, LAMA**

Data analysis and interpretation: **RDG, CS, AQD, LAMA**

Collection and/or assembly of data: **CS, AQD, LAMA**

Writing the article: **WT, MUA, RDG, AQD**

Critical revision of the article: **WT, MUA, RDG, CS, AQD, LAMA**

Final approval of the article: **WT, MUA, RDG, LAMA**

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