

ORIGINAL RESEARCH

The Value of Complete Blood Count Parameters in Predicting Complicated Acute Appendicitis; a Prognostic Accuracy Study

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Abstract: **Introduction:** Low accuracy of clinical variables can result in delayed diagnosis and increase the incidence of complicated appendicitis in some cases. This study aimed to determine the value of simple complete blood count (CBC) biomarkers in predicting complicated appendicitis. **Methods:** This is a single-center retrospective cross-sectional study, which was conducted on cases referred to emergency department following acute appendicitis who underwent appendectomy, to evaluate the accuracy of some cell blood count variables (white blood cell count (WBC), neutrophil percent, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), mean platelet volume (MPV)) in predicting complicated cases (gangrenous and ruptured appendicitis). **Results:** There were 252 (68.3%) patients in the uncomplicated appendicitis group and 117 (31.7%) patients in the complicated appendicitis group. The mean age of patients was 34.1 ± 1.09 (Range: 18 -79) years (55.3% male). There were no differences between groups regarding the mean age ($p = 0.053$), gender distribution ($p=0.07$), Alvarado score ($p = 0.055$), platelet count ($p=0.204$), PLR ($p = 0.115$), and MPV ($p = 0.205$). The complicated appendicitis cases had longer onset of symptoms ($p < 0.001$), higher WBC count ($p = 0.011$), higher neutrophil count ($p < 0.001$), and higher NLR ($p < 0.001$). Neutrophil count (area under the curve (AUC) = 0.61, 95% confidence interval (CI) = 0.56-0.66; $p = 0.001$) and NLR (AUC = 0.65, 95% CI = 0.60-0.69; $p = 0.001$) had higher level of accuracy in this regard. In contrast, the area under the curve of WBC count (AUC = 0.57, 95% CI = 0.52-0.63; $p = 0.22$), platelet count (AUC = 0.44, 95% CI = 0.38-0.49; $p = 0.049$), PLR (AUC = 0.57, 95% CI = 0.52-0.62; $p = 0.026$), and MPV (AUC = 0.54, 95% CI = 0.49-0.60; $p = 0.193$) showed low accuracy in predicting complicated acute appendicitis. **Conclusion:** Based on the findings of present study it seems that WBC, neutrophil percent, NLR, PLR, and MPV have failed to poor accuracy in predicting cases with complicated appendicitis in emergency department.

Keywords: Appendicitis; Biomarkers; Leukocyte Count; Emergencies

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1. Introduction

Acute appendicitis is the most common emergency surgical condition, with a 229 per 10,000-person incidence and a lifetime risk of 6.7% to 8.6%. Peak incidence is usually between the ages of 15 and 20 (1, 2). The clinical diagnosis of acute appendicitis has a sensitivity of 54%, specificity of 75%, positive and negative predictive values of 92.3% and 83.3%, respectively, and an accuracy of 89.8%, according to the Alvarado score (3). However, the diagnostic accuracy is relatively low in women of reproductive age, which can result in diagnostic

delays (4, 5).

Delayed or missed diagnosis of acute appendicitis can occur in 15-24% of cases, leading to complicated appendicitis (such as gangrenous, ruptured appendicitis and appendiceal abscess) and an increase in postoperative morbidity and mortality (6, 7).

Currently, computed tomography (CT) scans play an important role in the diagnosis of acute appendicitis, with sensitivity and specificity of 96.7% and 95.5%, respectively (8). However, CT scans may not be available in rural hospitals in developing countries.

White blood cell count (WBC), neutrophil percent, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and mean platelet volume (MPV) are all CBC biomarkers that are important in the response to acute inflammation and useful in the diagnosis of acute appendicitis. Nevertheless, the value of those biomarkers in predict-

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ing complicated appendicitis is uncertain, as the sensitivity and specificity of WBC were reported as 53% and 67%, respectively and the sensitivity and specificity of NLR were reported as 70.7% and 56.3% (9, 10). The goal of this study was to assess the value of simple CBC biomarkers such as WBC, neutrophils, NLR, PLR, and MPV in predicting complicated appendicitis.

2. Methods

2.1. Study design and setting

This is a single-center retrospective cross-sectional study, which was conducted on cases referred to emergency department following acute appendicitis who underwent appendectomy to evaluate the accuracy of some blood cell count variables (WBC, neutrophil percent, NLR, PLR, MPV) in predicting the complicated cases with peritonitis. The study was done in Emergency Surgical unit, Department of Surgery, Faculty of Medicine, Srinakharinwirot University, Ongkharak Nakhon-nayok, Thailand, between January 1, 2016 and March 31, 2022.

The method of research was approved by the institutional ethics committee of Srinakharinwirot University (Ethics code: SWUEC/E-253/2564). Patient information was gathered in accordance with the Standards for the Protection of Personally Identifiable Health Information.

2.2. Participants

The study included participants aged 18 to 70 who had acute appendicitis and were treated at our institute with an appendectomy (both open and laparoscopic surgery).

Those with advanced age, pregnancy, atherosclerotic disease, diabetes mellitus, hematologic disease, or use of steroids or immune-suppressants, which can affect serum biomarker interpretation, were excluded. Patients who had previous laparotomies were not excluded from the study.

2.3. Data gathering

From April 1 to November 1, 2022, the patient's data were obtained from an institutional computerized database program using the keywords acute appendicitis, appendicitis with peritonitis, and appendectomy for potential recruitment.

Acute appendicitis was confirmed by clinical, laboratory, and imaging tests, such as ultrasonography and computed tomography. Prior to administering antibiotics, a blood sample was drawn at the time of admission to evaluate the patient's WBC, neutrophils, lymphocytes, platelet count, and MPV. Laboratory data was used to calculate the NLR and PLR. The patients were operated on by our department's surgical staff, and 98.7% of the patients were approached using the open appendectomy technique. Both authors extracted pa-

tient information from the electronic database of the institution. For each patient, demographic data, intraoperative findings, and treatment outcomes (including postoperative complications and length of stay) were collected.

Patients were divided into two groups based on pathologic and intraoperative findings: uncomplicated acute appendicitis (acute focal and suppurative appendicitis) and complicated acute appendicitis (gangrenous and ruptured appendicitis). The postoperative outcomes were assessed during a 14–30-day follow-up period.

2.4. Statistical analysis

SPSS 22.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Clinical and demographic factors were assessed using descriptive analysis (percentage, mean, standard deviation, minimum-maximum), and compared between groups using student t-tests for continuous variables, and Mann Whitney-U tests for non-normal parameters. P-value less than 0.05 was considered statistically significant.

The receiver operating characteristic (ROC) curve was used to determine the diagnostic value of studied serum biomarkers for complicated appendicitis considering the operative findings as gold standard. The best cut-off point for each biomarker was calculated using the area under the ROC curve (AUC) and specificity, sensitivity, positive and negative predictive values; in addition, positive and negative likelihood ratio of studied markers were calculated and reported with 95% confidence interval (CI). The area under the ROC curves were classified as excellent (0.90-1), good (0.80-0.89), fair (0.70-0.79), poor (0.60-0.69) or fail (0.50-0.59).

3. Results

3.1. Baseline characteristics of studied cases

Appendectomy procedures were performed on 390 patients, but only 369 consecutive patients were recruited for the study. Twenty-one cases were excluded since they met the exclusion criteria or lacked sufficient data. There were 252 (68.3%) patients in the uncomplicated appendicitis group and 117 (31.7%) patients in the complicated appendicitis group. The mean age of patients was 34.1 ± 1.09 (Range: 18-79) years (55.3% male). Almost all of the procedures were performed via the open approach.

Table 1 compares the baseline characteristics of the patients between studied groups. There were no differences between the groups regarding mean age ($p = 0.053$), gender distribution ($p=0.07$), Alvarado score ($p = 0.055$), platelet count ($p = 0.204$), PLR ($p = 0.115$), and MPV ($p = 0.205$). The complicated appendicitis cases had longer onset of symptoms ($p < 0.001$), higher WBC count ($p = 0.011$), higher neutrophil count ($p < 0.001$), and higher NLR ($p < 0.001$).

The length of stay for patients with complicated appendici-

tis was significantly longer (4.67 ± 0.22 days versus 2.29 ± 0.70 days; $p < 0.001$). There was no statistically significant difference between groups in operative time ($p = 0.069$) or postoperative complication rate ($p = 0.523$).

3.2. Screening performance characteristics of studied parameters

The area under the ROC curve of studied parameters in predicting the cases with complicated appendicitis are shown in table 2 and figure 1. Neutrophil count (AUC = 0.61, 95% CI = 0.56-0.66; $p = 0.001$) and NLR (AUC = 0.65, 95% CI = 0.60-0.69; $p = 0.001$) had higher level of accuracy in this regard. In contrast, the area under the curve of WBC count (AUC = 0.57, 95% CI = 0.52-0.63; $p = 0.22$), platelet count (AUC = 0.44, 95% CI = 0.38-0.49; $p = 0.049$), PLR (AUC = 0.57, 95% CI = 0.52-0.62; $p = 0.026$), and MPV (AUC = 0.54, 95% CI = 0.49-0.60; $p = 0.193$) showed low accuracy in predicting the complicated acute appendicitis.

The sensitivity and specificity of neutrophil count in predicting complicated appendicitis in cut-off point of 83% were 64.02% (95% CI = 0.52-0.70) and 52.37% (95% CI = 0.48-0.61), respectively. These measures for NLR in cut-off point of 7.4 were 62.54% (95% CI = 0.52-0.70) and 58.92% (95% CI = 0.54-0.66), respectively.

4. Discussion

Appendectomy is currently the gold standard in the treatment of acute appendicitis, with a 0.09-0.24 percent mortality rate. A delayed diagnosis may result in complicated appendicitis, requiring more complex surgery and increasing morbidity by 35%. (e.g., wound infection and intra-abdominal abscess) (11, 12). Even in this study, there was no difference in the rate of postoperative complications between the two groups; however, complicated appendicitis required a longer hospital stay.

According to the results of a study, delayed presentation is a strong risk factor for developing complicated appendicitis; other risk factors included pediatric patients, those over the age of 70, male sex, and more than three comorbidities (13). Thereby, basic biomarkers in the CBC that can be collected in the emergency department become a potential predictor of complicated appendicitis, encouraging the decision to perform emergency surgery in this group of patients.

The primary goal of this study was to determine the value of CBC biomarkers in predicting complicated appendicitis. However, the results of this study indicate that complete blood counts parameters, including WBC, neutrophil count, NLR, platelet counts, PLR, and MPV, failed to accurately predict cases of complicated appendicitis in the emergency department.

Previous studies demonstrated that $WBC > 15,000/mm^3$ can

predict acute appendicitis, whereas $WBC > 18,000/mm^3$ can predict complicated appendicitis (14, 15). However, the results of this study indicate that a neutrophil with a cut-off value of 83% was unable to predict complicated appendicitis with adequate sensitivity and specificity. Similarly, the results demonstrated that WBC was incapable of predicting complicated appendicitis. WBC has a sensitivity of 67% and a specificity of 43% in the diagnosis of complicated appendicitis, according to a study by Sevinç et al. (16).

NLR and PLR are biomarkers associated with systemic inflammation. Several studies have demonstrated that NLR has diagnostic value for acute appendicitis (17). In addition, Hajibandeh et al. discovered that $NLR > 4.7$ and > 8.8 were independent predictors of simple and complicated appendicitis, respectively (18). In contrast to the study's findings, NLR at a cut-off level of 7.4 has a low predictive potential for complicated appendicitis, with a sensitivity and specificity of 62% and 58%, respectively.

Previous studies demonstrated that PLR at a cut-point value of 284 (AUC: 0.647; sensitivity: 42%; specificity: 86%) has predictive capabilities in pediatric patients for the diagnosis of complex appendicitis (19). According to the findings of the present study, PLR did not demonstrate value as a diagnostic biomarker for complicated appendicitis in adult populations.

A recent meta-analysis found that a lower MVP value could be used to predict acute appendicitis but failed to demonstrate the diagnostic value of MPV for complicated appendicitis (20). Consistent with the findings of the study, this can be explained by increase in MPV during the period of severe infection or sepsis as a result of platelet activation, due to an increase in the production of young platelets, which could affect MPV interpretation (21).

Given that there is currently no clinical scoring system to predict complicated appendicitis, future research may use the findings of this study to develop a clinical score that uses serum biomarkers as parameters to encourage early surgical management of complicated appendicitis patients, potentially improving their postoperative outcomes.

5. Limitations

The current study has two limitations: 1) it was retrospective, and 2) pregnant women and patients over 70 were excluded since they may present with unusual symptoms, delaying appendicitis diagnosis. However, this study's large patient population provides accurate data for analysis.

Furthermore, if blood test was delayed, the progression of the disease could have exacerbated the inflammatory response, affecting the interpretation of serum biomarkers. This may lead to data bias or imprecision. In this study, if the patient was suspected to have acute appendicitis, a blood sam-

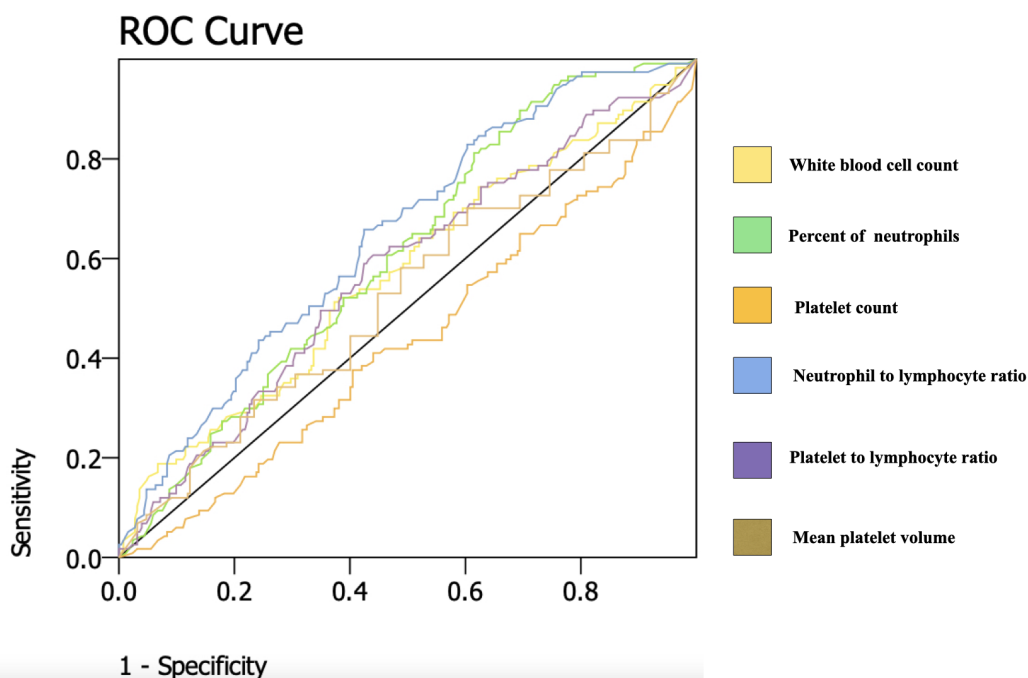


Figure 1: Receiver operating characteristics (ROC) curves of the studied biomarkers in predicting complicated appendicitis cases.

Table 1: Comparing the baseline characteristics as well as outcomes of studied patients between cases with complicated and uncomplicated appendicitis

Parameters	Appendicitis group		P-value
	Complicated	Uncomplicated	
Age (year)			
Mean ± SD	38.3±1.27	35.22±1.17	0.053
Gender			
Male/Female ratio	128/124	77/40	0.07
Alvarado score			
Mean ± SD	7.67 ± 1.44	7.14 ± 2.11	0.055
Onset of symptom (Hour)			
Mean ± SD	30.13 ± 2.15	15.15 ± 1.22	< 0.001
WBC (cell/mm³)			
Mean ± SD	16507 ± 403	15394 ± 389	0.011
WBC differential			
PMN (%)	85.00 ± 0.45	81.10 ± 0.66	< 0.001
Platelet count (cell/mm ³)	264333±6064.2	280581±6020	0.204
NLR	13.3±1.27	8.2±0.51	< 0.001
PLR	267.9 ± 35.0	204.8 ± 22.2	0.115
MPV	9.98 ± 0.08	9.80 ± 0.07	0.205
Treatment outcomes			
Operative times (minutes)	67.38 ± 2.70	61.25 ± 2.60	0.069
Length of stay (days)	4.67± 0.22	2.29 ± 0.70	<0.001
Overall post-operative complications	4 (1.60)	3 (2.610)	0.523

Data are presented as mean ± standard deviation (SD) or frequency (%). WBC = White blood cell count; PMNs = Polymorph nuclear neutrophils; NLR = Neutrophil to lymphocyte ratio; PLR = Platelet to lymphocyte ratio; MPV = Mean platelet volume.

ple was drawn immediately and results were provided within 30–45 minutes. The patient's biomarker-affecting comorbidities were eradicated, and surgical care was administered

within 24 hours of diagnosis, this could mimic the risk of bias in this study.

Table 2: Screening performance characteristics of studied markers in predicting the complicated cases of acute appendicitis

Variable	Cut-off	Sensitivity	Specificity	PPV	NPV	+LR	-LR	Accuracy
WBC	15150	62 (0.53-0.71)	50 (0.43-0.55)	36.13 (0.30-0.43)	73.66 (0.66-0.80)	1.22 (1.01-1.47)	0.77 (0.59-1.00)	53.12 (0.45-0.58)
Neutrophil	83	64 (0.52-0.70)	52 (0.48-0.61)	38.89 (0.31-0.46)	75.03 (0.68-0.81)	1.34 (1.10-1.63)	0.72 (0.56-0.92)	56.47 (0.51-0.62)
Platelet	242500	61 (0.52-0.70)	50 (0.45-0.57)	28.12 (0.23-0.34)	60.19 (0.51-0.69)	0.84 (0.72-0.99)	1.43 (1.05-1.94)	37.94 (0.33-0.43)
NLR	7.4	62 (0.53-0.70)	58 (0.54-0.66)	41.61 (0.34-0.49)	77.05 (0.70-0.83)	1.54 (1.25-1.89)	0.64 (0.50-0.82)	60.43 (0.55-0.65)
PLR	144.4	55 (0.46-0.64)	44 (0.37-0.50)	34.58 (0.28-0.41)	72.41 (0.65-0.73)	1.14 (0.96-1.35)	0.82 (0.62-1.08)	50.15 (0.45-0.55)
MPV	10	61 (0.55-0.66)	47 (0.37-0.56)	35.25 (0.28-0.43)	70.90 (0.64-0.70)	1.17 (0.92-1.50)	0.83 (0.73-1.08)	55.83 (0.51-0.61)

Data are presented with 95% confidence interval. WBC = White blood cell count; NLR = Neutrophil to lymphocyte ratio; PLR = Platelet to lymphocyte ratio; MPV = Mean platelet volume; PPV: positive predictive value; NPV: negative predictive value; +LR: positive likelihood ratio; -LR: negative likelihood ratio.

6. Conclusion

Based on the findings of present study it seems that cell blood count parameters such as WBC, neutrophil percent, NLR, PLR, and MPV have failed to poor accuracy in predicting the cases with complicated appendicitis in emergency department.

7. Declarations

7.1. Acknowledgments

The authors thank the surgical staff at Department of Surgery, Faculty of Medicine, Srinakahrinwirot University for the acquisition of data.

7.2. Conflict of Interest

The authors declare no conflict of interest in this study.

7.3. Findings

None.

7.4. Authors' contribution

Dr. Thawatchai Tullavardhana worked on study conception and design, acquisition, analysis, interpretation of data, editing.

Dr. Natchanok Mekrugsakit worked on study design, data collection, data analysis, the preparation of a manuscript. All authors read and approved the final version of manuscript.

7.5. Data availability

The Standards for the Protection of Personally Identifiable Health Information were used to safeguard patient information.

7.6. Disclosure

The findings of this study are presented at Annual Scientific Congress of the International College of Surgeons, Thailand. 21-22 November 2022.

7.7. Using artificial intelligence chatbots

This study made no use of artificial intelligence chatbots.

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