ORIGINAL ARTICLE

The role of complete blood count parameters in diagnosing acute appendicitis and measuring the severity of inflammation

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ABSTRACT

BACKGROUND: The diagnosis and severity of acute appendicitis (AA) are still challenging despite all the improvements in diagnosis and treatment. This study aimed to evaluate the efficacy of complete blood count (CBC) parameters in diagnosing AA and measuring severity.

METHODS: Data of 521 patients were reviewed retrospectively. Fifty-three patients with CBC results influenced by various reasons were excluded from the study. Age, gender, length of stay, CBC parameters, and histopathological results were examined.

RESULTS: The study included 468 patients: 90 patients with a preliminary diagnosis of AA, not undergoing surgery but receiving medical treatment (Group I), 227 patients with uncomplicated appendicitis (Group II), and 151 patients with complicated appendicitis (Group III). Of the patients, 279 were male (59.6%) and 189 were female (40.4%). The mean age was 33.37±13.05 years. Groups I and III had the lowest and highest white blood cell (WBC), neutrophil, and neutrophil-to-lymphocyte ratio (NLR), respectively. There was a statistically significant difference between the groups ($p<0.05$). The highest and lowest mean platelet volume (MPV) values were in Groups II and III, respectively. There was no statistically significant difference between the groups ($p>0.05$).

CONCLUSION: AA is the most common cause of abdominal surgery. The CBC is a cost-effective and easily-accessible test with acceptable diagnostic accuracy. It provides fast results and can be used in the diagnosis of appendicitis. Neutrophil, WBC, and NLR are helpful and useful parameters for physical examination and other diagnostic methods in diagnosing AA and measuring severity. However, the use of MPV is not recommended as it has a low diagnostic rate and contradictory results.

Keywords: Acute appendicitis; leukocyte, neutrophil, neutrophil-to-lymphocyte ratio, mean platelet volume, severity of appendicitis.

INTRODUCTION

Acute appendicitis (AA) is the most common cause of abdominal surgery. Patients with AA typically experience abdominal pain, tenderness in the right lower quadrant, the presence of defense, and rebound tenderness on physical examination. However, the clinical diagnosis of AA can be difficult in women in the reproductive age group, children, and elderly. Thus, negative appendectomy rates can reach 20–30%.[1,2] Complications may develop in case of a delay in the diagnosis of AA. The incidence of complicated AA (perforation, gangrenous appendicitis, intra-abdominal abscess, plastron formation, and generalized peritonitis) is ranging from 20% to 30%. Complication increases the risk of morbidity and mortality. Due to these serious problems, early diagnosis and treatment of appendicitis are of great importance to prevent the development of complications.[3,4]

The definitive diagnosis of AA can only be made through histopathological examination. Thus, having a marker with a high diagnostic value that is cost-effective, easily accessible in health-care institutions, and can provide results fast

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will provide considerable convenience for physicians in establishing diagnosis before surgery. Predicting the perforation of appendicitis before the surgery with these markers is important to predict the treatment plan to be followed. [5] This study aimed to investigate the effectiveness of complete blood count (CBC) parameters, which were important markers in diagnosing AA and measuring its severity, were easily accessible in many healthcare institutions, and could be evaluated quickly.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of Erzurum Regional Training and Research Hospital. The data of 521 patients aged 17–65 years who were followed and operated with the preliminary diagnosis of AA between 20 August 2018 and 1 October 2019 were analyzed retrospectively. Fifty-three patients whose CBC measurements were influenced by reasons other than AA were excluded from the study (Table 6). A total of 468 patients who met the inclusion criteria were included in the study. The age, gender, length of stay, and CBC results of the patients were reviewed through the information management system (Kardelen software) of the hospital. The patients were divided into three groups, namely, control group, uncomplicated appendicitis group, and complicated appendicitis group. The CBC parameters were analyzed using a hematology analyzer (Cell-Dyn Ruby Hematology Analyzer).

Statistical Analysis

Descriptive data were expressed as mean and standard deviation for the numerical variables and as number and percentages for the categorical variables. The distribution of the data was examined with histogram graphics. Kruskal–Wallis Test and Tamhane test, a post hoc analysis, were used to analyze data. Receiver operating characteristic (ROC) curves were created to measure the ability of laboratory values to distinguish pathology positivity. The area under curve (AUC) and cutoff value of each measurement were determined. Sensitivity, specificity, and positive likely-hood ratio (LR+) cutoff values were calculated and evaluated together. P<0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 23.0 software.

RESULTS

The study included 468 patients. Of the patients, 279 were male (59.6%) and 189 were female (40.4%), with a mean age of 33.37±13.05 years. Patients were divided into three groups namely Group I including 90 patients who received outpatient or inpatient medical treatment with a preliminary diagnosis of AA (19.2%), Group II including 227 patients who were diagnosed with uncomplicated AA (inflamed, phlegmonous appendicitis) according to the histopathology result (48.5%), and Group III including 151 patients who were diagnosed with complicated AA (gangrenous, perforated, and plastron appendicitis) (32.3%) (Tables 1 and 2). Blood samples were collected from the patients at the time of admission to the emergency department. Three hundred patients were operated under general and 78 patients under spinal anesthesia. Operations were performed as open in 337 patients and laparoscopic in 41 patients. The length of stay in the hospital was 1.08/day in Group I, 1.94/day in Group II, and 2.56/day in Group III, respectively, in ascending order. There was a significant difference between the groups in terms of length of stay (p<0.001) (Table 3).

Eleven CBC parameters were evaluated. However, only the parameters with high diagnostic value were discussed. There was a significant difference between the groups in terms of white blood cell (WBC), neutrophil, neutrophil-to-lym-

Table 1. Gender distrubition and histopathologic features of patients

Features	n	%
Gender		
Male	279	59.6
Female	189	40.4
Histopathology		
Normal appendix	90	19.2
Uncomplicated acute appendicitis	227	48.5
Complicated acute appendicitis	151	32.3

Table 2. Demographic, clinical features and laboratory findings of patients

	Min	Max	Mean	SD
Age	18	65	33.37	13.05
Length of hospital stay/day	0	9	1.97	1.33
WBC (x10^3/µl)	2.40	26.70	13.12	4.06
NEU (x10^3/µl)	1.30	25.24	9.90	4.01
LYM (x10^3/µl)	0.40	9.80	2.19	0.92
MCHC (g/dl)	29.46	42.50	33.54	1.42
RDW (%)	9.60	25.29	11.83	1.44
PLT (x10^3)	78.57	473.50	252.50	63.99
MPV (fL)	5.24	16.20	7.93	1.36
PCT (%)	0.07	0.48	0.19	0.04
PDW (%)	11.70	24.60	19.73	1.67
PLR	32.75	744.20	135.28	72.77
NLR	0.17	31.29	5.62	4.16

SD: Standard deviation; NEU: Neutrophil; LYM: Lymphocyte; WBC: White blood cell; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; PLT: Platelet; MPV: Mean platelet volume; PCT: Plateletcrit; PDW: Platelet distribution width; PLR: Platelet lymphocyte ratio; NLR: Neutrophil-lymphocyte ratio; Min: Minimum; Max: Maximum.

phocyte ratio (NLR) values (p<0.05) whereas no significant difference was observed in terms of mean platelet volume (MPV) (p>0.05).

Some descriptive data of all patients are presented in Tables 1 and 2. The distribution of some numerical data according to the appendicitis pathology was examined. A significant difference was observed according to the pathology except MPV in all of the laboratory values given in Table 3. Post hoc analysis performed to evaluate the significance between the groups showed significant differences between patients with normal appendix and those with complicated and uncomplicated AA.

The ability of laboratory values to distinguish pathology positivity was investigated by creating ROC curves. Cut-off values and AUC of some values were determined and sensitivity, specificity, and LR+ cut-off values were calculated. The tables and graphs below present the results obtained from ROC analyzes performed separately for complicated and uncomplicated cases (Table 4 and Fig. 1). A separate ROC analysis was

Table 3. Comparison of demographic, clinical features and laboratory findings of patients

		n	Mean	SD	Minimum	Maximum	p-value
Age	Normal appendix	90	37.60	14.560	19	78	0.03
	Uncomplicated AA	227	32.23	12.174	16	68	
	Complicated AA	151	32.55	12.956	15	71	
	Total	468	33.37	13.051	15	78	
Length of hospital stay/ day	Normal appendix	90	1.08	1.538	0	6	<0.001
	Uncomplicated AA	227	1.94	.905	1	7	
	Complicated AA	151	2.56	1.450	1	9	
	Total	468	1.97	1.337	0	9	
White blood cell (x10^3/µl)	Normal appendix	90	10.05596	2.684047	4.465	15.450	<0.001
	Uncomplicated AA	227	12.50867	3.687139	4.636	26.700	
	Complicated AA	151	15.87217	3.581277	2.400	26.470	
	Total	468	13.12223	4.063467	2.400	26.700	
Neutrophil (x10^3/µl)	Normal appendix	90	6.96600	2.623254	2.560	12.180	<0.001
	Uncomplicated AA	227	9.23247	3.606232	2.400	21.900	
	Complicated AA	151	12.66207	3.597543	1.300	25.240	
	Total	468	9.90317	4.013037	1.300	25.240	
Mean platelet volume (fl)	Normal appendix	90	7.95014	1.354573	5.709	11.640	0.06
	Uncomplicated AA	227	8.11985	1.444752	5.244	16.200	
	Complicated AA	151	7.64048	1.200002	5.591	11.050	
	Total	468	7.93255	1.366397	5.244	16.200	
Neutrophil-lymphocyte ratio	Normal appendix	90	3.91818	2.789699	.716	16.226	<0.001
	Uncomplicated AA	227	4.85596	3.259286	.828	21.385	
	Complicated AA	151	7.79069	5.113433	.173	31.291	
	Total	468	5.62251	4.169884	.173	31.291	

AA: Acute appendicitis; SD: Standard deviation.

Table 4. Comparison of complicated and uncomplicated appendicitis groups

Parameters	Cut-off value	AUC (p)	Sensitivity (%)	Specificity (%)	+LR
WBC (x10^3/µl)	13.99	0.766 (<0.000)	73	72	2.65
Neutrophil (x10^3/µl)	10.89 (77.8%)	0.768 (<0.000)	72	73	2.73
MPV (fl)	7.68	0.404 (0.002)	44	59	0.75
NLR	5.08	0.720 (<0.000)	67	67	2.04

AUC: Area under the curve; +LR: Positive likelihood ratio; WBC: White blood cell; NEU: Neutrophil; NLR: Neutrophil-lymphocyte ratio; MPV: Mean platelet volume.

Table 5. Evaluation of patients with and without acute appendicitis

Parameters	Cut-off value	AUC (p)	Sensitivity (%)	Specificity (%)	+LR
WBC (x10^3/µl)	11.74	0.783 (<0.000)	71	71	2.47
NEU (x10^3/µl)	8.40 (71.5%)	0.773 (0.024)	70	70	2.33
MPV (fl)	7.78	0.501 (0.034)	46	53	1.07
NLR	3,79	0.681 (0.032)	64	66	1.92

AUC: Area under the curve; +LR: Positive likelihood ratio; WBC: White blood cell; NEU: Neutrophil; NLR: Neutrophil-lymphocyte ratio; MPV: Mean platelet volume.

Table 6. Exclusion criterias

Exclusion criteria	n	%
Patients over 65 years of age	12	22.6
Pathologies other than appendectomy during surgery	12	22.6
Pregnant women	12	22.6
Patients with malignant appendix histopathology result	9	17
Comorbid chronic diseases	6	11
Patients whose blood results could not be reached	2	3.8
Total number of patients	53	100

performed for patients diagnosed with appendicitis and those with normal appendix (Table 5 and Fig. 2).

DISCUSSION

AA is one of the most common emergencies requiring surgery, with a lifetime prevalence of 7%.[6,7] It is 1.4 times more common in men than in women.[8–10] In the literature, the mean age of patients with normal appendix, uncomplicated appendicitis, and complicated appendicitis varies 22.5–32.8 years, 21.2–35.1 years, and 25.4–43 years, respectively.[3,9,11–13] Compatible with the literature data, the mean age of the control group, which included patients with normal appendix receiving medical treatment, was 37.6 years, and the mean age of the patients with uncomplicated and complicated appendicitis was 32.23 and 32.55 years, respectively, in the present study. The age of patients in the complicated appendicitis group has been found to be younger than those in the literature since the incidence of complicated appendicitis is higher in the elderly patient population, but individuals over 65 years of age have been excluded from our study.

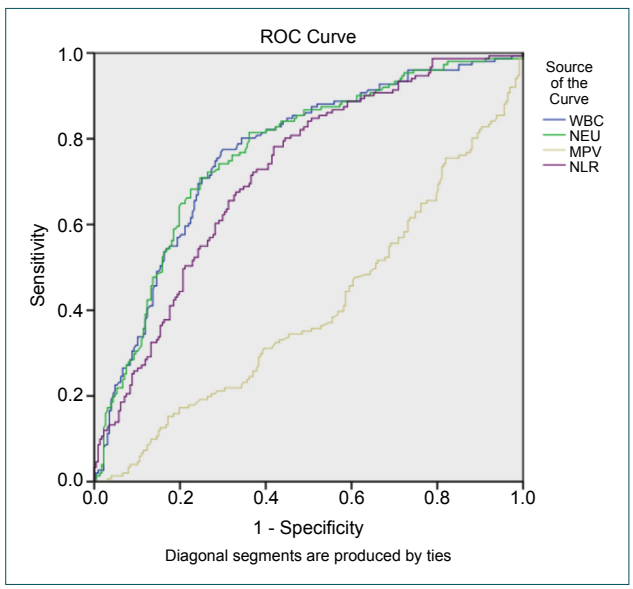

Figure 1. ROC analysis for complicated and uncomplicated cases. ROC: Receiver operating characteristic.

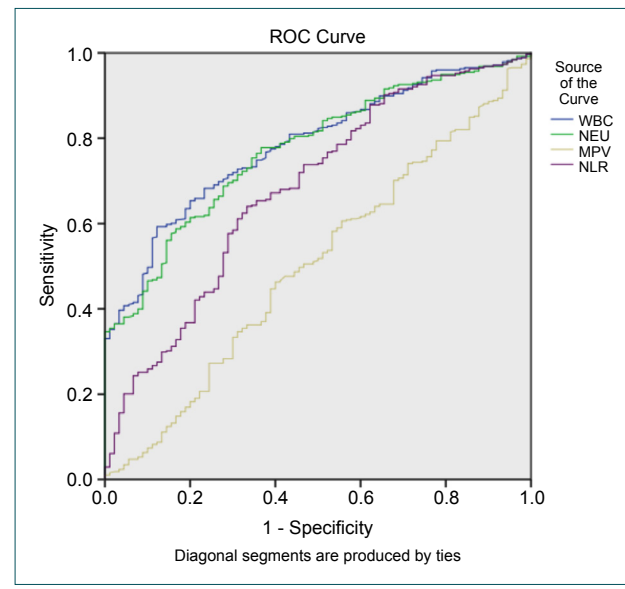

Figure 2. ROC analysis for those with appendicitis and those without appendicitis. ROC: Receiver operating characteristic.

Anamnesis, physical examination, laboratory tests, and imaging techniques are used in the diagnosis of AA. Accurate diagnosis of AA is of vital importance. If the diagnosis is delayed, AA inflammation progresses to abscess formation or perforation with widespread peritonitis whereas an unnecessary laparotomy poses a 5% risk of developing intestinal obstruction after surgery.[11,14] The complicated form of appendicitis increases both the length of stay in the hospital and cost.[15] In the present study, the length of hospital stay in the complicated appendicitis group was longer and there was a significant difference between the groups in this regard ($p<0.001$).

Early diagnosis of AA can prevent perforation, abscess formation, and post-operative complications, and decrease the length of stay and cost burden accordingly. However, the diagnosis of AA is still challenging despite all the studies conducted.[16] In particular, surgeons working in rural areas may not easily access to advanced imaging methods such as ultrasonography or computed tomography to establish a diagnosis.[17] This has led researchers to search for easily accessible and cost-effective markers that can be used for the early diagnosis of the disease.[13,17,18] The CBC is an ideal marker in terms of the features mentioned above. It is a test that can be easily accessed and evaluated quickly in health-care institutions, particularly in emergency departments. Parameters of CBC have been investigated in various studies and are used in the diagnosis of diseases.[10,13,17–19] White blood cell count parameters vary depending on the presence of hematological diseases, allergic diseases, malignancies, inflammatory diseases, and use of medication, or according to the patient groups such as pregnant women and elderly patients.[20,21] It is necessary to exclude these patient groups to correctly evaluate the effect of CBC values in patients with AA; however, these patient groups are excluded in a limited number of studies. About 10% of patients were excluded from the present study (Table 6). This study is also important in this aspect. There is a need for more comprehensive studies considering these criteria.

The WBC count has been reported to be higher in patients with AA than those with normal appendix[12] in patients with complicated appendicitis than those with uncomplicated appendicitis.[11,14] Studies have reported that WBC has a sensitivity and specificity of 67–97.8% and 31.9–81%, respectively, in the diagnosis of AA when the cut-off value is set at 10–12.08.[3,11,22–24] In a meta-analysis study, the sensitivity and specificity of WBC for diagnosis of AA have been found to be 83% and 67%, respectively, when the cut-off value is set at >10.[25] When the cut-off value is set at 14.45–15.8, WBC has been found to have the sensitivity, specificity, and LR+ of 67–75%, 59.9–70.2%, and 1.62, respectively, in the differential diagnosis of complicated and uncomplicated appendicitis.[19,20] Similar to the literature, WBC levels in the present study were higher in patients with a normal appendix, those with uncomplicated appendicitis and those with complicated appendicitis, respectively. We found that WBC had the sensitivity, specificity, and LR+ of 71%, 71%, and 2.65 (AUC=0.78), respectively, when the cut-off point was set at 11.74, compatible with the literature data. The sensitivity and specificity were found to be 73% and 72% (AUC=0.76) when WBC cut-off value was taken as 13.99 in the comparison of complicated and uncomplicated groups. The diagnostic value rates were very close to the group involving patients with and without appendicitis. According to these results, the likelihood of AA increases as the WBC value increases and if the values are higher, the risk of complicated AA becomes higher. Therefore, it can be said that WBC values play an important role in determining the severity of AA. The cut-off value of WBC was taken as 11 in our laboratory where blood samples were analyzed. As in some studies, the rate of diagnostic values in our study will be higher based on these values.

The neutrophil value, a WBC component, is a good diagnostic marker used in the diagnosis of AA.[14] In a meta-analysis involving 14 studies, the neutrophil count was measured to be >6500/mm^3 in the diagnosis of AA, and sensitivity and specificity were found to be 71–89% and 48–80%, respectively.[25] In other studies, the neutrophil count was reported to have a sensitivity and specificity of 78.8–98.9% and 25–76.9% when the cut-off point was taken as 6.9–9.3 in the diagnosis of AA.[1,11,26,27] In a study by Ayrık et al.,[11] the sensitivity, specificity, and LR+ of the neutrophil value were reported as 54%, 59.8%, and 1.34, respectively, when the cut-off value was taken as 9.84 in the differential diagnosis of complicated and uncomplicated appendicitis. The present study has revealed that AA diagnosis can be made for a neutrophil value >71.5. The diagnostic value of neutrophil value in the differentiation between normal appendix and AA cases is similar to its diagnostic value in the differentiation between uncomplicated and complicated appendicitis cases. When the neutrophil cut-off value was taken as 8.4 in diagnosing AA, sensitivity and specificity were found to be 70% and 70% (AUC=0.77), respectively. A statistically significant difference was found between the AA group and the control group without appendicitis ($p<0.05$). The sensitivity and specificity were found to be 72% and 73% (AUC=0.77) in the evaluation of complicated and uncomplicated patients when the cut-off value was set at 10.89. There was a statistically significant difference between the patient groups in measuring the severity of the complicated AA ($p<0.001$). Although the neutrophil sensitivity was found to be relatively lower than the literature, the specificity values were higher.

Neutrophilia and lymphocytopenia are cellular response elements in systemic inflammation. The increase in the difference between neutrophil and lymphocyte reflects the severity of the inflammatory response. Therefore, NLR has been used as a marker in many pathological conditions such as malignancies, chronic inflammatory diseases, and post-operative complications for many years.[28] The NLR value has been

used as a more sensitive parameter than WBC in many studies for many years. Different cut-off values were determined for NLR and its sensitivity and specificity in the diagnosis of AA were found to be 44–92.5% and 22–59.3%, respectively.[13,17,29,30] Similarly, sensitivity, specificity, and LR+ were found to be 61–78.4%, 41.7–61%, and 1.56 when the cut-off value of NLR was set at 5.5–6.94 in the differential diagnosis of uncomplicated and complicated appendicitis.[13,17,20] In the present study, when NLR cut-off value was taken as 3.79 in the differential diagnosis of AA, sensitivity, specificity, and LR+ were found to be 64%, 66%, and 1.92 (AUC=0.68), respectively, and a statistically significant difference was observed between Group I and Group II ($p<0.05$). When the cut-off value was set at 5.08, sensitivity, specificity, and LR + values of NLR in the differential diagnosis of complicated AA were found to be 67%, 67%, and 2.04, respectively (AUC=0.72). A significant difference was observed between Group II and Group III ($p<0.001$). In contrast to the literature, although NLR values in our study have a slightly lower diagnostic value than WBC values sensitivity rates have been similar to the literature and specificity rates have been higher than the literature.

MPV, which has been frequently studied in recent years and easily accessible in routine CBC measurements, is a marker of platelet size and functions. It has been studied as a diagnostic or prognostic parameter in various inflammatory and thrombotic diseases.[22,31] However, whether a high MPV value or a low MPV value has a diagnostic value in AA has not been clarified yet. In the literature, MPV levels have been reported to be significantly higher in the AA group than in the control group, with a sensitivity of 66% and specificity of 51%.[32,33] However, there are also studies reporting higher MPV levels in the control group than in the AA group. In these studies, the sensitivity and specificity of MPV have been found to be 73% and 54%, respectively. There was a significant difference between the groups in terms of MPV values.[34,35] In the study by Leader et al.,[36] the clinical value of MPV was reported to be limited although there were statistically significant differences. These results show that MPV levels vary in AA cases and do not have a diagnostic advantage over other parameters of CBC. In the present study, the highest and lowest MPV values were in the uncomplicated appendicitis group and the complicated group, respectively. When the cut-off value was set at 7.78, MPV was found to have a sensitivity and specificity of 46% and 53% (AUC=0.5) in the differential diagnosis of AA. There was no statistically significant difference between the groups in terms of MPV values ($p>0.05$). When the cut-off point was set at 7.68, MPV was found to have a sensitivity and specificity of 44% and 59% (AUC=0.4) in the comparison of complicated and uncomplicated appendicitis groups. A statistically significant difference was observed between the groups ($p<0.05$). In this study, although there was a significant difference between complicated and uncomplicated appendicitis groups, AUC value, sensitivity and specificity values were found to be low. Furthermore, MPV value was found to be lower in the patient group with normal appendix than in the AA group although it was expected to decrease as the severity of complication increased. Therefore, we don't recommend the use of MPV in the diagnosis for the diagnosis of AA and the determination of the severity of inflammation as it provides contradictory results and has low diagnostic rates.

Conclusion

The diagnosis of AA, which is a common disease, is still difficult. There is no gold standard test to predict AA and its complications. However, CBC is a cost-effective test that is easily accessible by almost all physicians, provides rapid results, and has acceptable diagnostic efficiency. Neutrophil, WBC, and NLR, which are among the CBC parameters, can be considered as a useful variable that helps physical examination and other diagnostic methods in diagnosing AA and predicting uncomplicated and complicated appendicitis. We do not recommend the use of MPV as a diagnostic marker due to its low diagnostic rates reported in many studies and conflicting results between groups.

Ethics Committee Approval: This study was approved by the Health Sciences University Erzurum Regional Training and Research Hospital Ethics Committee (Date: 02.12.2019, Decision No: 2019/15-142).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Akut apandisit tanısını koymada ve ciddiyetini belirlemede hemogram parametre değerlerinin rolü

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AMAÇ: Tanı ve tedavideki tüm gelişmelere rağmen akut apandisitin tanısının ve ciddiyetinin değerlendirilmesi halen zor olabilmektedir. Bu çalışmada, birinci basamak sağlık kuruluşlarında dahil rahatça ulaşılabilen ve hızlıca sonuçlanan hemogram parametrelerinin akut apandisitin tanısı ve hastalığın ciddiyetini ortaya koymadaki etkinliğini değerlendirmeyi amaçladık.
GEREÇ VE YÖNTEM: Beş yüz yirmi bir hasta geriye dönük incelendi. Çeşitli sebeplerle hemogram sonucunu etkileyen 53 hasta çalışma dışı bırakıldı. Hastaların yaş, cinsiyet, hastanede yatış süresi, hemogram alt parametreleri ve histopatolojik sonuçları incelendi.
BULGULAR: Çalışmada 468 hasta incelendi. Hastaların 279'u erkek %59.6, 189'u kadın %40.4 olup tüm hastaların yaş ortalaması 33.37±13.05 yıl idi. Akut apandisit ön tanısıyla ameliyat yapılmayıp tıbbi tedavi uygulanan 90 hasta (grup I), akut apandisit tanısı alan nonkomplike 227 apandisit (grup II), komplike apandisit 151 (grup III) olarak üç grup halinde incelendi. beyaz kan hücresi (WBC), nötrofil, nötrofil-lenfosit oranı (NLR) değerleri en az grup I'de, en fazla grup III'te görüldü. Gruplar arasında istatiksel olarak anlamlı fark saptandı ($p<0.05$). ortalama trombosit hacmi (MPV) değerleri en fazla grup II'de en az grup III'de görüldü. Gruplar arasında istatiksel anlamlı fark saptanmadı ($p>0.05$).
TARTIŞMA: Akut apandisit karnın en sık görülen cerrahi hastalığıdır. Hemogram hemen tüm sağlık kuruluşlarında kolay ulaşabilen, hızlı sonuçlanan, maliyet etkin ve kabul edilebilir düzeylerde tanısal etkinliği olan hastalığın tanısında kullanılabilen bir testtir. Hemogram parametrelerinden WBC, nötrofil, NLR akut apandisit tanısı koymada ve şiddetini belirlemede fiziki muayene ve diğer tanı yöntemlerine yardımcı ve kullanışlı değişkenlerdir. Ancak MPV değerinin düşük tanısal oranları ve çelişkili sonuçları nedeniyle kullanımını önermiyoruz.
Anahtar sözcükler: Akut apandisit; apandisitin ciddiyeti; lökosit; MPV; NLR; nötrofil.

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