ORIGINAL RESEARCH

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The Role of the Count and Percentage of Immature Granulocytes in the Differentiation of Acute Complicated and Non-Complicated Appendicitis

Onur Karabay[1], Özgür Dikme[2], Gözde Karabay[3], Özgür Karcıoğlu[2]

[1]University of Health Sciences Türkiye, Taksim Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Türkiye
[2]University of Health Sciences Türkiye, İstanbul Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Türkiye
[3]University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Türkiye

Abstract

Objective: The objective of this study was to ascertain the effectiveness of the immature granulocyte (IG) count and percentage in diagnosing and discriminating between non-complicated acute appendicitis (NCAA) and complicated acute appendicitis (CAA).

Materials and Methods: This study was conducted using data from 244 adult patients who underwent appendectomy. A retrospective assessment of demographic details, preoperative white blood cell (WBC) count, number and percentage of neutrophils, neutrophil-to-lymphocyte ratio (NLR), lymphocyte (LYM) count, IG count and IG percentage, operation findings, and pathology results was conducted. Patients diagnosed with acute appendicitis (AA) were categorised as NCAA and CAA according to pathology reports and surgical outcomes.

Results: The WBC, NLR, IG count and IG% did not differ significantly ($p>0.05$) between the CAA and NCAA groups.

Conclusion: The findings of this study indicate that AA is statistically more prevalent in the early 30s.The number and percentage of neutrophil counts, NLR, IG in the diagnoses of AA, in conjunction with the elevated number of WBC, prove negligible in differentiating between CAA and NCAA. In the emergency room, examining the hemogram parameters merely reveals that the prediction of complications is rendered meaningless. The study revealed no statistically significant relationship between the groups. Consequently, hemogram parameters (LYM, WBC, NLR, IGC, and IG%) were deemed unreliable for distinguishing between CAA and NCAA.

Keywords: Appendicitis, immature granulocytes, complicated, emergency medicine

Introduction

Acute appendicitis (AA) is one of the most common causes of acute abdomen requiring surgical intervention in the emergency department (ED) [1]. The highly variable clinical presentation of AA makes its diagnosis in the ED challenging. The time taken to establish a diagnosis is known to increase the risk of appendiceal perforation and complications [2]. Approximately 10% of ED visits are due to abdominal pain [3]. AA is the most common abdominal surgical emergency worldwide, with a lifetime incidence of 8.6% in men and 6.9% in women [4].

The physical examination findings and clinical presentation of AA can vary considerably. The classic triad of pain radiating to the right lower quadrant, right lower quadrant tenderness, and leukocytosis is observed in only 50% of patients [5]. Despite advances in laboratory tests and imaging, the diagnosis of AA remains challenging. In particular, early surgical intervention in women of childbearing age results in a negative appendectomy (NA) rate of 20-30% [6]. The increase in NA rates leads to unnecessary morbidity and complications, increases treatment costs, and exposes physicians to malpractice lawsuits [7].

Address for Correspondence: Onur Karabay, University of Health Sciences Türkiye, Taksim Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Türkiye
E-mail: onurkarabay@windowslive.com **ORCID-ID:** orcid.org/0000-0002-0164-9536
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A plethora of biochemical and haematological tests are requested in EDs with a view to detecting AA in its early stages. However, studies have demonstrated that the specificity and sensitivity of these tests are low [7]. Consequently, various parameters have been proposed for the early diagnosis of AA. One such parameter is the immature granulocyte (IG), which is known to increase in cases of infection and inflammation [8].

IG [Delta Neutrophil Index, (DNI)] refers to myelocytes, promyelocytes, and metamyelocytes, precursors of granulocytes, which are normally found in the bone marrow and absent in peripheral blood except in the neonatal period [9]. The clinical significance of IG count has been scientifically demonstrated by counting metamyelocytes, myelocytes, and promyelocytes [9]. To ensure accurate diagnosis, band cells, myeloblasts, and type 1 myelocytes must be excluded, as these cells share a similar granule formation but belong to different categories. The presence of IG in peripheral blood, with the exception of newborns and pregnant women, signifies a serious infection, inflammation, or the onset of a bone marrow disorder [10].

The accelerated granulopoiesis observed in acute systemic inflammatory or infectious states is mechanistically driven by proinflammatory cytokine cascades-principally interleukin-1, tumor necrosis factor-alpha, and interleukin-6- which induce the upregulation of granulocyte colony-stimulating factor. This pivotal hematopoietic cytokine orchestrates the proliferation and premature egress of immature myeloid progenitors from medullary compartments into peripheral circulation, a process substantiated in prior experimental and clinical models [8,9].

This hematologic derangement, pathognomonically termed a “left shift” frequently precedes detectable leukocytosis, functioning as a sentinel marker of nascent innate immune activation. In complicated acute appendicitis (CAA), characterized by transmural necrosis or perforation, localized tissue devitalization and microbial translocation elicit a systemic inflammatory milieu, via pathogen- and damage-associated molecular pattern signaling, culminating in elevated circulating IG concentrations. Consequently, IG quantification, whether absolute or proportional, has been validated as a prognostically robust biomarker, reflecting both the magnitude of inflammatory dysregulation and its correlation with advanced disease phenotypes, as demonstrated in recent clinical cohorts [9,10].

IG appears in peripheral blood as immature polymorphonuclear cells present following bone marrow activation. Research has demonstrated the potential of IG as an early marker in inflammatory and infectious processes, as it emerges in the peripheral blood prior to the observation of leukocytosis [10]. Early and assertive treatment is paramount in cases of AA, as there is a 16% to 36% risk of perforation within the first 36 hours of abdominal pain. This risk escalates by 5% for every 12-hour delay [11]. Perforation, the most common complication of AA, has been shown to significantly increase mortality and morbidity [12].

Notably, IGs exhibit superior kinetic fidelity relative to conventional leukocytic indices. Total leukocyte and neutrophil (NEU) counts may demonstrate diagnostic latency during incipient inflammation or resolution phases, with further susceptibility to perturbation by exogenous variables (e.g., glucocorticoid therapy, adrenergic demargination) [10,11]. In contrast, IG elevation manifests with greater temporal concordance to inflammatory onset and persists during protracted or severe infections, underscoring their pathophysiologic specificity. This discriminative capacity positions IG enumeration as a critical adjunct for delineating complicated inflammatory pathologies (e.g., gangrenous/perforated AA) from uncomplicated counterparts [12]. The operational efficiency of automated hematology analyzers in delivering rapid, reproducible IG quantification further augments their integration into evidence-based diagnostic frameworks, circumventing subjectivity inherent to manual methodologies [8,9].

Therefore, it is vital that AA is accurately diagnosed and treated without delay in the ED [12]. The present study aims to evaluate the diagnostic power of IG, a hemogram parameter frequently employed by ED physicians to confirm diagnoses, in differentiating CAA from uncomplicated acute appendicitis (NCAA).

Materials and Methods

Ethics Committee Approval

This study was approved by the Ethics Committee of University of Health Sciences Türkiye Hamidiye Faculty of Medicine (decision number: 84, date: 20.08.2019). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Population

This observational-retrospective study included patients over the age of 18 who presented to the ED with abdominal pain, and underwent surgery with a preliminary diagnosis of AA between 6 September 2018 and 31 March 2019. Patients with a pathology report confirming AA were included in the study, while those with other pathologies or missing data were excluded. Data were accessed through the hospital information system.

Patients who presented to the ED with abdominal pain, underwent evaluation and testing, had complete access to laboratory and pathology records, and were operated on with a preliminary diagnosis of AA, were included at the age

of 18 or older. Patients with hematological diseases affecting hemogram parameters, pregnant women, those followed up for plastron appendicitis, those recently undergoing chemotherapy, those with a clearly identifiable infectious focus on examination, patients under 18 years, and those with recurrent abdominal pain admissions were excluded.

The diagnosis of AA in this study was ultimately confirmed by. **Histopathological examination**, which served as the **definitive diagnostic reference.** During the clinical decision-making process in the ED, imaging modalities such as ultrasonography and computed tomography were frequently used at the discretion of the treating physician to support the diagnosis. However, in the context of this retrospective study, radiological findings were not used as inclusion criteria or outcome measures, and classification into complicated or uncomplicated AA was based exclusively on histopathological reports.

Patients were stratified into two groups based on postoperative histopathological evaluation: positive appendectomy (PA) and NA. The PA group consisted of patients with histologically confirmed AA, which was further subclassified into NCAA and CAA. In this study, CAA was strictly defined by histopathological criteria, including specimens demonstrating gangrenous changes, necrosis, or perforation. NCAA was characterized by histologically confirmed AA without evidence of these complications. Final categorization into CAA or NCAA subgroups relied solely on histopathological findings, with no consideration given to intraoperative observations or preoperative imaging results.

Data Collection

A comprehensive statistical comparison was conducted on various hemogram parameters, including IG count, IG percentage, white blood cell count (WBC), lymphocyte count (LYM), NEU, and neutrophil-to-lymphocyte ratio (NLR), which have been previously associated with acute inflammation. Receiver operating characteristic analyses were performed to evaluate the diagnostic performance of statistically significant hemogram parameters. Biochemical markers, such as C-reactive protein and procalcitonin-which are not included in routine practice-as well as urinalysis results were excluded.

Statistical Analysis

Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics included mean, standard deviation, median, minimum, maximum, frequency, and proportions. The **Kolmogorov-Smirnov test was used to assess the distribution of continuous variables**, and since the data **did not show a normal distribution**, **non-parametric tests** were selected for analysis. The **Mann-Whitney U test** was used for comparing independent quantitative variables, while the **chi-square test** was applied for categorical variables. Statistical significance was set at $p<0.05$.

Results

A total of 266 patients who underwent surgery with a preliminary diagnosis of AA at University of Health Sciences Türkiye, İstanbul Training and Research Hospital between September 6, 2018, and March 31, 2019 were included in our study. According to pathology reports, 17 patients who were not diagnosed with appendicitis were excluded from the study, and pathology reports for 5 patients were unavailable. Thus, a total of 244 patients with accessible pathology reports were included in the study (Figure 1).

When examining the demographic characteristics of these patients, 147 (60.2%) were male, and 97 (39.8%) were female (Table 1). The median age of the patients was calculated as 32.77.

The patients included in the study were divided into two groups based on pathology reports: CAA and NCAA. In the NCAA group, 88 patients (40.7%) were female, and 128 patients (59.3%) were male (Table 2). There was no significant difference in gender distribution between the CAA and NCAA groups ($p>0.05$).

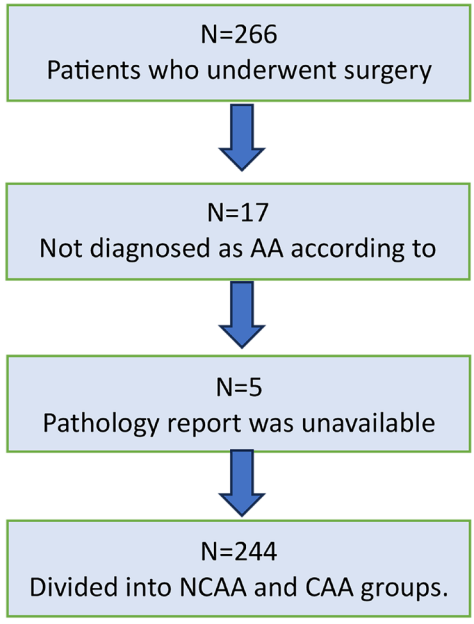

Figure 1. Patient flowchart

NCAA: Non-complicated acute appendicitis, CAA: Complicated acute appendicitis

Table 1. Gender distribution

Gender	Frequency	Percentage (%)
Male	147	60.2
Female	97	39.8
Total	244	100.0

The mean age of patients in the CAA group was 40.75±19.48, while the mean age of patients in the NCAA group was 31.73±13.22 (Table 2). The age of patients in the CAA group was found to be significantly higher compared to the NCAA group ($p<0.05$) (Table 2).

In our study, NEU count and percentage, LYM, NLR, IG count and percentage, and WBC values were calculated and compared between CAA and NCAA patients. No statistically significant difference was found between these parameters.

In the CAA group, the mean WBC was 13.59±3.95, while in the NCAA group, it was 13.88±4.14. The median WBC value was 13.44 in the CAA group and 13.88 in the NCAA group. No significant difference was detected between the two groups in terms of WBC ($p=0.708$) (Table 3).

In the CAA group, the mean IG was 0.06±0.04, similar to that in the NCAA group. The IG percentage was 0.43±0.20 in the CAA group and 0.42±0.32 in the NCAA group. No significant difference was observed between the two groups in terms of IG count and percentage ($p=0.884$; $p=0.374$) (Table 3).

Regarding NEU count and percentage, the mean NEU count was 10.54±4.05 in the CAA group and 10.81±4.12 in the NCAA group. The median values were 10.71 in the CAA group and 10.81 in the NCAA group. No significant difference was found between the two groups in terms of NEU count and percentage ($p=0.839$; $p=0.672$) (Table 3).

Regarding LYM count, the mean value was 1.88±1.16 in the CAA group and 1.97±0.92 in the NCAA group. No significant difference was found between the two groups in terms of LYM count ($p=0.348$, Table 3).

Finally, the NLR was 7.94±5.31 in the CAA group and 7.33±6.46 in the NCAA group. The median NLR was 6.85 in the CAA group and 5.57 in the NCAA group. There was no significant difference in NLR between the two groups ($p=0.348$) (Table 3).

Discussion

AA is one of the most common causes of surgical acute abdomen, affecting all age groups. The CAA condition is a serious clinical situation that can lead to prolonged recovery time, increased hospital stay, higher costs, and negatively affected treatment outcomes [13]. In addition to physical examination and clinical history, laboratory tests, scoring systems, and imaging methods are widely used in the diagnosis of AA [14]. However, despite these advancements, perforation rates are still reported at high levels. In particular, complication rates in elderly patients can reach up to 50% [15]. Therefore, determining whether appendicitis is complicated plays an important role in selecting the treatment method [16]. In our study, we examined hemogram parameters in adult AA patients and revealed the role of these parameters in distinguishing CAA from NCAA.

Table 2. Relationship between age, gender, and CAA/NCAA

Variable	NCAA (n=216)	Median	CAA (n=28)	Median	p
Age	(Mean ± SD) 31.73±13.22	28.00	(Mean ± SD) 40.75±19.48	39.00	0.040[m]
Gender					
Female	88 (40.7%)	-	9 (32.1%)	-	0.382[x2]
Male	128 (59.3%)	-	19 (67.9%)	-	-

[m]Mann-Whitney U test/[x2]chi-square test.

CAA: Complicated acute appendicitis, NCAA: Non-complicated acute appendicitis, SD: Standard deviation

Table 3. Relationship between IG count and percentage, WBC, NEU count and percentage, LYM, NLR with NCAA and CAA

Variable	NCAA (mean ± SD)	NCAA (median)	CAA (mean ± SD)	CAA (median)	p
WBC	13777±1892	1395	13480±1700	1370	0.070[m]
IG count	0.06±0.08	0.05	0.08±0.05	0.07	0.065[m]
IG %	0.42±0.32	0.40	0.30±0.20	0.28	0.048[m]
NEU count	10530±7735	7550	9989±7580	7000	0.089[m]
NEU %	74.12±10.65	75.00	72.05±10.45	70.50	0.052[m]
LYM	1987±1092	1800	1520±820	1500	0.033[m]
NLR	7.33±4.65	5.57	7.94±5.31	6.85	0.041[m]

[m]Mann-Whitney U test.

IG: Immature granulocyte, WBC: White blood cell count, NEU: Neutrophil counts, LYM: Lymphocyte, NLR: Neutrophil/lymphocyte ratio, NCAA: Non-complicated acute appendicitis, CAA: Complicated acute appendicitis

Finding appropriate, easily accessible, and cost-effective markers for the early diagnosis of diseases frequently attracts researchers' interest [17]. Due to increased morbidity and mortality caused by diagnostic delays in patients presenting to the ED with abdominal pain, researchers widely investigate biochemical tests that can be used for early diagnosis [18]. One of the easily accessible and rapidly evaluated tests in the ED is the complete blood count. Inflammatory markers such as IG, NEU, WBC, and NLR, which are included in the complete blood count, have been examined in many studies. In recent years, determining appropriate threshold values for these parameters and evaluating their sensitivity and specificity have also become important research topics [19].

In our study, significant differences were found between the groups in terms of demographic characteristics such as age and gender. In the literature, AA diagnosis is reported to be more common in males. In our study, 60.2% of the patient group was male, and 39.8% was female, which is consistent with the literature. However, no difference was found between the CAA and NCAA groups. The mean age of patients in the CAA group was found to be higher than in the NCAA group. Similar results have been reported in the literature [19,20]. This can be explained by the fact that AA presents with more atypical symptoms in geriatric patients, making diagnosis more challenging than in younger patients [21]. Additionally, although the literature states that CAA cases are more common in males, no significant difference was found in our study.

There are numerous reports in the literature on the relationship between complete blood count parameters and inflammatory or infectious pathologies. Although WBC elevation is frequently observed in AA diagnosis, it is not sufficient as a standalone diagnostic marker. Paragiotopoulou et al. [22] reported that WBC could be used in the diagnosis of appendicitis, but was not sufficient for distinguishing perforation. Yang et al. [23] stated that an increase in WBC and NEU percentage correlated with the degree of appendix inflammation. A meta-analysis reported that the sensitivity of leukocytosis (WBC>10,000/mm^3) in AA diagnosis was 83%, and specificity was 67%, while the sensitivity of neutrophilia (NEU>6,500/mm^3) ranged between 71-89% and specificity between 48-80% [24]. Guraya et al. [25] also stated that leukocytosis is frequently observed in AA patients. In our study, leukocytosis was observed in all patients diagnosed with AA. However, no statistically significant relationship was found in distinguishing CAA from NCAA (p=0.708).

NLR is used as an inflammatory marker that reflects the physiological leukocyte response [26,27]. Kahramanca et al. [28] reported that NLR could be used in both the diagnosis of appendicitis and the distinction between CAA and NCAA. However, in our study, NLR values were not found to be statistically significant in CAA patients (p=0.348).

In the study conducted by Yılmaz Ünal [29] the role of IG count and percentage in the diagnosis of CAA was investigated. This study reported that the sensitivity and specificity of IG count and percentage in CAA diagnosis were high (sensitivity 93% and specificity 93.8%) [29].

In the study by Turkes et al. [30], WBC, polymorphonuclear leukocyte, monocyte, IG count, and IG percentage were found to be significantly higher in CAA patients compared to AA patients (p=0.009, p=0.047, p=0.001, p=0.018, respectively). The negative predictive value of IG for AA was calculated as 85%, and this value was found to be the same as that of WBC [30].

In the study by Yazla et al. [31], IG percentage, IG count, WBC, and NEU values were reported to be significantly higher in CAA patients compared to the NCAA group (p<0.001). The specificity of IG percentage in predicting CAA was found to be 92.6%, while its sensitivity was 23.5%. The low sensitivity rate of IG percentage suggests that these parameters should be used in combination with clinical evaluation and other diagnostic methods [31]. Studies have shown that IG's sensitivity and specificity rates are variable, indicating the need for further research on IG in CAA diagnosis. These data suggest that IG alone is insufficient for detecting CAA and should be evaluated together with other inflammatory parameters. In our study, no statistically significant difference was found between the CAA and NCAA groups in terms of IG count and percentage (p=0.884 and p=0.374).

Study Limitations

Our study was designed retrospectively and observationally, which brings certain limitations. Firstly, the study was based on pathology reports and was conducted within a limited time frame, which may have contributed to the lack of statistical significance in the results. Additionally, only hemogram parameters obtained at the initial ED presentation were evaluated in our study. Possible changes in parameters after treatment could not be monitored. The time of surgical intervention following diagnosis was also not specified, and the risk of perforation and complications developing during this period was not considered. Furthermore, the duration of abdominal pain in patients presenting to the ED was not recorded, making it impossible to determine the stage of the inflammatory process they were at. These limitations should be taken into account when interpreting the results.

Conclusion

IG count and percentage is not an effective hemogram parameter in distinguishing between CAA and NCAA.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences Türkiye

Hamidiye Faculty of Medicine (decision number: 84, date: 20.08.2019).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.K., Concept: O.K., Design: O.K., Data Collection or Processing: O.K., G.K., Analysis or Interpretation: O.K., G.K., Ö.K., Literature Search: O.K., Ö.D., G.K., Writing: O.K., Ö.D.

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