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Investigation of Systemic Immune Inflammatory Index and Other Complete Blood Parameters in Cases with Amoebiasis

Amoebiasisli Olgularda Sistemik İmmüno Enflamatuvar İndeks ve Diğer Tam Kan Parametrelerinin Araştırılması

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ABSTRACT

Objective: *Entamoeba histolytica* is a major parasitic cause of acute gastroenteritis. In this study, hematological inflammatory indices were assessed in adhesin-positive amoebiasis cases.
Methods: Adhesin test results and hemogram parameters were evaluated simultaneously in cases who were referred to Necmettin Erbakan University Faculty of Medicine, Medical Parasitology laboratory with suspicion of amoebiasis and whose *Entamoeba histolytica* specific adhesin enzyme-linked immunosorbent assay test was found to be positive between January 2022 and December 2023. In this study, the indices were calculated using haemogram parameters. Age- and sex-matched groups were formed, consisting of cases with adhesin test-positive acute gastroenteritis (APAG) and those with adhesin test-negative acute gastroenteritis (ANAG). In addition to common statistical analyses, the diagnostic performance of various hematologic inflammatory parameters in predicting adhesin positivity was evaluated by receiver operating characteristic analysis.
Results: The results of 340 cases were analyzed, including 136 cases under the age of 18. Blood lymphocyte and monocyte levels were significantly lower in the APAG group compared to the ANAG group (p=0.004 and p=0.048, respectively), while no significant differences were observed in the remaining haemogram parameters. There was also no statistically significant difference in C-reactive protein levels between the groups (p=0.061). Among the calculated indices, only the platelet-to-lymphocyte ratio (PLR) showed a significant difference between groups (p=0.017). In the gender-based subgroup analysis of the APAG group, red blood cell levels were found to be lower in female cases (p=0.026), while no significant differences were observed in the calculated indices.
Conclusion: This study evaluated the predictive performance of various hematologic inflammatory parameters in determining adhesin test positivity. Although the PLR showed a statistically significant difference between groups, the positive and negative predictive values of all evaluated parameters remained moderate. These findings suggest that the diagnostic utility of these biomarkers is limited.
Keywords: Amoebiasis, adhesin test, SIRI, PLR, NLR

ÖZ

Amaç: *Entamoeba histolytica*, akut gastroenteritlerin önde gelen paraziter etkenlerinden biridir. Bu çalışmada, adezin pozitif amoebiasis olgularında hematolojik enflamatuvar indeksler değerlendirilmiştir.
Yöntemler: Ocak 2022-Aralık 2023 tarihleri arasında Necmettin Erbakan Üniversitesi Tıp Fakültesi, Tıbbi Parazitoloji laboratuvarına amibiyazis şüphesi ile gönderilen ve *Entamoeba histolytica* spesifik adezin enzim bağlı immünosorbent analiz testi pozitif bulunan hastalarda adezin test sonuçları ve hemogram parametreleri eş zamanlı olarak değerlendirilmiştir. Bu çalışmada, indeksler hemogram parametreleri kullanılarak hesaplanmıştır. Adezin testi pozitif akut gastroenterit (APAG) ve adezin testi negatif akut gastroenterit (ANAG) hastalarından oluşan, yaş ve cinsiyet açısından eşleştirilmiş gruplar oluşturulmuştur. Genel istatistiksel analizlere ek olarak, çeşitli hematolojik enflamatuvar parametrelerin adezin pozitifliğini öngörmedeki tanısal performansı alıcı işletim karakteristiği analizi ile değerlendirilmiştir.
Bulgular: Çalışmada 136'sı 18 yaş altı olmak üzere 340 hastanın sonucu incelenmiştir. APAG grupta kan lenfosit ve monosit düzeyleri ANAG gruba göre anlamlı olarak (p=0,004, p=0,048, sırasıyla) düşük bulunurken, kalan hemogram parametrelerinde farklılığa rastlanmamıştır. C-reaktif protein düzeyinde de istatistiksel olarak fark tespit edilmemiştir (p=0,061). Platelet lenfosit

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oranı (PLR) indeksinde iki grup arasındaki fark anlamlı bulunurken (p=0,017) diğer indekslerde gruplar arasında anlamlı farklılık saptanmamıştır. APAG grubunun cinsiyete dayalı alt grup analizinde, kırmızı kan hücresi seviyeleri kadın hastalarda daha düşük bulunurken (p=0,026), hesaplanan diğer indekslerde anlamlı bir farklılık gözlenmemiştir.

Sonuç: Bu çalışmada, çeşitli hematolojik enflamatuvar parametrelerin adezin pozitifliğini öngörme performansları değerlendirilmiştir. Her ne kadar PLR indeksinde gruplar arası fark saptansa da genel olarak tüm parametrelerde pozitif ve negatif prediktif değerler orta düzeyde kalmaktadır. Bu sebeple, söz konusu biyobelirteçlerin tanısal performansının kısıtlı olduğu sonucuna varılmıştır.

Anahtar Kelimeler: Amibiyazis, adezin test, SIRI, PLR, NLR

INTRODUCTION

Amebiasis is a communicable enteric parasitic infection caused by *Entamoeba histolytica (E. histolytica)* (1). It is predicted that approximately 50 million individuals worldwide, particularly in developing countries, are affected by *E. histolytica*, with almost 100,000 of these resulting in death (1,2). The primary route of transmission of *E. histolytica* is the ingestion of food or water contaminated with amebic cysts (1). In developed countries, where water- and food-borne transmission is rare, sexually transmitted infections among men who have sex with men have also been reported (3). Most *E. histolytica* infections are asymptomatic; however, individuals on immunosuppressive therapy, pregnant women, and infants are at higher risk of developing invasive disease, which may include dysentery or extra-intestinal manifestations such as amebic liver abscesses (1,3).

Asymptomatic patients typically show normal colonoscopic findings and no history of bloody stools. Diagnostic microscopy, including observation of erythrocyte-engulfed trophozoites, may not always detect infection (4). Direct microscopy is often used as the initial diagnostic step due to its low cost, practicality, and accessibility. However, differentiation of pathogenic *E. histolytica* from the non-pathogenic *E. dispar* is essential, as reliance on microscopy alone can result in diagnostic errors (4,5). Modern serological tests offer high sensitivity and specificity, allow differentiation from non-pathogenic species, and can process large numbers of samples rapidly, making them especially useful during outbreaks (6).

Prompt diagnosis and treatment of *E. histolytica* are essential to prevent complications and reduce mortality (7,8). Although serological and molecular methods with higher sensitivity and specificity are available, traditional fecal microscopy remains the most commonly used diagnostic approach worldwide (9). However, this method cannot reliably distinguish *E. histolytica* from other non-pathogenic Entamoeba species, leading to false-positive results and missed asymptomatic cases. Therefore, practical and cost-effective supplementary diagnostic parameters are needed (6-9).

Hemogram-derived indices, including mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), have emerged as accessible and cost-effective markers of systemic inflammation (10-12). These parameters have been increasingly studied in various infectious and inflammatory conditions due to their ability to reflect the balance between different immune cell populations and platelet activity. Evidence on the utility of these indices in parasitic infections is limited (13-15), though they could help assess inflammation and severity in amoebiasis.

In *E. histolytica* infection, neutrophils constitute the first line of defense, contributing to parasite clearance through phagocytosis, degranulation, and the formation of neutrophil extracellular traps (16). However, trophozoites can interact with β_2 integrins on the neutrophil surface, triggering a phosphatidylinositol 3-kinase dependent pathway that leads to excessive reactive oxygen species generation and subsequent neutrophil apoptosis. This mechanism allows the parasite to effectively counteract neutrophil-mediated killing, facilitating tissue invasion and immune evasion. Monocytes also play a central role in the early innate immune response against *E. histolytica*, contributing to phagocytosis, cytokine-mediated inflammation, and the recruitment of other immune cells, while the parasite employs monocyte locomotion inhibitory factor and additional mechanisms to suppress monocyte activity and facilitate tissue colonization (17).

Despite the established role of neutrophils in amoebiasis (16,17), no studies have directly evaluated NLR or related indices as diagnostic or prognostic markers. Since excessive neutrophil activation contributes to tissue injury and inflammation, composite markers such as SII (platelet×neutrophil/lymphocyte) and SIRI (neutrophil×monocyte/lymphocyte) (11-14) may serve as practical tools to estimate inflammatory burden and disease severity in amoebiasis, especially in resource-limited settings.

In this planned study, the properties of haemogram-derived indices as inflammatory markers in adult and paediatric cases with adhesin test positive *E. histolytica* infection will be investigated.

METHODS

Population of Study and The Ethical Approval

This study was conducted with the approval of Necmettin Erbakan University Drug and Non-Medical Device Research Ethics Committee (decision no: 2025/5656, date: 21.03.2025).

In this study, the adhesin test results and hemogram parameters [e.g., neutrophils (10^3/µL), lymphocytes (10^3/µL), monocytes (10^3/µL), platelets (10^3/µL)] of the cases who were referred to the Medical Parasitology Laboratory of Necmettin Erbakan University Medical Faculty for testing between January 2022 and December 2023 with suspicion of amoebiasis were examined simultaneously.

Between these dates, cases with acute gastroenteritis were assigned to the adhesin test-positive acute gastroenteritis (APAG) or adhesin test-negative acute gastroenteritis (ANAG) group according to fecal adhesin antigen results. Cases with positive adhesin test results were evaluated with age- and sex-matched controls and compared with blood parameters. Fecal samples from (range 0-86 years) 204 adult and 136 paediatric cases were included in the study. The study design was retrospective, and the necessary information was obtained from the hospital record system.

E. histolytica was detected in fresh stool samples using the commercial immunoassay Entamoeba CELISA Path (Cellabs Pty Ltd., Australia), which has high sensitivity and specificity. Stool

samples were analyzed strictly according to the manufacturer's instructions without any modifications. The kit's performance has been previously validated, showing sensitivities ranging from 93% to 100% and specificities from 93% to 100% across studies involving 44 to 757 fecal specimens, with comparisons made against culture or Zymodeme methods. Results were interpreted following the recommended cut-offs, and all assays were performed under standardized laboratory conditions. This test provides rapid detection of the adhesin of *E. histolytica* in fecal samples. In spectrophotometric measurement, samples with optical density$_{450}$≥0.150 are considered "positive." An automated analyzer was used to detect hemogram parameters.

The indices were calculated using the following formulas (11-14):

NLR: Neutrophil count/lymphocyte count

LMR: Lymphocyte count/monocyte count

Monocyte-to-lymphocyte ratio (MLR): Monocyte count/lymphocyte count

PLR: Platelet count/lymphocyte count

SIRI: Neutrophil count×monocyte count/lymphocyte count

SII: Platelet count×neutrophil count)/lymphocyte count

MPVPCR: Mean platelet volume/platelet count ratio

Statistical Analysis

Tests were selected based on the normality of the numerical data (assessed by the Shapiro-Wilk test) and whether the data were paired. For numerical data, t-tests were used to compare two independent groups if the data were normally distributed, and ANOVA was used to compare more than two groups. In paired data, repeated measures ANOVA was used. When data were not normally distributed, the Wilcoxon rank test for two groups or the Kruskal-Wallis test for more groups was used. For categorical data, chi-square tests were used if the number of cell counts was sufficient, and Fisher's exact test was implemented for small sample sizes. In all tests, $p<0.05$ is statistically significant was considered statistically significant.

In this study, the diagnostic performances of various haematological inflammatory parameters in predicting adhesin positivity were evaluated by receiver operating characteristic (ROC) analysis. In ROC analysis, the diagnostic discriminative power of a parameter is expressed by the "area under the curve (AUC)" value. An AUC value close to 0.5 indicates that the question test is indistinguishable from random guessing in terms of discriminative power, while an AUC value close to 1.0 indicates high discriminative power.

RESULTS

The study included 340 participants, 169 women (49.71%) and 171 men (50.29%). The mean age of those included in the study was 29.83±24.83 years (range 0-86; median 26), 136 were <18 years, and 204 were ≥18 years. No significant difference was found in terms of age and gender differences for amoebiasis cases (p>0.999). A total of 340 cases were included in the study and equally divided into two groups according to the adhesin test results: adhesin-negative (ANAG, n=170) and adhesin-positive (APAG, n=170). The comparison of hematological and inflammatory parameters between the groups is presented in Table 1. Although the C-reactive protein (CRP) level was slightly higher in the APAG group compared to the ANAG group, the difference was not statistically significant (p=0.061). Lymphocyte counts (×10^3/µL) were significantly higher in the adhesin-negative group compared to the adhesin-positive group (p=0.004). Monocyte counts (×10^3/µL) were also significantly higher in the adhesin-negative group (0.79±0.54) than in the adhesin-positive group (0.69±0.39) (p=0.048). No statistically significant differences were observed between the groups for other hematological parameters, including white blood cell (WBC), neutrophil, red blood cell (RBC), hematocrit, mean corpuscular volume (MCV), red cell distribution width (RDW), platelet, MPV, hemoglobin (Hb), and platelet distribution width values (p>0.05 for all).

When the indexes in both groups are examined, PLR was found to be significantly higher in the APAG group compared to those with the ANAG group [Wilcoxon test (W)=12212, p=0.017]. Nevertheless, there was no statistically significant difference in the LMR, MLR, MPVPCR, NLR, SII, and SIRI indexes obtained from haemogram between APAG and ANAG groups (Table 2).

In the adhesin-negative group, there were 84 females (49.7%) and 86 males (50.3%), while in the adhesin-positive group, there were 85 females (50.3%) and 85 males (49.7%). Considering the values of haemogram parameters among the amoebiasis cases, only the RBC value was found to be significantly higher in male sex than in female sex (W=2897, p=0.026). Similarly, there was no significant difference in CRP values between male and female cases with amoebiasis (p=0.849). There was no difference in the values of haemogram derivative indexes; NLR (p=0.747), PLR (p=0.855), MLR (p=0.286), LMR (p=0.176), MPVPCR (p=0.421), SII (p=0.756), and SIRI (p=0.807) between male and female amoebiasis cases.

Of 170 cases with positive adhesin test, 102 were ≥18 years of age and 68 were <18 years of age. Significant differences were observed between adult and paediatric amoebiasis cases in neutrophil (p=0.029), lymphocyte (p=0.013), eosinophil (p=0.031), MCV (<0.001), and MPV (p=0.04) values. Lymphocytes were higher in patients under 18, while the other parameters were higher in adults. Significant age-related differences were found in all haemogram-derived indices. NLR (W=2253, p=0.000), PLR (W=2841, p=0.046), MLR (W=2355.5, p=0.000), MPVPCR (W=2630, p=0.008), SII (W=2447, p=0.001), and SIRI (W=2276, p=0.000) were significantly higher in adults, while LMR was higher in patients under 18 years (W=4376.5, p=0.001).

According to the findings of the analysis, PLR showed a statistically significant difference with AUC=0.576 (p=0.016). The 95% confidence interval of PLR is between 0.515-0.637, and although it has statistical significance, the low AUC value indicates that it is not a clinically powerful marker. When the AUC values of other indexes were examined, AUC=0.551 for NLR (p=0.103), AUC=0.530 for MLR (p=0.338), AUC=0.470 for LMR (p=0.338), AUC=0.518 for MPVPCR (p=0.565), AUC=0.529 for SII (p=0.354), and AUC=0.513 for SIRI (p=0.689). In all of these parameters, AUC values did not show statistical significance and were found to be very close to 0.5 (Table 3 and Figure 1).

Additionally, this study evaluated the predictive performance of various haematological inflammatory parameters for adhesin positivity by ROC analysis. The most appropriate cut-off points for each parameter were determined by ROC analysis according to Youden index and diagnostic accuracy measures were calculated. In the results obtained with ROC analysis, SII has the highest sensitivity with 50.6%, and LMR has the highest specificity with

Table 1. Comparison of haemogram values according to adhesin test results

	Overall (n=340)	ANAG (n=170)	APAG (n=170)	p
CRP				0.061
Mean	28.59±50.33	26.57±50.53	30.61±50.19	
WBC				0.425
Mean	8.79±4.2	9.04±4.25	8.54±4.16	
Neutrophils (10^3/uL)				0.706
Mean	5.45±3.43	5.55±3.55	5.36±3.32	
Neutrophils (%)				0.166
Mean	59.24±17.46	58.14±16.57	60.35±18.28	
Lymphocytes (10^3/uL)				0.004
Mean	2.4±1.74	2.58±1.73	2.23±1.73	
Lymphocytes (%)				0.034
Mean	29.25±15.78	30.83±15.33	27.67±16.11	
Monocytes (10^3/uL)				0.048
Mean	0.74±0.47	0.79±0.54	0.69±0.39	
Monocytes (%)				0.312
Mean	9.28±7.94	9.88±9.65	8.68±5.7	
Eosinophils (10^3/uL)				0.514
Mean	0.18±0.4	0.16±0.17	0.21±0.53	
Eosinophils (%)				0.722
Mean	2.09±3.22	1.92±2.15	2.26±4.01	
Hb (g/dL)				0.325
Mean	12.35±2.33	12.47±2.33	12.22±2.33	
RBC (10^6/uL)				0.106
Mean	4.51±0.84	4.57±0.8	4.44±0.87	
HCT (%)				0.067
Mean	37.96±8.14	38.79±9.04	37.13±7.06	
MCV (fL)				0.911
Mean	84.31±8.94	84.09±8.85	84.54±9.05	
RDW (%)				0.414
Mean	16.04±21.82	14.96±2.81	17.11±30.74	
PLT (10^3/uL)				0.164
Mean	306.82±133.76	320.17±141.45	293.55±124.65	
MPV (10^3/uL)				0.087
Mean	10.08±1.33	10.21±1.06	9.96±1.56	
PDW (fL)				0.150
Mean	11.53±2.46	11.67±2.19	11.39±2.71	

ANAG: Adhesin test-negative acute gastroenteritis, APAG: Adhesin test-positive acute gastroenteritis, CRP: C-reactive protein, WBC: White blood cell, Hb: Hemoglobin, RBC: Red blood cell, HCT: Haemotocrit, MCV: Mean corpuscular volume, RDW: Red cell distribution width, PLT: Platelet, MPV: Mean platelet volume, PDW: Platelet distribution width

95.3% among the other indexes. Positive and negative predictive values were calculated at rates close to each other for all indexes (Table 4).

DISCUSSION

E. histolytica is an important cause of morbidity and mortality, especially in developing tropical regions with poor sanitation (18). There is currently no effective vaccine for prevention. The diagnosis of intestinal amoebiasis is based on clinical symptoms and laboratory diagnosis. Traditional methods, immunological tests, and molecular modalities are used in diagnosis. Microscopic evaluation is the primary used method throughout the world because it is relatively cheap, easy, and accessible. Another commonly used method is the identification of *E. histolytica* specific antigens by enzyme-linked immunosorbent assay (ELISA)

Table 2. The comparison of haemogram-derived inflammatory indices according to adhesin test result

	Overall (n=340)	ANAG (n=170)	APAG (n=170)	p
NLR				0.091
Mean	8.2±73.75	11.21±103.9	5.19±9.91	
PLR				0.017
Mean	211.59±415.96	156.45±101.86	266.41±574.16	
MLR				0.394
Mean	0.51±1.08	0.39±0.32	0.64±1.48	
LMR				0.338
Mean	3.78±2.82	3.85±2.98	3.71±2.65	
MPVPCR				0.578
Mean	0.04±0.04	0.04±0.05	0.04±0.03	
SII				0.323
Mean	2611.33±26836.57	3807.11±37810.59	1415.56±3485.33	
SIRI				0.764
Mean	5.06±34.55	6.13±47.78	3.99±10.49	

ANAG: Adhesin test-negative acute gastroenteritis, APAG: Adhesin test-positive acute gastroenteritis, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, MPVPCR: Mean platelet volume/platelet count ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index

Table 3. Area under the curve values calculated for haemogram-derived indices

Test result variable(s)	Area	Standard error	p	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
NLR	0.551	0.031	0.103	0.490	0.613
PLR	0.576	0.031	0.016	0.515	0.637
MLR	0.530	0.032	0.338	0.468	0.592
LMR	0.470	0.032	0.338	0.408	0.532
MPVPCR	0.518	0.032	0.565	0.456	0.580
SII	0.529	0.031	0.354	0.468	0.591
SIRI	0.513	0.032	0.689	0.451	0.574

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, MPVPCR: Mean platelet volume/platelet count ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index

tests. The advantage of these tests is that they are largely capable of distinguishing between *E. histolytica* and non-pathogenic *E. dispar*. In addition, the sensitivity of ELISA tests is 80-94% and specificity ranges from 94-100%, which means that perform better than microscopic and culture methods (19-20). Although the sensitivity of molecular and serological diagnostic methods for the determination of intestinal amoebiasis is quite high, microscopic examination is widely used especially in developing countries. Haemogram parameters may be useful in diagnosing symptomatic cases of amoebiasis wherever access to advanced laboratory facilities is limited (19).

Platelet size has been shown to represent platelet function. It appears to be a beneficial predictive and prognostic biomarker in cardiovascular disorders, rheumatological diseases and cancers. Evidence from the literature demonstrates that MPV can reveal valuable data on the outcome and prognosis of various pathological disorders, for instance cardiovascular illnesses, respiratory disorders, rheumatological diseases and malignancies (21). In preliminary studies, MPV was evaluated as a positive acute phase reactant, whereas in some studies it was reported as a negative acute phase reactant. Turhan et al. (22) detected much higher MPV levels in the inactive hepatitis B group compared to the controls. In one former investigation, it was observed that while platelet count decreased in the first three days of infection, MPV value increased significantly in patients with sepsis caused by Gram-positive bacteria (23). On the contrary, Mete et al. (24) reported that MPV value was significantly lower in children with rotavirus gastroenteritis compared to the control group. In another study, increased platelet counts and lower MPV levels were determined in patients with amoebiasis compared to the control group (25). In a current study conducted in Türkiye, with adult amoebiasis cases, MPV level was detected to be lower than the control, but the difference found statistically insignificant (26). In our study, similar to the previous study, mean MPV levels were found decreased in the APAG group compared to the ANAG group, but this difference was not statistically significant (p=0.087). This result suggests

that low MPV level may be associated with increased platelet activation in cases with amoebiasis, but it is not possible to reach a definite conclusion due to the small sample size in order to reach statistically significant results. Similar to the data of Tatliparmak et al. (26), no significant difference was found between APAGs and ANAG group in terms of CRP value and WBC count in our study. Furthermore, in our study, blood monocyte, and lymphocyte levels among haemogram parameters were found to be statistically lower in the APAG group. These findings could suggest that host innate and adaptive immune system cells play important roles together in the elimination of *E. histoloytica* trophozoites. Macrophages, well known as the tissue form of monocyte cells in the blood, are actively involved in host defense in intestinal amoebiasis. Macrophages activated with interferon-gamma released by lymphocytes, show amoebicidal activity with the nitric oxide that they produce (27). It is thought that macrophages are localized in the intestinal tissue and therefore blood monocyte levels are low in our cases with intestinal amoebiasis.

Figure 1. Predictive values of some complete blood count parameters and hemogram-derived markers for amoebiasis

ROC: Receiver operating characteristic, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, MPVPCR: Mean platelet volume/platelet count ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index

The difference in RBC values between male and female patients is most likely due to physiological and hormonal factors rather than amoebiasis. Males generally have higher erythrocyte and Hb levels because androgens stimulate erythropoiesis, while menstrual blood loss plays only a minor role (28,29). Therefore, the sex-based variation in RBC values observed in this study is considered a normal physiological finding rather than a disease-related alteration.

In accordance with the recent literature findings, the levels of indices such as SII, SIRI, PLR and NLR, which are calculated from hemogram parameters, has shown an elevated level in bacterial infections (12,23,30). In one recent study, NLR was reported as a potential biomarker for disease severity and mortality in COVID-19 patients (31). In a former study including viral, bacterial and parasitic gastroenteritis cases, the lowest NLR value was found in the viral group, while the difference in level of the NLR between the groups was not significant (32). A recent study in children with rotavirus gastroenteritis reported that higher values of NLR and PLR were related to hospitalization severe clinical course and enhanced inflammation (33). Studies in parasitic infections have demonstrated the clinical relevance of hemogram-derived indices. In children with malaria, NLR and MLR were significantly higher in complicated cases compared to uncomplicated ($p=0.023$) and healthy groups ($p<0.001$), and both indices correlated positively with parasite density ($r=0.623$, $p=0.022$) (13).

Similarly, another study (34) showed that malaria patients had higher systemic inflammatory biomarkers (NLR, MLR, PLR) than healthy individuals, with NLR exhibiting excellent diagnostic accuracy (AUC=0.937; sensitivity 86.7%, specificity 92.0%), highlighting its potential as a simple and cost-effective marker of inflammation and disease severity in parasitic infections.

Additionally, platelet parameters such as platelet count and plateletcrit (PCT) were significantly altered, with platelet count and PCT together serving as highly sensitive and specific markers for malaria diagnosis (99.0% and 95.0%, respectively), underscoring the utility of hemogram and platelet indices as cost-effective indicators of disease severity in endemic areas (35). In patients with schistosomiasis mansoni, splenomegaly was found to be directly associated with hematological alterations, including thrombocytopenia, leukopenia, and anemia, indicating the diagnostic and prognostic value of blood indices in parasitic diseases (36).

It has been reported that cases with hepatic alveolar echinococcosis with low preoperative NLR and PLR values have a superior 5-year survival in compared to cases with high values. In these cases, the lower SII values have been associated with a better prognosis (37).

Table 4. Sensitivity, specificity, PPV and NPV values of diagnostic parameters according to ROC analysis results

Parametre	Cut-off	Sensitivite	Spesifite	PPV	NPV
NLR	5.019	0.247	0.876	0.667	0.538
PLR	164.796	0.471	0.716	0.625	0.573
MLR	0.506	0.259	0.824	0.595	0.526
LMR	7.581	0.089	0.953	0.652	0.513
MPVPCR	0.034	0.5	0.559	0.531	0.528
SII	696.576	0.506	0.582	0.548	0.541
SIRI	2.002	0.371	0.682	0.538	0.52

PPV: Positive predictive value, NPV: Negative predictive value, ROC: Receiver operating characteristic, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, MPVPCR: Mean platelet volume/platelet count ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index

In previous research, NLR, MLR, PLR, and SII rates were observed to be positively correlated with malaria parasitaemia (38). In a retrospective study investigating *Enterobius vermicularis*-associated appendicitis in comparison to acute appendicitis, no statistically significant differences were identified in commonly used inflammatory markers, including CRP, WBC, RDW, lymphocyte, and neutrophil counts, NLR, monocyte and eosinophil counts, platelet, and PLR ($p>0.05$). However, the SII was found to be significantly lower in pediatric patients with Enterobius-associated appendicitis. Histopathological examination further revealed that most of these patients exhibited no evidence of inflammation in their biopsy specimens (39). Hematological indices such as NLR and PLR, previously shown to correlate with disease severity in malaria, also hold potential as accessible markers in amebiasis. In malaria, elevated NLR and MLR were associated with higher parasite densities and complicated cases, demonstrating their utility in early risk stratification and monitoring therapeutic response (13).

Similarly, in amebiasis, these ratios may reflect systemic inflammation and immune-mediated alterations, providing adjunctive information beyond conventional diagnostic methods. However, their clinical applicability is limited. Despite PLR reaching statistical significance in our study (AUC=0.576, p=0.016), the overall low AUC values of PLR and other hematological indices (NLR, MLR, LMR, MPV/PC, SII, SIRI) highlight their limited clinical relevance, indicating that these parameters may assist in evaluating *E. histolytica* infections but are insufficient as independent diagnostic tools. Factors such as variable cut-off values, demographic differences, comorbid conditions, nutritional status and methodological inconsistencies further restrict their standalone use (40). Therefore, while NLR and PLR can serve as supportive markers, they should complement, rather than replace, standard diagnostic approaches, and further research is needed to validate their routine application in parasitic infections like amebiasis.

To our knowledge, there are no previous studies directly comparing age-related differences in immune or inflammatory responses in amoebiasis. However, the observed differences in haemogram-derived indices between paediatric and adult cases in our study may reflect the maturation and functional shifts of the immune system that occur with age. Higher NLR, PLR, MLR, SII, and SIRI values in adults suggest a more pronounced innate and proinflammatory response, whereas higher LMR values in younger patients may indicate a relatively stronger adaptive lymphocyte-mediated activity. These findings may therefore represent age-dependent variations in the host's immune response to *E. histolytica* infection.

Numerous studies are available for the prognostic use of indices derived from haemogram parameters in a wide range of conditions, including bacterial infections, sepsis, cancer, and autoimmune diseases (11,12,23,30,31). Nevertheless, there are limited number of analyses investigating these parameters in parasitic infections (13-15). To the best of our knowledge, this is the first study evaluating the biomarker potential of NLR, PLR, MLR, LMR SII, SIRI indices in the differentiation of cases with amoebiasis from healthy controls. In the present study, PLR was observed to be significantly elevated in the APAG group, aligning with the findings of Idemudia et al. (38), who demonstrated a positive correlation between PLR and malaria parasitemia. The lack of significant differences in parameters such as NLR, SII, SIRI, MLR, and LMR may be attributed to the fact that intestinal amebiasis typically presents as a localized disease, without inducing a marked systemic inflammatory response.

Study Limitations

The study's insights should be interpreted within the context of several inherent limitations, including its retrospective design, limited sample size, and the insufficient data regarding extraintestinal involvement in amoebiasis cases. Furthermore, the lack of standardized cut-off values for inflammatory indices, the single-center nature of the study, and the absence of testing for other viral or bacterial gastroenteritis pathogens may have influenced the results. A further limitation is that observed differences in RBC, neutrophil, lymphocyte, eosinophil, MCV, and MPV across sex and age groups likely reflect normal physiological variation rather than amoebiasis-related changes. Changes in NLR, PLR, SIRI and SII are not specific to *E. histolytica* infection and may be influenced by other conditions. Therefore, relying solely on these biomarkers could lead to misclassification of patients, especially in cases with other enteric infections or inflammatory diseases.

Nevertheless, the key strength of this study is that, to the best of our knowledge, it is the first to investigate contemporary hemogram-derived indices, such as the SIRI and the SII, in the context of diagnosing a pathogen as prevalent as *E. histolytica*. This study can contribute a valuable foundation for future research in the field.

CONCLUSION

In conclusion, while only monocyte, lymphocyte, and PLR levels were found to be statistically significant among the hematological inflammatory parameters evaluated in the study, these biomarkers alone do not demonstrate sufficient sensitivity and specificity in predicting adhesin positivity. Therefore, to increase the prediction accuracy, comprehensive studies are needed in larger patient groups, where clinical findings are standardized and other causes of gastroenteritis are excluded.

*Ethics

Ethics Committee Approval: This study was conducted with the approval of Necmettin Erbakan University Drug and Non-Medical Device Research Ethics Committee (decision no: 2025/5656, date: 21.03.2025).

Informed Consent: Informed consent was not obtained because this was a retrospective study using previously collected data.

*Authorship Contributions

Surgical and Medical Practices: S.U., F.E.T., Concept: S.U., F.E.T., Design: S.U., F.E.T., Data Collection or Processing: S.U., B.Y., Analysis or Interpretation: S.U., F.E.T., Literature Search: S.U., Writing: S.U., F.E.T.

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