

Sensitivity and specificity of neutrophil-to-lymphocyte ratio in pediatric patients with acute complicated appendicitis

Sensibilidad y especificidad de la relación neutrófilos a linfocitos en pacientes pediátricos con apendicitis aguda complicada

Manuel Gil-Vargas^{1*}, Ivonne Cruz-Peña², and Mary S. Saavedra-Pacheco³

¹Pediatric Surgery Service, "Eduardo Vazquez Navarro" General Hospital of Puebla; ²Pediatric Service, General Hospital of Puebla "Eduardo Vazquez Navarro"; ³Faculty of Medicine, Meritorious Autonomous University of Puebla. Puebla, Mexico

Abstract

Objective: Establish the sensibility and specificity of the neutrophil-lymphocyte rate (NLR) in pediatric patients with acute complicated appendicitis. **Method:** Cross-sectional, observational, descriptive, and retrospective study. Patients between 4 to 16 years old with diagnosis of acute appendicitis, who had appendectomy, from December 2017 to January 2019 were selected. We calculated the NLR in every patient. To analyze the variables, we used the test of Mann-Whitney and we value the sensibility and specificity of the NLR. **Results:** There were 245 patients, 81 with simple appendicitis and 144 with complicated appendicitis. Just 27 of them were laparoscopic appendectomy. The NLR had a media of 10.48 in simple appendicitis, and 13.03 in complicated ones, with a p value of 0.02. The area under the curve was 0.622. There was a rate of 8.2 in complicated appendicitis to the NLR. **Conclusions:** The NLR has been poorly studied in pediatric patients with acute appendicitis. In this study the NLR had a significant value in the patients with acute complicated appendicitis, with medium sensibility and a relatively low specificity.

Keywords: Neutrophil-lymphocyte rate. Appendicitis. Children. Appendectomy.

Resumen

Objetivo: Establecer la sensibilidad y especificidad de la tasa de neutrófilos-linfocitos (NLR) en pacientes pediátricos con apendicitis aguda complicada. **Método:** Estudio transversal, observacional, descriptivo y retrospectivo de pacientes pediátricos de 4 a 16 años con diagnóstico de apendicitis aguda, a los que se les realizó apendicectomía, desde diciembre de 2017 hasta enero de 2019. Se calculó el INL en cada paciente. Para analizar las variables utilizamos el test de Mann-Whitney y valoramos la sensibilidad y especificidad del NLR. **Resultados:** Hubo 245 pacientes, 81 con apendicitis simple y 144 con apendicitis complicada. Solo 27 de ellos fueron apendicectomía laparoscópica. El NLR tuvo una media de 10.48 en apendicitis simple y de 13.03 en complicadas, con un valor de p de 0.02. El área bajo la curva fue de 0.622. Hubo una tasa de 8.2 en apendicitis complicada a la NLR. **Conclusiones:** El INL ha sido poco estudiado en pacientes pediátricos con apendicitis aguda. En este estudio el NLR tuvo un valor significativo en los pacientes con apendicitis aguda complicada, con una sensibilidad media y una especificidad relativamente baja.

Palabras clave: Tasa de neutrófilos-linfocitos. Apendicitis. Niños. Apendicectomía.

*Correspondence:

Manuel Gil-Vargas

E-mail: gilvm@yahoo.com

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Introduction

Acute appendicitis is the most common surgical emergency in childhood¹. In most cases its diagnosis depends on the patient's symptoms, but in pediatric patients it is difficult to distinguish appendicitis from other conditions. Only 10 to 36% of pediatric patients will present the classic symptoms of an appendiceal condition, unlike adults, who present it in 60-70%^{2,3}. Hence the importance of using diagnostic aids for timely treatment.

The neutrophil/lymphocyte (NLR) rate has been reported as a useful adjunct in predicting the severity of appendicitis, postoperative complications, and length of stay. It is a marker of inflammation, which results from dividing the absolute number of neutrophils by the absolute number of lymphocytes. NLR can be useful for diagnosis and prognosis in various inflammatory pathologies⁴. Some publications report that NLR is related to severe bacterial infection and systemic inflammatory response⁵. There are few studies in the pediatric population that analyze the utility of the NLR in the diagnosis of acute appendicitis⁶.

Acute appendicitis is the leading cause of acute surgical abdomen in children. Timely detection of an appendiceal condition leads to the reduction of numerous complications, such as surgical site infection, appendiceal perforation, appendiceal abscess, generalized peritonitis, adhesions, and sepsis; in addition, it reduces mortality and hospital stay, and therefore avoids high hospital costs.

The main objective of this study was to determine the sensibility and specificity of the NLR in pediatric patients with complicated acute appendicitis.

Method

A cross-sectional, observational, descriptive and retrospective study was carried out. Data was collected from pediatric patients operated on for appendectomy from January 2017 to December 2019. The clinical records of patients between 4 and 16 years of age treated at the Hospital General Zona Sur de Puebla Eduardo Vázquez Navarro with the main diagnosis of acute appendicitis were included. Incomplete clinical records, patients with surgical intervention in another unit and patients with prophylactic appendectomy were excluded. The clinical records of the patients operated on for appendectomy who were transferred to another unit in the postoperative period were eliminated.

The following variables were recorded: age, sex, leukocyte count, absolute neutrophil count, absolute lymphocyte count, NLR, surgical approach for appendectomy, type of appendicitis, and days of hospital stay. The blood count was taken as a reference at the patient's admission and the NLR was calculated by dividing the absolute number of neutrophils by the absolute number of lymphocytes in each patient.

Uncomplicated appendicitis is one that does not have perforation data. Acute perforated appendicitis, with or without localized abscess, or with purulent peritonitis were considered complicated.

The sample was conventional, being the number of cases that presented in this hospital unit during the study period.

A data collection sheet was prepared, the information was concentrated in the *software* Microsoft Excel version 2013 and the data was analyzed with the *software* IBM SPSS Statistic, version 25.

In the statistical analysis, continuous variables were expressed as mean and standard deviation. For the normally distributed continuous variables, the Student's t-test of independent samples was used, and the Mann-Whitney test was used to analyze the non-normally distributed continuous data. Statistical significance was established at $p < 0.05$.

Sensibility and specificity for the diagnosis of complicated acute appendicitis were determined using ROC curves (*Receiver Operating Characteristic*). The maximum diagnostic precision cut-off point for each analytical parameter was also calculated using the Youden index.

This study was approved by the research ethics committee of the Eduardo Vázquez Navarro General Hospital.

Results

295 clinical records of pediatric patients diagnosed with acute appendicitis were analyzed and 70 were excluded due to incomplete data, resulting in a sample of 225 clinical records: 81 with a transoperative diagnosis of simple acute appendicitis and 144 with a diagnosis of complicated acute appendicitis (Fig. 1). Of the clinical records of patients with simple acute appendicitis, 51 were male and 30 female, with a mean age of 11 years (standard deviation [SD]: ± 3). Of the records of patients with complicated acute appendicitis, 94 were male and 50 female, with a mean age of 10 years (SD: ± 4).

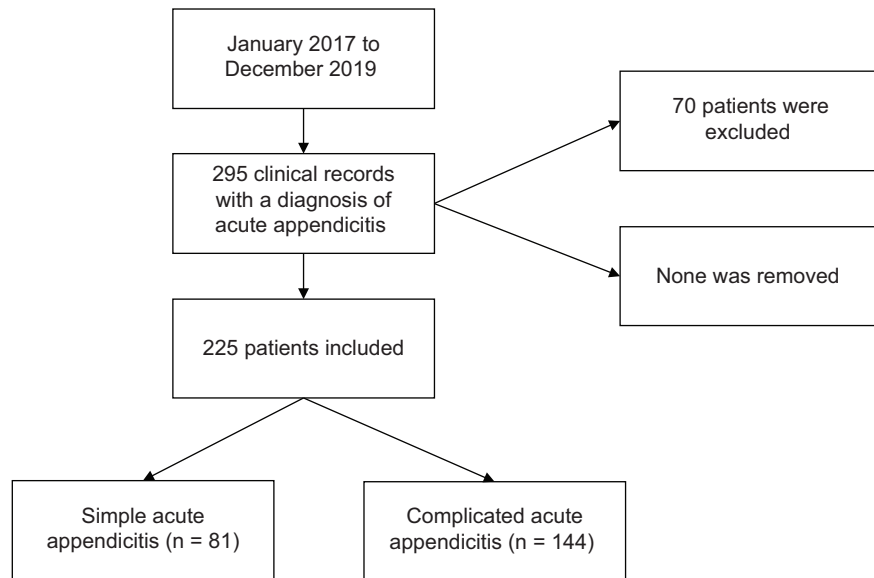


Figure 1. Flowchart of the patients included in the study.

Table 1. Analytical variables studied

Variable	Simple appendicitis (n = 81)			Complicated appendicitis (n = 144)			
	Mean	OF	Range	Mean	OF	Range	p
Leukocytes	14636	5406	1344-1583	16886	5.117	1604-1772	0.02*
Neutrophils	12066	5010	1095-1317	14118	4.604	1336-1487	0.02*
Lymphocytes	1638	863	1447-1829	1442	818	1307-1577	0.062 [†]
Bands	2.23	2.55	1.67-2.80	3.77	4.11	3.09-4.45	0.07 [†]
Hospital stay	2.36	1.34	2.06-2.66	4.31	2.25	3.94-4.68	0 [†]

SD: standard deviation.

*Student's t-test for independent samples.

[†]Mann-Whitney U test.

Regarding the surgical approach to appendectomy, the technique was open in 198 patients (71 with simple acute appendicitis and 127 with complicated acute appendicitis) and laparoscopic in 27 patients (10 with simple acute appendicitis and 17 with complicated acute appendicitis).

In patients with simple appendicitis, the NLR resulted in a mean of 10.48 (SD: ± 8.4) and a range of 8.6-12.36, while in patients with complicated appendicitis the mean was 13.03 (OF: ± 10.24) and the range was 11.34-14.72 ($p = 0.02$). Table 1 shows the other variables studied.

The NLR in patients with complicated appendicitis had an area under the curve (AUC) of 0.622 and a 95% confidence interval (95%CI) of 0.542-0.702, considering its cut-off point at 8.2, with a sensitivity of

70% and a specificity of 46% ($p = 0.02$). For neutrophils, an AUC of 0.621 (95%CI: 0.545-0.697), with a cut-off point of 17.390, with a sensitivity of 25% and a specificity of 99% ($p = 0.03$). For leukocytes, an AUC of 0.12 (95%CI: 0.536-0.688), with a cut-off point of 19.785, with a sensitivity of 27% and a specificity of 99% ($p = 0.05$) (Table 2 and Fig. 2).

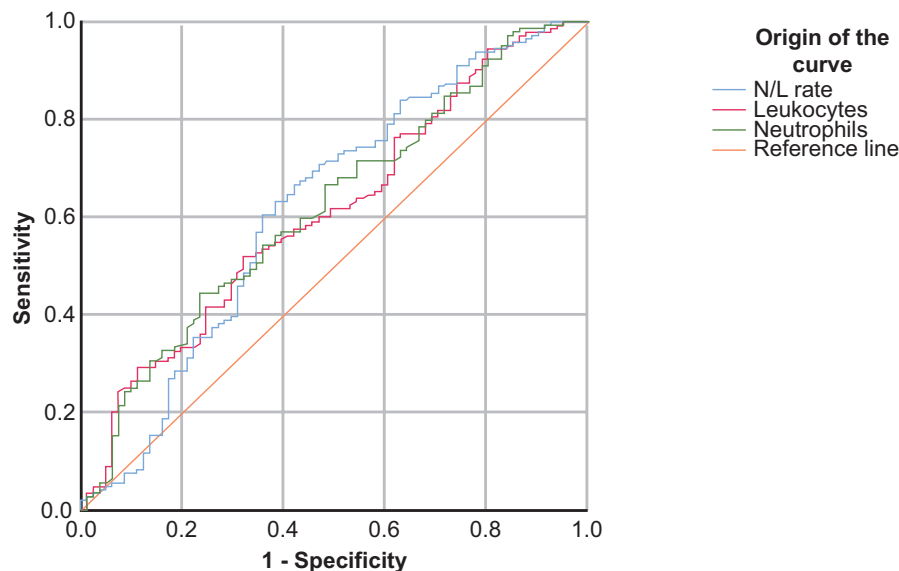
Discussion

The NLR is a marker of systemic inflammation that may be suitable for predicting the severity of cardiovascular, oncological, and infectious diseases. This index is also valuable at the time of diagnosis of acute appendicitis.

Table 2. ROC area under the curve for the diagnosis of complicated appendicitis

Complicated appendicitis	AUC	95%CI	Cut-off point	Sensibility (%)	Specificity (%)	p
Neutrophil-lymphocyte rate	0.622	0.542-0.702	8.2	70	46	0.02
Neutrophils	0.621	0.545-0.697	17.390	25	99	0.03
Leukocytes	0.12	0.536-0.688	19.785	27	99	0.05

AUC: area under the curve; 95% CI: 95% confidence interval.

**Figure 2. ROC curve for the diagnosis of complicating acute appendicitis.**

The objective was achieved by determining the sensitivity and specificity of the NLR in pediatric patients with complicated acute appendicitis. In our sample, more than 50% of the patients presented this diagnosis and it is important to highlight that their NLR had a high cut-off point and intermediate diagnostic sensitivity.

There are reports that NLR is a promising marker that can predict both the diagnosis and severity of appendicitis, with acceptable sensitivity and specificity, potentially facilitating decision-making when having pediatric patients diagnosed with acute appendicitis, giving them priority to perform your emergency surgical treatment⁷.

Yazici et al.⁸ published a study with 240 patients aged 3 to 16 years, which they divided into two groups: the first, 183 patients diagnosed with acute appendicitis, and the second, 57 patients with non-specific abdominal pain. They found an NLR of 3.5 as the cut-off point for patients with acute appendicitis, with a

specificity of 88% and a sensitivity of 90%. The association with complicated appendicitis was not analyzed in this study.

Tuncer et al.⁹ reported in their study the great utility of the NLR to differentiate pediatric patients with acute appendicitis from patients with familial Mediterranean fever or mesenteric lymphadenitis. However, they do not specifically associate complicated appendicitis either.

Yilmaz et al.¹⁰ reported similar data in a descriptive and retrospective study, in patients under 18 years of age, with a mean age of 11.35 years, who investigated in two groups: one of 628 patients with acute appendicitis and treated with appendectomy, and another with other abdominal pathologies. In the first group, the AUC results were 0.694 for the NLR, with a cut-off value of 3.5, with a sensitivity of 84.2% and a specificity of 56.7% ($p = 0.008$). They also evaluated the NLR as a predictor in the diagnosis of acute appendicitis in the pediatric population.

Delgado et al.⁶ evaluated the analytical parameters of the complete blood count in children between 5 and 16 years of age diagnosed with peritonitis secondary to complicated acute appendicitis, and found the NLR with an AUC of 0.783, a cut-off point of 8.3, a sensitivity of 75%, and a specificity of 72.2%. The NLR does not have fixed values, but depends on the pathology under study and the patient's clinical evolution, and therefore modifies the sensitivity and specificity, with this value being higher in patients with complicated acute appendicitis.

Nazik et al.¹¹ conducted a study in which they assessed the relationship between appendicitis and different markers, one of them NLR. They included 63 pediatric patients: 30 with appendicitis and 33 controls. They reported that the group of patients with appendicitis obtained a significantly higher NLR than the healthy patients.

Godínez et al.⁵ published a retrospective study in young adult patients, with a mean age of 36.4 years, in which they compared NLR with other biomarkers, as well as with severity scales. The severity of the pathology related to complicated acute appendicitis was determined, with an NLR cut-off point of 12, related to generalized peritonitis and perforated appendicitis, with a sensitivity of 86%, a specificity of 68%, and an AUC of 0.756 ($p = 0.023$). This study concludes that the NLR can be used to identify those patients with a higher risk of complications and, therefore, those cases that require closer postoperative monitoring.

Ozaydin et al.¹² point out that NLR is a relatively new marker that is associated with poor survival in many diseases. The authors evaluated 154 patients between the ages of 18 and 65 (mean: 34.2 years) in two groups: with complicated acute appendicitis and with uncomplicated appendicitis. In the first group, they obtained an NLR AUC of 0.856, with a cut-off value of 7.3, a sensitivity of 75.8%, and a specificity of 81.8%. On the other hand, Çelik et al.¹³ analyzed pediatric patients in two groups, with complicated and uncomplicated acute appendicitis, and obtained an AUC of 0.717, a sensitivity of 61.1%, and a specificity of 73.2% for differentiating complicated appendicitis.

The results of the previously mentioned studies are similar to those obtained in ours; however, most have not evaluated pediatric patients with complicated acute appendicitis and in Mexico we found no studies conducted in the pediatric population. We invite other researchers to carry out more studies related to this approach to increase the evidence, and we propose that it be applied in clinical practice.

Conclusions

In some cases, the patient's symptoms are not enough to establish the diagnosis of appendicitis and it is necessary to resort to other diagnostic tools. In this study the NLR had a significant value in the patients with acute complicated appendicitis, with medium sensibility and a relatively low specificity. Applying this index in clinical practice can support early diagnosis in patients with appendicitis and provide timely surgical treatment.

We propose that the cut-off point obtained for the NLR be taken into consideration, since together with a high clinical suspicion of acute appendicitis it can help to reduce surgical examinations with negative appendicitis, days of hospital stay and complications in pediatric patients with appendiceal symptoms.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments were carried out on humans or animals for this research.

Data confidentiality. The authors declare that no patient data appears in this article.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

References

1. Kohan R, Zavala B, Zavala P, Vera O, Schonhaut B. Acute appendicitis in the child. *Rev Chil Ped.* 2012;83:474-81.
2. Mendoza MR, Alonso MF. Appendicitis in pediatric ages. *Cir Gen.* 2005;27:238-44.
3. Alvarado A. How to improve the clinical diagnosis of acute appendicitis in resource limited settings. *World J Emerg Surg.* 2016;11:1-4.
4. Seclén HD, Perales CLFA, Díaz VC. Diagnostic value of the neutrophil-lymphocyte ratio to identify complicated acute appendicitis. *Magazine of the Medical Corps.* 2018;11:81-7.
5. Godínez VA, Sashida MH, Cruz RC, Bandeh MH, Gutiérrez BC, Gracida MN. Comparison of the neutrophil-to-lymphocyte ratio, SOFA score and serum procalcitonin as biomarkers of acute appendicitis. *Cir Cir.* 2019;87:12-7.
6. Delgado MC, Muñoz SA, Barrena DS, Núñez C V, Estefanía K, Velayos M. Neutrophil-lymphocyte index as a predictor of peritonitis in acute appendicitis in children. *Cir Ped.* 2019;32:185-9.
7. Hajibandeh S, Hobbs N, Mansour M. Neutrophil-to-lymphocyte ratio predicts acute appendicitis and distinguishes between complicated and uncomplicated appendicitis: a systematic review and meta-analysis. *Am J Surg.* 2020;219:154-63.

8. Yazici M, Ozkisacik S, Oztan MO, Gürsoy H. Neutrophil/lymphocyte ratio in the diagnosis of childhood appendicitis. *Turkish J Pediatr.* 2010;52:400-3.
9. Tuncer AA, Cavus S, Balcioglu A, Silay S, Demiralp I, Calkan E et al. Can mean platelet volume, neutrophil-to-lymphocyte, lymphocyte-to-monocyte, platelet-to-lymphocyte ratios be favourable predictors for the differential diagnosis of appendicitis? *J Pak Med Assoc.* 2019;69:647-53.
10. Yilmaz B, Acar Y. Investigation of the diagnostic value of neutrophil to lymphocyte ratio in pediatric appendicitis cases. *Iran J Pediatr.* 2017;27:e9593.
11. Nazik S, Avcı V, Kiraz ZK. İskemi Modifiye Albümin Ve Diğer Enflamatuvar Belirteçlerin Çocuk Apandisit Tanısındaki Yeri. *Ulus Travma ve Acil Cerrahi Derg.* 2017;23:317-21.
12. Özaydin V, Dogruyol S, Bagdigen S, Katipoglu B, Gul M. Does neutrophil lymphocyte ratio have a clinical value to determine the seriousness of the acute appendicitis cases? *Eurasian J Emerg Med.* 2017;19:6-9.
13. Çelik B, Nałçacıoğlu H, Özçatal M, Torun YA. Role of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in identifying complicated appendicitis in the pediatric emergency department. *Ulus Travma ve Acil Cerrahi Derg.* 2019;25:222-8.