

Hematological parameters and histopathological outcomes in appendicitis patients: A retrospective study

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Abstract. Appendicitis remains the most common cause of abdominal complaints in the emergency setting. Clinicians and surgeons often place greater reliance on ultrasonography result than on hematological parameters. This mindset may present challenges, particularly in low-resource settings. The aim of current study to investigate the correlation between hematological parameters and histopathological outcomes in patients with appendicitis. We conducted a retrospective analysis of data from 188 patients who underwent appendectomy and histopathological examinations. We found that there were correlations between white blood cell count (WBC) ($p < 0.001$), platelet count ($p = 0.029$), neutrophil-to-lymphocyte ratio (NLR) ($p < 0.001$), platelet-to-lymphocyte ratio (PLR) ($p = 0.040$), lymphocyte-to-monocyte ratio (LMR) ($p < 0.001$), and percentage eosinophils ($p = 0.019$) with histopathological outcomes. We concluded that hematological parameters can aid clinicians and surgeons assessing appendicitis and in planning surgical procedures.

1 Introduction

Appendicitis remains the most common cause of abdominal complaints in emergency settings. It is still become the leading cause of abdominal complaints followed with abdominal surgery [1]. Around 7% of the population is expected to experience acute appendicitis during their lifetime [2]. Diagnosing appendicitis in practice can sometimes overlap with other abdominal complaints [3]. There is reported case where dengue fever mimicked symptoms of appendicitis [4]. This highlights the need for caution among clinicians and surgeons when evaluating patient complaints and conducting subsequent examinations. Laboratory parameters serve as crucial tools in diagnosing appendicitis and assessing its severity [3], [5], [6], [7]. These parameters are especially valuable in low-resource settings where modalities like ultrasonography or CT scans are unavailable [8]. Also where post-surgical histopathology examinations may not be feasible. White Blood Cell count (WBC), Neutrophil-to-Lymphocyte Ratio (NLR), and Platelet-to-Lymphocyte Ratio (PLR) have been validated as predictors for appendicitis and its severity [5], [6], [9].

Post-surgical hitopathology is used to examine the tissue cells of inflamed or infected appendix. This actually helps the surgeon and the patient to know the cause of appendicitis. Also to noted the surgeon is the celles were benign or malignant, for further therapy. But this

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technology are rare in low-resource setting, because it needed advanced tools and pathologist. Thus, the examination rarely done in rural areas [8]. Research on the relationship between hematological parameters and histopathological outcomes in appendicitis patients remains limited. This study aims to investigate this correlation, aiming to assist clinicians and surgeons in evaluating and planning surgical procedures for appendicitis patients, particularly in resource-limited settings. Our research is part of the of the agenda of Sustainable Development Goals (SDG's) which were to ensure healthy lives and promote well-being for all, at all ages.

2 Material and Methods

This retrospective cohort study included all consecutive patients who diagnosed with appendicitis at PKU Muhammadiyah Bantul Hospital (Bantul, Indonesia) from January 1, 2016, to December 31, 2020. We searched for medical records by using the ICD-10 code for appendicitis in the hospital's electronic system. We also gathered data on patients who had appendectomy from the operating room register. The information collected included age, gender, address, symptoms, vital signs, physical exams, laboratory tests, ultrasound results, histopathology findings, postoperative diagnoses, incidence of peritonitis, and length of hospital stay. These records were analyzed using an online research form, excluding any data that did not meet our criteria. A total of 601 patient records met the inclusion and exclusion criteria for further analysis.

Among these, only 188 patients underwent histopathology examination, which constituted the focus of our research. We divided the histopathology examination into five categories: (1) acute appendicitis, (2) acute appendicitis with peri-appendicular infiltrate, (3) perforated acute appendicitis, (4) chronic appendicitis with acute exacerbation, and (5) chronic appendicitis with acute exacerbation et peri-appendicular infiltrate. The data were processed and analyzed using IBM-SPSS Statistics version 25.0. Initially, we conducted a normality test using the Kolmogorov-Smirnov test on numerical data; only hemoglobin data showed normal distribution, while the remaining numerical data yielded *p*-values less than 0.05, indicating non-normal distribution. Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada (FK-KMK UGM), under ethical eligibility number KE/0067/01/2021.

3 Results and Discussion

3.1 Subjects Characteristics

This study included 188 patients diagnosed with appendicitis. Tabel 1 shows the characteristics and *p*-value from the bivariate analysis results of this research. A total of 56.38% of the subject is female patients. All patients underwent histopathology examination, revealing findings of 15 patients with acute appendicitis, 39 patients with acute appendicitis with peri-appendicular infiltrate, 16 patients with perforated appendicitis, 90 patients with chronic appendicitis with acute exacerbations, and 28 patients with chronic appendicitis with acute exacerbations et peri-appendicular infiltrate. In total, 104 patients diagnosed with complicated appendicitis. In this study, we did not set an age limit for the data we analyzed. The average age was 28.5 years, ranging from 1 to 78 years. When categorized by age, 47.87% (n=90) were young adult patients, 28.72% (n=54) were children patients, 21.28% (n=40) were adult patients, and only 2.13% (n=4) were geriatric patients. This finding is consistent with Lima (2016), whose study also found that the majority of appendicitis cases occurred in the young adult age group (60.3%) [10]. Other studies, have similarly categorized patients into groups, often focusing on children [6], [11]. Due to the subjective nature of some

medical history questions, there is a need for more accurate scoring or screening methods for pediatric patients [12]. The highest incidence of appendicitis occurs between the ages of 20 and 30 years, with lower rates observed in children under 5 years old and adults over 50 years old [2].

Table 1. Subject's characteristics

Characteristic	All	Group* 1	Group* 2	Group* 3	Group* 4	Group* 5	p-value
N	188	15	39	16	90	28	
Age	28.5 (1 – 78)	23.4 ± 13.52	31.46 ±17.40	31.06 ± 22.15	30.71 ± 15.82	35.93 ± 14.33	0.22
Gender							
Male	43.62%	40%	61.5%	56.25%	31.11%	53.5%	0.11
Female	56.38%	60%	38.5%	43.75%	68.88%	46.4%	
Laboratory							
Hemoglobin (g/dl)	13.4 ± 1.62	13.2 ± 1.40	13.79 ± 1.68	13.46 ± 1.73	13.46 ± 1.53	13.03 ± 1.82	0.442
WBC (x10 ⁶ /ml)	9.64 (3.32 – 25.1)	7.87 ± 1.86	13.4 ± 4.40	14.23 ± 6.24	9.65 ± 3.43	10.34 ± 3.95	< 0.001
Platelet count (x 10 ⁶ /ml)	277.7 (33.1 – 802)	295.62 ± 64.64	276.37 ± 85.94	242.63 ± 106.29	310.62 ± 85.23	287.35 ± 130.01	0.029
NLR	3.56 (0.84 – 23.35)	2.25 ± 1.19	6.73 ± 4.56	10.06 ± 4.93	3.61 ± 2.63	5.81 ± 5.05	< 0.001
PLR	1.46 (0.11 – 9.75)	1.40 ± 0.58	1.59 ± 0.69	2.44 ± 1.53	1.56 ±0.59	2.00 ± 1.65	0.04
LMR	3.49 (0.71 – 17.41)	5.30 ± 1.57	3.40 ± 2.22	2.31 ± 2.77	4.61 ± 2.94	3.59 ± 1.94	< 0.001
Eosinophil (%)	1.37 (0 – 8.31)	2.14 ±1.27	1.56 ±1.50	0.89 ± 0.87	2.06 ± 1.71	1.92 ± 1.38	0.019
Final diagnosis							
Uncomplicated appendicitis	44.68%	100%	7.69%	6.25%	67.78%	14.2%	< 0.001
Complicated appendicitis	55.32%	0%	92.3%	93.75%	32.22%	85.8%	

*Histopathological outcomes group: (1) acute appendicitis, (2) acute appendicitis et peri appendicular infiltrate, (3) perforated acute appendicitis, (4) chronic appendicitis with acute exacerbation, and (5) chronic appendicitis with acute exacerbation et peri appendicular infiltrate. WBC: white blood cells count, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, LMR: lymphocyte-to-monocyte ratio. Categorical values are expressed as n (%); continuous values are expressed as median and its range or mean ± SD

3.2 Laboratory findings

Table 1 demonstrates that all hematology parameters exhibit a statistically significant relationship with histopathological outcomes, except for hemoglobin, which shows no significant relationship ($p = 0.042$). White blood cell (WBC) count plays a crucial role in the diagnosis of appendicitis, as evidenced by its statistically significant relationship with histopathological outcomes in our study. This finding is consistent with Tanrikulu et al.'s study, which also noted that elevated WBC levels support the diagnosis of acute appendicitis [13]. However, Zuhoor et al. study mentioned that WBC counts are often overlooked, as normal levels can still indicate appendicitis [14]. Additionally, another study stated that even with normal WBC counts, if ultrasonography reveals an appendix diameter larger than 8 mm,

appendectomy is still recommended [15], [16]. In our study, a higher mean WBC count was observed in Group 3 (perforated appendicitis), suggesting that elevated WBC levels may indicate severe or complicated appendicitis [17]. In this study, platelet count was found to have statistically significant relationships with histopathological outcomes. However, as of the writing of this paper, no similar or contrasting research results have been identified. Several studies have reported that platelet count shows no relationship with appendicitis, whether uncomplicated or complicated appendicitis [18], [19]. One study reported thrombocytopenia as a complication from appendicitis [20]. Another study reported about dengue fever mimicking as acute appendicitis [4]. Further research about platelet count and appendicitis needs to be conducted.

Nowadays, Neutrophil-to-Lymphocyte Ratio (NLR) has emerged as a novel parameter for assessing appendicitis. This study demonstrates that NLR has a statistically significant relationship with histopathological outcomes. This finding is consistent with Ahmad et al.'s research, which highlighted NLR's effectiveness in distinguishing between normal appendices and acute appendicitis, as well as its potential for predicting appendicitis severity [21]. One meta-analysis has also affirmed NLR as a predictor for diagnosing and assessing the severity of appendicitis. It assists surgeons in planning surgical procedures, monitoring conservatively managed patients, and in cases where CT scans are not routinely performed (such as in pregnant or pediatric patients) [5]. In this study, Platelet-to-Lymphocyte Ratio (PLR) results demonstrated a statistically significant relationship with histopathological outcomes ($p = 0.04$). Rajalingam et al. also reported similar findings, indicating that PLR correlates significantly with histopathological outcomes ($p < 0.001$) and is reliable for assessing the severity of appendicitis [22]. Additionally, Lymphocyte-to-Monocyte Ratio (LMR) in our study also showed a statistically significant relationship with histopathological outcomes ($p < 0.001$). This aligns with Nissen et al.'s research on LMR as a tool to differentiate the severity of appendicitis in pediatric patients, which included histopathological validation [6].

Eosinophils are a type of immune cell containing granules with enzymes released during infections, allergic reactions, and asthma [23]. Eosinophilia is defined as an increase in circulating eosinophils $>500/\text{mm}^3$ [24]. Increased eosinophils in the muscularis propria of the appendix may indicate early symptomatic appendicitis [25]. Our recent study shows that eosinophils have a statistically significant relationship with histopathological outcomes in appendicitis patients ($p = 0.019$). This finding is consistent with Karabulut et al.'s study ($p = 0.033$), which also suggested that eosinophils can differentiate between acute appendicitis and lymphoid hyperplasia [26]. Eosinophils represent a potential marker that can assist clinicians and surgeons in assessing appendicitis due to their biological characteristics.

4 Conclusion

Most of hematological parameters can aid clinicians and surgeons assessing appendicitis and in planning surgical procedures. Several parameters like NLR, PLR, LMR, and eosinophil also proven as a strong parameters to differ the severity of appendicitis. This research still have limitation such as the number of data and the depth of its analysis. We suggest further research can analyzed hematology values as predictor for histopathology outcomes. Thus, there will be a cost effective in term of examination.

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Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors disclose no conflict.

Author contribution statement

Bunga Fatimah and Mochammad Junaidy Heriyanto conceived and designed the study. Bunga Fatimah performed the computational analysis and wrote the manuscript. Mochammad Junaidy Heriyanto provided the funding and revised the manuscript. All authors have read and approved the manuscript and have made significant contributions to this study.

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