The Predictive Value of Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratio for Diagnosis of Acute Appendicitis and Distinguishing Between Complicated and Uncomplicated Appendicitis at King Abdul-Aziz Medical City-Jeddah

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Abstract: Background: The study aimed to evaluate the predictive value of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in diagnosing acute appendicitis and distinguishing between complicated and uncomplicated cases at King Abdul-Aziz Medical City-Jeddah.

Methods: This retrospective cohort study reviewed data from adult patients who underwent appendectomy between 2018 and 2023. Data were collected from electronic medical records and included demographic information, clinical presentation, laboratory results (including NLR, PLR, CRP, and total bilirubin levels), surgical history, and histopathological findings. Statistical analysis involved descriptive statistics, Chi-squared test ($\chi 2$), and Mann-Whitney tests to compare variables between groups, with significance set at $p < 0.05$.

Results: The study included 387 participants with a mean age of 33.4 ± 12.78 years, ranging from 18 to 98 years. The cohort was predominantly male (223 males, 57.6%). The most common clinical sign was right lower quadrant tenderness (332 participants, 85.8%). Blood tests showed a mean total bilirubin level of 14.88 ± 10.82, mean WBC 12.73 ± 5.49 with mean neutrophil 9.18 ± 4.05. Mean platelet count was 287.96 ± 118.05. The mean NLR was 6.65 ± 5.87, and the mean PLR was 186.86 ± 115.67. NLR and PLR were significantly higher among complicated appendicitis with ($p=<0.01$) and ($p=<0.05$) respectively. Approximately half of the participants had a modified Alvarado score of 4-6 (49.1%). Most patients (359, 92.8%) underwent laparoscopic appendectomy. The majority of hospital stays were under one week (368 participants, 95.1%). Complications were reported in 16 participants, including infections (7 cases), perforation (1 case), bleeding (1 case), abdominal collection (3 cases), pelvic collection and abscess (2 cases), ileus (1 case), sepsis and pulmonary embolism (1 case).

Conclusion: NLR and PLR demonstrated a significant relationship and effectively differentiate between complicated and

uncomplicated appendicitis. However, further studies are still needed to refine diagnostic tools for appendicitis.

1. Introduction

Notable as the principal cause of abrupt abdominal pain, acute appendicitis (AA) is classified as a surgical emergency [1]. Due to the high degree of overlap between the symptoms of AA and other acute abdominal diseases, making a correct diagnosis is a formidable challenge for surgeons [1]. Radiological tests are reserved for rare cases and used as an adjunct to clinical signs for diagnosing acute appendicitis. The worst outcomes, including perforation, which may cause significant morbidity and, in extreme instances, death, can result from acute appendicitis being detected too late [2].

A number of evaluation instruments have been developed to facilitate the diagnosis of acute appendicitis, including the RIPASA score [4] and the Alvarado score [3]. Present grading methods are not sensitive enough or detailed enough to reliably differentiate between basic and complicated appendicitis cases [5]. Also, studies have shown that scoring systems are just as good, if not better, than an increased white blood cell (WBC) count for predicting severity [6]. Apendix perforation may be indicated by elevated blood bilirubin levels [7, 8]. Perforation in patients of acute appendicitis may be more easily detected with elevated C-reactive protein levels, according to research [9]. Numerous studies continue to be interested in finding a dependable indication or tool that may properly predict the diagnosis of acute appendicitis and differentiate between simple and complex cases [2].

From differential white blood cell counts (WBC), the neutrophil-to-lymphocyte ratio (NLR) arises as an easy-to-understand and inexpensive indicator of inflammation. Because it sheds light on separate immunological and inflammatory mechanisms, NLR shows promise as a tool for appendicitis prediction and severity assessment [10].

This study aimed to evaluate the prognostic relevance of the neutrophil-to-lymphocyte ratio (NLR) and/or the platelet-to-lymphocyte ratio (PLR) in patients presenting with symptoms suggestive of acute appendicitis and assess their ability to differentiate between uncomplicated and severe cases. Specifically, the objectives were to evaluate the efficacy of NLR and/or PLR in diagnosing acute appendicitis and to determine their effectiveness in distinguishing between complicated and uncomplicated appendicitis. Additionally, the study sought to establish appropriate cut-off values for NLR and/or PLR in relation to appendicitis severity and to compare the diagnostic accuracy of total bilirubin and C-reactive protein (CRP) with that of NLR and PLR.

2. Methods

Study Design

This study was an observational retrospective cohort study conducted over a period of six years, from 2018 to 2023. The proposal was submitted to the King Abdullah International Medical Research Center (KAIMRC) for approval.

Study Setting

The study was performed at King Abdul-Aziz Medical City-Jeddah, a major healthcare facility providing Urgent and Emergent care.

Population

All individuals aged 18 years and above who underwent appendicectomy (either laparoscopic or open) at King Abdul-Aziz Medical City-Jeddah between 2018 and 2023 were included.

Sample and Sampling technique

The study included all eligible patients who met the inclusion criteria, employing a nonprobability consecutive sampling technique. The inclusion criteria consist of adults aged 18 years and older who underwent appendicectomy and confirmed Acute Appendicitis by histopathology finding, while exclusion criteria were cases of appendicular neoplasm.

Data Collection

Data were obtained retrospectively from the medical records. A data sheet was used to extract demographic data, clinical presentation, laboratory findings, operative history, type of surgery (laparoscopic/open), and histopathological findings.

Instruments

The primary instruments for data collection were the electronic medical records, which were reviewed to fill out a structured data sheet. This sheet captured essential variables such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), total bilirubin, and C-reactive protein (CRP) levels.

Statistical Analysis

Microsoft Excel has been used for data entry and analyzed using SPSS version 26. To investigate the association between the variables, the Chi-squared test ($\chi 2$) was applied to qualitative data that was expressed as numbers and percentages. The association between the quantitative non-parametric variables that were expressed as mean and standard deviation (Mean ± SD) was examined using the Mann Whitney test. A p-value of less than 0.05 was considered statistically significant.

Ethical Consideration

Ethical approval was sought from the King Abdullah International Medical Research Center (KAIMRC). Patient confidentiality and data privacy were maintained throughout the study, and only de-identified data were used in the analysis.

3. Results

The study included 387 participants. The mean age among study participants was 33.4 + 12.78. Age ranged from 18 to 98 years. More than half of study participants were males (n= 223, 57.6%). All study participants had a definitive diagnosis of acute appendicitis. The most common clinical presentation was tenderness in right lower quadrant (85.8%), migratory right lower quadrant pain (77.8%) and nausea or vomiting (72.1%). Almost half of patients (49.1%) had a Modified Alvarado score of 4-6, 16.8% had complicated appendicitis and the majority (92.8%) underwent a Laparoscopic appendectomy. Most of patients (95.1%) had a length of hospital stay less than one week. Only 16 patients (4.2%) had postoperative complications, with infection the most common (1.8%).

Table 1. Distribution of studied patients according to their demographic characters, surgical and clinical data, length of hospital stay and postoperative complications.

Variable	No. (%)
Age (Mean ± SD) (years)	33.4 ± 12.78
Gender	
Female	164 (42.4)
Male	223 (57.6)
Clinical Presentation	
Migratory right lower quadrant pain	301 (77.8)
Anorexia	230 (59.4)
Nausea or vomiting	279 (72.1)
Tenderness in right lower quadrant	332 (85.8)
Rebound tenderness in right lower quadrant	232 (59.9)
Fever > 37.5	46 (11.9)
Modified Alvarado score	

0-3	68 (17.6)
4-6	190 (49.1)
≥7	129 (33.3)
Complicated appendicitis	
Complicated (perforated &gangrenous appendicitis)	65 (16.8)
Not complicated	322 (83.2)
Type of surgery	
Laparoscopic appendectomy	359 (92.8)
Open appendectomy	28 (7.2)
Length of hospital stay	
<1 week	368 (95.1)
1-2 weeks	15 (3.9)
>2 weeks	4 (1)
Presence of postoperative complications	
No	371(95.8)
Yes	16 (4.2)
If yes, specify:	
Infection	7 (1.8)
Perforation	1 (0.3)
Bleeding	1 (0.3)
Other	7 (1.8)

The mean and SD values of laboratory results of WBC, Neutrophil, Lymphocyte, NLR, Platelets, PLR, MPV, CRP and Total Bilirubin are illustrated in (Table 2).Based on the NLR and the PLR classification,293 (75.7%) of patients had an abnormal NLR (≥3) and 183 (47.3%) had an abnormal PLR (> 163.27) (Figure 1).

Table 2. Mean and SD of laboratory results

Variable	Mean ± SD
WBC	12.73 ± 5.49
Neutrophil	9.18 ± 4.05
Lymphocyte	1.92 ± 1.22
NLR	6.65 ± 5.87
Platelets	287.95 ± 118.05
PLR	186.86 ± 115.67
MPV	12.6 ± 52.4
CRP	62.91 ± 90.66
Total Bilirubin	14.88 ± 10.82

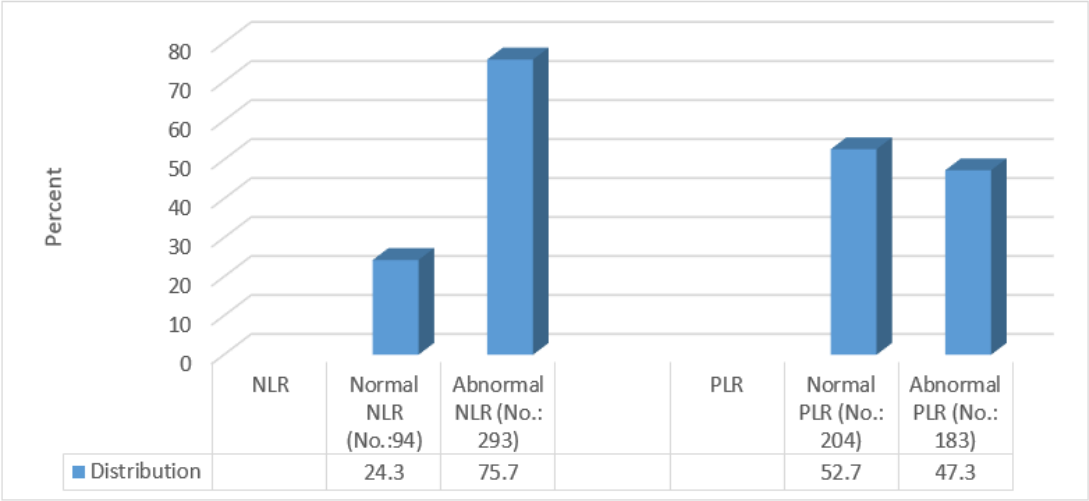

Figure 1. Percentage distribution of NLR and PLR level
N.B.: Normal NLR =less than 3, abnormal NLR = 3 or more, normal PLR = less than 163.27, abnormal PLR = 163.27 or more)

(Table 3, and Figure 2) illustrates that the prevalence of abnormal NLR (≥3) was significantly higher among patients whose clinical presentation was nausea or vomiting, who had Modified Alvarado score of 4-6, and who had an abnormal PLR level (p=<0.05). As for complicated appendicitis, abnormal NLR was significantly higher among patients having complicated appendicitis (20.8% vs. 4.3%) (p=<0.01). On the other hand, despite that a higher prevalence of abnormal NLR (≥3) was present among patients who had postoperative complications, this association was not significant (p=>0.05).

Table 3. Relationship between NLR and patients' demographics, surgical and clinical data, length of hospital stay, postoperative complications and PLR level.

Variable	NLR		χ^2	p-value
	Normal NLR (<3) No. (%)	Abnormal NLR (≥3) No. (%)		
Age (Mean SD) (years)	30.72 ± 9.68	34.26 ± 13.53	1.91*	0.055
Gender				
Female	39 (41.5)	125 (42.7)	0.04	0.841
Male	55 (58.5)	168 (57.3)		
Clinical Presentation				
Migratory right lower quadrant pain	68 (72.3)	233 (79.5)	2.12	0.145
Anorexia	55 (58.5)	175 (59.7)	0.04	0.834
Nausea or vomiting	54 (57.4)	225 (76.8)	13.23	<**0.001**
Tenderness in right lower quadrant	75 (79.8)	257 (87.7)	3.66	0.055
Rebound tenderness in right lower quadrant	52 (55.3)	180 (61.4)	1.1	0.292
Fever > 37.5	9 (9.6)	37 (12.6)	0.97	0.615
Modified Alvarado score				
0-3	23 (24.5)	45 (15.4)	21.54	<**0.001**
4-6	58 (61.7)	132 (45.1)		
≥7	13 (13.8)	116 (39.6)		
Complicated appendicitis				
Complicated	4 (4.3)	61 (20.8)	13.97	<**0.001**
Not complicated	90 (95.7)	232 (79.2)		
Type of surgery				
Laparoscopic appendectomy	93 (98.9)	266 (90.8)	7.04	0.008
Open appendectomy	1 (1.1)	27 (9.2)		
Length of hospital stay				
<1 week	92 (97.9)	276 (94.2)	2.36	0.307
1-2 weeks	2 (2.1)	13 (4.4)		
>2 weeks	0 (0.0)	4 (1.4)		
Presence of postoperative complications				
No	94 (100)	282 (96.2)	3.63	0.057
Yes	0 (0.0)	11 (3.8)		
If yes, specify:				
Infection	0 (0.0)	7 (2.4)	2.28	0.13
Perforation	0 (0.0)	1 (0.3)	0.32	0.571
Bleeding	0 (0.0)	1 (0.3)	0.32	0.571
Other	0 (0.0)	7 (2.4)	2.28	0.13
PLR				
Normal PLR (No.: 204)	78 (83)	126 (43)	45.62	<**0.001**
Abnormal PLR (No.: 183)	16 (17)	167 (57)		

N.B.: * = Mann Whiteney test

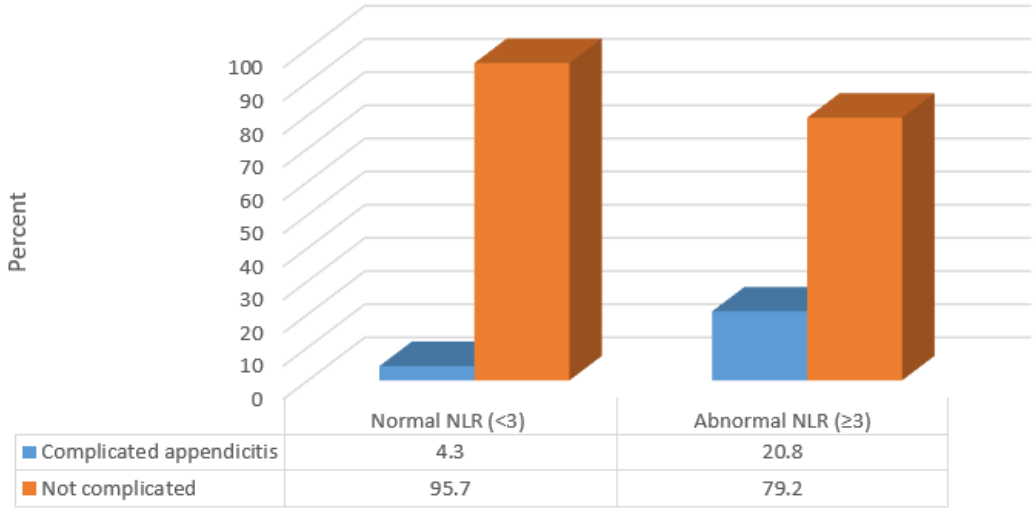

Figure 2. Relationship between NLR and complicated appendicitis.
N.B.: ($\chi 2$ = 13.97, p-value =<0.001)

At the same time, abnormal NLR (≥3) was significantly higher among patients with higher mean WBC, higher mean PLR, and higher mean Total Bilirubin (p=<0.05). On contrary, non-significant relationship was found between NLR and all other mean laboratory results (p=>0.05). (Table 4).

Table 4. Relationship between NLR and mean laboratory results

Variable	NLR		Mann Whitney test	p-value
	Normal NLR (<3) (Mean ± SD)	Abnormal NLR (≥3) (Mean ± SD)		
WBC	11.55 ± 8.12	13.11 ± 4.28	4.73	**<0.001**
Platelets	316.59 ± 197.86	278.76 ± 74.87	1.86	0.062
PLR	124.67 ± 58.51	206.81 ± 122.27	7.86	**<0.001**
MPV	8.79 ± 1.49	13.82 ± 60.19	0.28	0.776
CRP	43.43 ± 56.06	68.8 ± 98.12	0.94	0.347
Total Bilirubin	11.51 ± 7.51	15.85 ± 11.44	3.5	**<0.001**

As for PLR, higher prevalence of abnormal PLR was significantly higher among male patients, whose clinical presentation was nausea or vomiting, rebound tenderness in right lower quadrant or fever > 37.5 (p=<0.05). At the same time, abnormal PLR was significantly higher among patients having complicated appendicitis (22.4% vs. 11.8%) (p=<0.05). Despite that a higher prevalence of abnormal PLR was found among patients who had postoperative complications, this association was not significant (p=>0.05) (Table 5 and Figure 3).

Table 5. Relationship between PLR and patients' demographics, surgical and clinical data, length of hospital stay, postoperative complications and PLR level.

Variable	PLR		$\chi 2$	p-value
	Normal PLR No. (%)	Abnormal PLR No. (%)		
Age (Mean SD) (years)	32.33 ± 11.3	34.6 ± 14.19	1.05*	0.291
Gender				
Female	73 (35.8)	91 (49.7)	7.67	**0.006**
Male	131 (64.2)	92 (50.3)		
Clinical Presentation				
Migratory right lower quadrant pain	160 (78.4)	141 (77)	0.1	0.744
Anorexia	125 (61.3)	105 (57.4)	0.6	0.436

Nausea or vomiting	138 (67.6)	141 (77)	4.23	**0.04**
Tenderness in right lower quadrant	169 (82.8)	163 (89.1)	3.06	0.08
Rebound tenderness in right lower quadrant	112 (54.9)	120 (65.6)	4.57	**0.032**
Fever > 37.5	17 (8.3)	29 (15.8)	6.41	**0.041**
Modified Alvarado score				
0-3	41 (20.1)	27 (14.8)	5.17	0.075
4-6	105 (51.5)	85 (46.4)		
≥7	58 (28.4)	71 (38.8)		
Complicated appendicitis				
Complicated	24 (11.8)	41 (22.4)	7.81	**0.005**
Not complicated	180 (88.2)	142 (77.6)		
Type of surgery				
Laparoscopic appendectomy	193 (94.6)	166 (90.7)	2.18	0.14
Open appendectomy	11 (5.4)	17 (9.3)		
Length of hospital stay				
<1 week	197 (96.6)	171 (93.4)	2.3	0.316
1-2 weeks	6 (2.9)	9 (4.9)		
>2 weeks	1 (0.5)	3 (1.6)		
Presence of postoperative complications				
No	200 (98)	176 (96.2)	1.21	0.271
Yes	4 (2)	7 (3.8)		
If yes, specify:				
Infection	3 (1.5)	4 (2.2)	0.27	0.598
Perforation	1 (0.5)	0 (0.0)	0.89	0.343
Bleeding	1 (0.5)	0 (0.0)	0.89	0.343
Other	2 (1)	5 (2.7)	1.66	0.197

N.B.: * = Mann Whiteney test

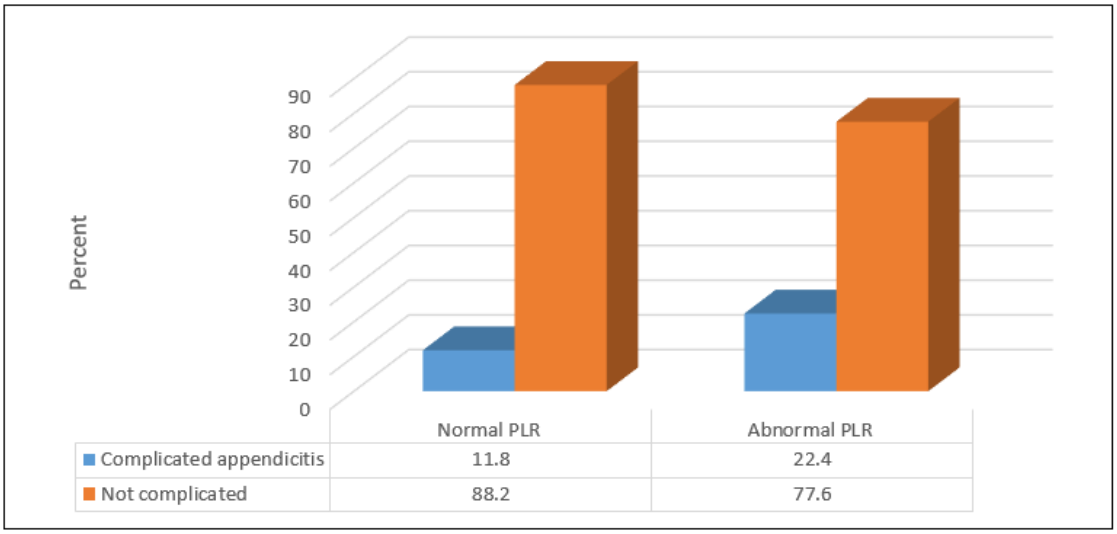

Figure 3. Relationship between PLR and complicated appendicitis.
N.B.: ($\chi 2 = 7.81$, p-value = 0.005)

The presence of abnormal PLR was significantly found among patients with higher mean values of Neutrophil or NLR (p=<0.05). While a non-significant relationship was found between PLR and all other mean laboratory results (p=>0.05) (Table 6).

Table 6. Relationship between PLR and mean laboratory results.

Variable	PLR		Mann Whitney test	p-value
	Normal PLR (Mean ± SD)	Abnormal PLR (Mean ± SD)		
WBC	12.68 ± 6.35	12.78 ± 4.37	1.12	0.259
Neutrophil	8.63 ± 3.86	9.79 ± 4.18	3.11	**0.002**

NLR	3.96 ± 2.34	9.65 ± 7.06	10.3	**<0.001**
MPV	13.63 ± 67.23	11.45 ± 27.92	1.77	0.075
CRP	58.4 ± 86.32	68.65 ± 96.01	0.71	0.475
Total Bilirubin	14.32 ± 8.45	15.53 ± 13.06	0.29	0.769

4. Discussion

The current study highlighted sociodemographic and clinical characteristics of patients with confirmed diagnosis of acute appendicitis as well as spotted light on laboratory work among these patients.

At Saudi Arabia's Aseer Central Hospital, researchers conducted an observational retrospective cohort study. Out of 103 patients included in the research, 50.5% were male and 49.5% were female. The age group with the highest prevalence was 36-45 years, with 56.3% of the patients falling into that category, followed by 18-25 years with 23.3%. Acute appendicitis was diagnosed in every single case. We observed that the means of neutrophils were 68.970%, lymphocytes were 22.067%, and NLR was 5.020. While 31% of cases included complications, 69% were classified as non-complicated appendicitis. There was a statistically significant correlation between NLR and the development of problems (p-value = 0.00001). All of the claims made in the literature review can be firmly backed up by this research. When it comes to detecting acute appendicitis and distinguishing between difficult and simple cases, the NLR shows a remarkable degree of accuracy [11].

There have been a number of published research that touch on the same subject as this one. Sipra et al. performed research in Saudi Arabia in the year 2022. The NLR was greater in children who had acute appendicitis compared to those who were healthy. Two NLR cutoff values were able to rule out acute appendicitis with a sensitivity of 94% and a specificity of 100%. With a high NLR of 3.5, acute appendicitis might be accurately diagnosed. The degree of appendicitis was likewise associated with significantly different NLR levels. Both studies indicated that NLR was an accurate predictor for acute appendicitis, with a high mean of 3.5 in the prior research and 4.5 [12].

It is evident by comparing the present research's findings to those of the prior study conducted by Ayeni et al. that the NLR and PLR ratios in the former study differed significantly ($p = 0.05$, Kruskal-Wallis). Area under the ROC curve (AUC) for uncomplicated appendicitis was 0.741, whereas the cut-off for neutrophil-to-lymphocyte ratio and PLR was 3.80. The AUC was 0.776 and the cut-off was 8.86 in complex appendicitis, when the neutrophil-to-lymphocyte ratio and PLR were used. A prior research indicated a substantial connection between NLR and the incidence of problems (p-value = 0.00001) [13].

In 2020, Hajibandeh et al. determined that a neutrophil-to-lymphocyte ratio of 4.7 was the diagnostic threshold for appendicitis. With an area under the curve (AUC) of 0.96, this cut-off value was shown to have a sensitivity of 88.89% and a specificity of 90.91%. A neutrophil-to-lymphocyte ratio of 8.8 was established as the diagnostic threshold for complicated appendicitis. With an area under the curve (AUC) of 0.91, this figure demonstrated a sensitivity of 74.92% and a specificity of 100%. There was a substantial indication of acute appendicitis when the neutrophil-to-lymphocyte ratio was more than 4.7 (odds ratio [OR]: 128, $p < 0.0001$). Moreover, a risk factor for complex appendicitis was shown to be a neutrophil-to-lymphocyte ratio higher than 8.8 (OR: 43, $p < 0.0001$) [14].

The median NLR levels for three separate groups were reported in a research by Ahmad et al. Groups 1, 2, and 3 had median values of 2.37, 5.25, and 9.27, respectively. Both groups 2 and 3 showed a statistically significant difference in NLR ($P < 0.001$), in addition to group 1 and group 2 ($P < 0.001$). The NLR was shown to have diagnostic values of 3.11 (sensitivity 75.23%, specificity 68.70%) for acute appendicitis and 6.17 (sensitivity 76.32%, specificity 58.72%) for perforated appendicitis. There was a statistically significant correlation between

the NLR and illness severity. In addition, there was a clear correlation between the NLR and the duration of hospitalization [15].

Finally, Prasetya et al. found that NLR and neutrophil count were significantly higher in the acute appendicitis group compared to the control group. However, when looking at the white blood cell counts, there was no discernible difference between the two groups. In addition, the research found that compared to cases of simple appendicitis, patients of complex appendicitis had a significantly higher number of neutrophils and a higher neutrophil-to-lymphocyte ratio. In terms of acute appendicitis, the following diagnostic performance metrics were found for the NLR: sensitivity of 83.5%, specificity of 57.7%, PPV of 81.4%, NPV of 61.2%, area under the receiver operating characteristic (ROC) curve of 0.764, and a cutoff point of 2.87. The area under the ROC curve, sensitivity, specificity, PPV, and NPV are important metrics to consider [16].

5. Limitations of the study

This study was conducted retrospectively, and clinical data provided by the patients were obtained from the medical records and physician documentation, with consideration of the patient's age. The number of patients diagnosed with complicated acute appendicitis was limited.

6. Conclusion

This study focused on participants with acute appendicitis and found a demographic trend towards younger males, most of whom exhibited tenderness in the right lower quadrant. The study showed that the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were significantly associated with the modified Alvarado score. Both PLR and NLR proved to be valuable in diagnosing acute appendicitis. Elevated levels of NLR and PLR offer higher diagnostic value compared to traditional inflammatory markers and are important risk indicators for identifying complicated cases, particularly when the cut-off value is 3 or more. Using NLR in the emergency room is an encouraging and recommended approach.

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The final version of the manuscript has been reviewed for publication; every author agreed to assume complete accountability for the entire document.

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Critical review of the manuscript: Shahd Alghamdi and Maryam BinBakr

Discloser

Human Subjects: King Abdullah International Medical Research Center issued approval NRJ24/002/4.

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Animal Subjects: The authors confirm that no animals or animal tissues were involved in this research.

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