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Predictive Factors for Acute and Complicated Appendicitis in Children: A Prospective Study

Çocukluk Yaş Grubunda Akut ve Komplike Apandisit Tanısında Prediktif Faktörlerin Belirlenmesi: Prospektif Bir Çalışma

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Abstract

Introduction: Acute appendicitis is one of the most common surgical emergencies in children, where early diagnosis is crucial to reducing morbidity and mortality. This study aimed to identify predictive factors for appendicitis and evaluate the diagnostic value of serum sodium and blood and urine ketone levels.

Methods: This prospective study included patients under 18 years of age who presented with acute abdominal pain and were clinically suspected of having appendicitis. Patients were divided into two groups: appendicitis and non-appendicitis. The appendicitis group was further categorized into acute and complicated cases. Demographic data, clinical symptoms, physical examination findings, symptom duration, preoperative laboratory values, blood and urine ketone levels, and pathology results were recorded.

Results: A total of 153 patients were included [100 with appendicitis (51 complicated) and 53 non-appendicitis]. In the appendicitis group, leukocyte count, neutrophil count, C-reactive protein (CRP), blood ketones [area under the curve (AUC)=0.618], and urine ketones (AUC=0.627) were significantly higher (p<0.001, p<0.001, p=0.001, p=0.03, and p=0.04, respectively). Among patients presenting within 24 hours of symptom onset, leukocyte count (p=0.013), neutrophil count (p=0.014), and blood ketones (p=0.035) were significantly higher in the appendicitis group. For patients with symptom duration longer than 24 hours, leukocyte count (p=0.005), neutrophil count (p=0.001), and CRP levels (p=0.001) were significantly elevated, while serum sodium levels were significantly lower (p=0.046) in appendicitis cases.

Öz

Giriş: Akut apandisit, çocuklarda en sık görülen cerrahi acil durumlardan biridir. Morbidite ve mortaliteyi azaltmak için erken tanı kritik öneme sahiptir. Bu çalışmanın amacı, apandisit için öngörücü faktörleri belirlemek ve serum sodyum ile kan ve idrar keton düzeylerinin tanı değerini değerlendirmektir.

Yöntemler: Çalışmaya, akut karın ağrısı ile başvuran ve fizik muayenede apandisit şüphesi olan 18 yaş altı hastalar ileriye dönük olarak dahil edildi. Hastalar apandisit olanlar ve olmayanlar olarak gruplandırıldı; apandisit olanlar da kendi içinde akut ve komplike apandisit olarak ayrıldı. Demografik veriler, semptomlar, fizik muayene bulguları, semptom süresi, ameliyat öncesi laboratuvar sonuçları, kan ve idrar keton düzeyleri ve patoloji raporları kaydedildi.

Bulgular: Çalışmaya toplam 153 hasta dahil edildi [100 apandisit (51 komplike) ve 53 apandisit olmayan]. Apandisit grubunda lökosit, nötrofil, C-reaktif protein (CRP), kan ketonları [eğri altında kalan alan (AUC)=0,618] ve idrar ketonları (AUC=0,627) düzeyleri anlamlı derecede yüksekti (sırasıyla p<0,001, p<0,001, p=0,001, p=0,03, p=0,04). Semptom süresi <24 saat olan hastalarda apandisit grubunda lökosit (p=0,013), nötrofil (p=0,014) ve kan ketonu (p=0,035) anlamlı olarak yüksek bulundu. Semptom süresi >24 saat olan hastalarda ise apandisit grubunda lökosit (p=0,005), nötrofil (p=0,001), CRP (p=0,001) anlamlı olarak yüksek, sodyum (p=0,046) anlamlı olarak düşük bulundu.

Sonuç: Çalışmamızda apandisitli çocuklarda kan ve idrar keton düzeyleri anlamlı olarak yüksek bulundu. Kan keton düzeyi özellikle

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Abstract

Conclusion: In our study, blood and urine ketone levels were significantly elevated in children with appendicitis. Blood ketones appeared particularly useful in early-stage presentations, whereas CRP elevation and decreased serum sodium were more prominent in delayed cases.

Keywords: Appendicitis, children, emergency, sodium, ketones

Öz

erken başvurularda faydalı olurken CRP artışı ve serum sodyum düşüklüğü hastaneye başvuru süresi uzadıkça daha anlamlı hale geldi.

Anahtar Kelimeler: Apandisit, çocuklar, acil, sodyum, keton

Introduction

Acute appendicitis (AA) is the most common non-traumatic surgical emergency in children.[1] However, diagnosing AA in pediatric patients can be particularly challenging due to non-specific clinical signs, a broad differential diagnosis of abdominal pain, and young children's limited ability to communicate symptoms or cooperate during physical examinations. Despite advancements in laboratory tests, imaging modalities, and clinical scoring systems, diagnostic delays, misdiagnoses, and unnecessary appendectomies still occur.

As a result, there is ongoing research to identify alternative biomarkers that may improve diagnostic accuracy for pediatric appendicitis. Recent studies suggest that, in addition to commonly used markers such as C-reactive protein (CRP), white blood cell (WBC) count, and absolute neutrophil count (ANC), hematological indices like the neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR) may serve as valuable diagnostic tools.[2,3] With the growing interest in conservative management approaches, there is an increasing need to distinguish complicated appendicitis (CA) from AA cases early in the clinical course.

Several studies examining hematological parameters in appendicitis have highlighted immune response patterns, particularly elevated neutrophil and monocyte counts in CA. Monocytes, as part of the innate immune system, tend to increase in inflammatory states, while lymphocyte counts-associated with adaptive immunity-often decline during infections. A decrease in lymphocytes has been linked to appendicitis and appears more pronounced in complicated cases.[4,5] These findings help explain the frequent observation of elevated NLR and decreased LMR in patients with appendicitis.

Hyponatremia has also been identified as a potential marker for CA.[2,6,7] Although the exact mechanism remains unclear, it is thought to involve systemic inflammation and the release of proinflammatory cytokines such as interleukin (IL)-1β and IL-6, which stimulate the secretion of antidiuretic hormone (ADH). These cytokines may cross the blood-brain barrier and activate neurons in the supraoptic and paraventricular nuclei, leading to non-osmotic ADH release, increased water reabsorption in renal tubules, and subsequent dilutional hyponatremia.[8]

During acute stress, when glucose reserves are rapidly depleted, ketone bodies become an alternative energy source for the brain and other tissues.[9] In children with appendicitis, elevated ketone levels may result from increased catabolism, vomiting, fasting, and dehydration. While urinary ketones correlate with serum levels, renal function may influence ketone excretion, potentially limiting their diagnostic reliability. Thus, evaluating both serum and urine ketone levels is necessary; however, only a few studies have investigated the association between ketosis and appendicitis in children.[10-12]

The aim of this study was to evaluate the diagnostic value of leukocyte, neutrophil, lymphocyte, and monocyte counts; CRP and procalcitonin (PCT) levels; NLR and LMR; and, in particular, serum sodium and blood/urine ketone levels in predicting appendicitis in pediatric patients.

Materials and Methods

Study Population

This single-center, prospective case-control study was conducted between April 2022 and October 2023. Pediatric patients under 18 years of age who presented to the Aydın Adnan Menderes University Faculty of Medicine, Department of Pediatric Emergency with an annual patient volume of approximately 30.000-were evaluated for inclusion. Eligible patients had acute abdominal pain and a clinical suspicion of appendicitis based on physical examination findings and a pediatric appendicitis score (PAS) greater than 3.[13] The following data were collected for each patient: socio-demographic characteristics, vital signs, physical examination findings, symptom duration, PAS value, serum sodium levels, WBC, ANC, absolute lymphocyte and monocyte counts, NLR, LMR, CRP, PCT, serum and urine ketone levels, surgical notes, pathology reports, length of hospital stay, and postoperative complications.

While some patients underwent surgical intervention, others were observed and subsequently discharged. For discharged patients, families were contacted within one month to

confirm whether surgery had been performed at another facility. The "non-appendicitis" group included patients who were discharged without surgery or underwent negative appendectomy. Patients with histopathologically confirmed appendicitis were further categorized into either AA or CA. CA was defined as cases involving perforation, gangrenous appendix, intra-abdominal abscess, or peritonitis.

Exclusion criteria included: prior appendectomy, abdominal trauma, malignancy, inflammatory bowel disease, Familial Mediterranean Fever, chronic systemic illness, long-term medication use, or administration of intravenous fluids containing dextrose and/or saline prior to laboratory evaluation.

Biochemical Analysis

Routine laboratory assessments at our institution included complete blood count, serum sodium, and CRP levels. Diagnostic thresholds were defined as follows: leukocytosis >10.000/mm^3, neutrophilia >7.500/mm^3, and hyponatremia <135 mEq/L. Blood samples for ketone [β-hydroxybutyrate (β-OHB)] and PCT analyses were centrifuged at 4.500 rpm for 10 minutes. Serum and urine samples were stored at -80 °C until analysis. Ketone levels were measured using the Cayman β-OHB (ketone body) colorimetric assay kit (item no: 700190). PCT levels were measured using the Abbott Alinity autoanalyzer, based on the chemiluminescent microparticle immunoassay principle.

Statistical Analysis

Sample size estimation was performed using G*Power software. Based on the association between appendicitis and serum sodium levels, a minimum of 128 patients was required to achieve a statistical power of 95% with a 5% significance level.

Statistical analyses were conducted using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages. Continuous variables with normal distribution were presented as mean ± standard deviation (SD), while non-normally distributed variables were reported as median and interquartile range (25th-75th percentiles). Comparisons between groups were made using the chi-square test for categorical variables, Student's t-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed variables. Pearson's correlation test was used for parametric data, while Spearman's rank correlation was applied for non-parametric data. A p-value <0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic and exclusionary performance of numerical variables, including sensitivity, specificity, and cut-off values.

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from parents or legal guardians prior to participation. Ethical approval was obtained from the Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine (approval no: 2022/62, date: 07.04.2022).

Results

Of the 169 eligible patients who presented with acute abdominal pain, physical examination findings suggestive of appendicitis, and a PAS greater than 3, a total of 153 patients were included in the final analysis (Figure 1). One patient in the observation group underwent surgery for ovarian torsion at our institution, and another was operated for AA at a different hospital one week later.

In the appendicitis group, the male-to-female ratio was 1.9:1, and the mean ± SD age of the patients was 132.3±45.5 months. No statistically significant difference was observed between the appendicitis and non-appendicitis groups (p=0.336 and p=0.111, respectively) and the AA and CA groups (p=0.536 and p=0.158, respectively) in terms of age or gender. The median PAS was significantly higher in patients with appendicitis compared to those non-appendicitis (p<0.001), and also significantly higher in patients with CA compared to those with AA (p=0.006).

Serum sodium, CRP, and hemogram parameters were studied for all 153 patients. However, additional serum samples were obtained from 115 patients (66 from the appendicitis group and 49 from the non-appendicitis group) for serum ketone and PCT analysis. β-OHB levels were measured in all 115 samples, and PCT levels were analyzed in 106 of them. Additionally, urine samples for β-OHB analysis were obtained from 83 patients (42 appendicitis and 41 non-appendicitis).

The laboratory findings are presented in Table 1. Patients in the appendicitis group had significantly higher values for WBC, ANC, monocyte count, leukocytosis, neutrophilia, NLR, CRP, and both serum and urine ketone levels, while LMR was significantly lower. The corresponding p-values were: p<0.001, p<0.001, p=0.028, p=0.003, p<0.001, p<0.001, p=0.001, p=0.032, p=0.047, and p=0.010, respectively. When comparing AA and CA subgroups, LMR was significantly higher in the AA group (p=0.006), whereas leukocytosis and CRP were significantly elevated in the CA group (p=0.011 and p<0.001, respectively).

ROC curve analysis demonstrated that a blood ketone level ≥0.205 mmol/L predicted appendicitis with a sensitivity of 63.6% and specificity of 58.3% [area under the curve (AUC: 0.618); 95% confidence interval (CI: 0.512-0.723); p=0.032].

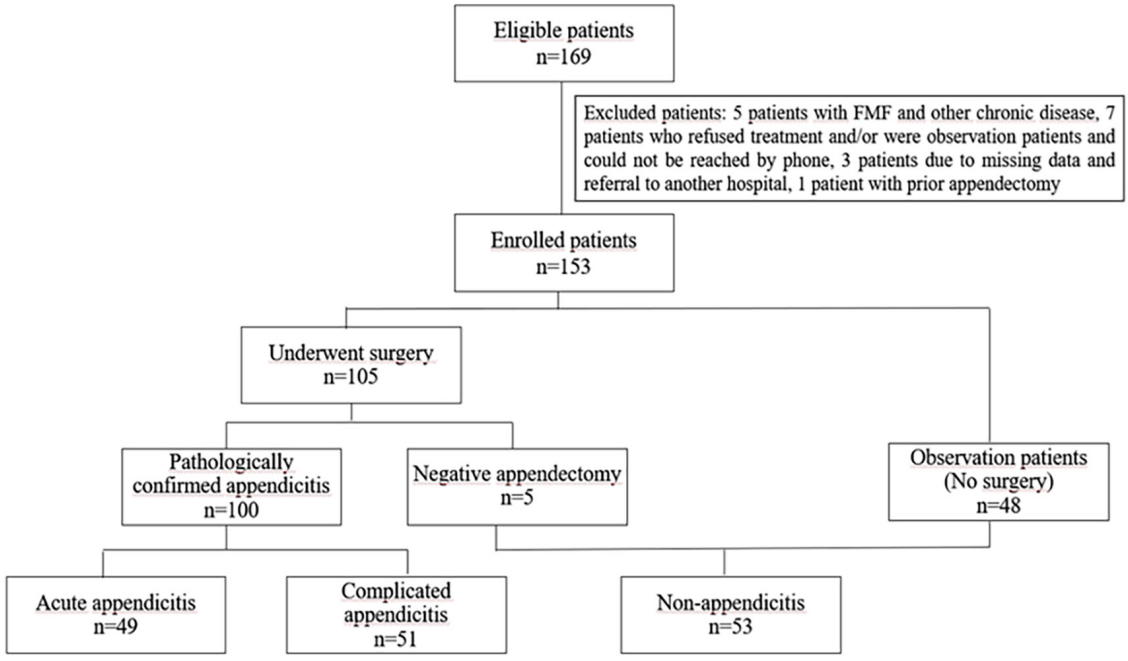

Figure 1. Flowchart of patients
FMF: Familial Mediterranean Fever

Table 1. Laboratory characteristics of the cases

	Appendicitis (n=100)	Non-appendicitis (n=53)	p-value	AA patients (n=49)	CA patients (n=51)	p-value
WBC (cells/mm³)	15510.00 (12790.00-19650.00)	12340.00 (8960.00-16180.00)	**<0.001***	15057.76±5113.43	16900.98±5006.49	0.072
ANC (cells/mm³)	12500.00 (9885.00-16380.00)	9300.00 (5220.00-12210.00)	**<0.001***	12204.49±5031.06	13849.22±4675.36	0.093
Leukocytosis (>10.000/mm³)	88 (88.0)	36 (67.9)	**0.003***	39 (79.6)	49 (96.1)	**0.011***
Neutrophilia (>7.500/mm³)	88 (88.0)	33 (62.3)	**<0.001***	40 (81.6)	48 (94.1)	0.055
Lymphocytes (cells/mm³)	1700.00 (1050.00-2225.00)	1770.00 (1340.00-2510.00)	0.073	1788.37±800.56	1680.39±838.98	0.512
Monocytes (cells/mm³)	1025.00 (775.00-1335.00)	860.00 (680.00-1100.00)	**0.028***	910.00 (740.00-1140.00)	1200.00 (850.00-1520.00)	0.005
NLR	7.53 (5.22-12.72)	4.79 (2.30-7.96)	**<0.001***	6.64 (4.11-12.03)	8.36 (5.65-14.22)	0.106
LMR	1.61 (1.04-2.28)	1.98 (1.29-3.22)	**0.010***	1.94 (1.11-2.55)	1.47 (0.76-1.96)	**0.006***
CRP (mg/L)	34.65 (8.55-89.50)	8.00 (2.00-68.10)	**0.001***	17.10 (4.60-37.60)	63.80 (24.90-144.60)	**<0.001***
PCT (ng/mL)	0.06 (0.02-0.18)	0.07 (0.02-0.20)	0.976	0.04 (0.02-0.17)	0.09 (0.03-0.19)	0.173
Serum sodium (mEq/L)	137.00 (135.00-138.50)	137.00 (136.00-139.00)	0.063	136.70±2.50	135.89±3.56	0.187
Hyponatremia (<135 mEq/L)	24 (24.0)	8 (15.1)	0.197	8 (16.3)	16 (31.4)	0.078
Blood ketone (mmol/L)	0.27 (0.18-0.38)	0.18 (0.15-0.28)	**0.032***	0.24 (0.18-0.35)	0.36 (0.19-0.38)	0.173
Urine ketone (mmol/L)	0.36 (0.13-0.45)	0.20 (0.09-0.39)	**0.047***	0.37 (0.12-0.49)	0.35 (0.15-0.44)	0.879

Categorical data is summarized as n (%), and numerical data is summarized as mean ± SD or median (25^{th}-75^{th} percentiles)
*: p<0.05, AA: Acute appendicitis, CA: Complicated appendicitis, WBC: White blood cell, ANC: Absolute neutrophil count, NLR: Neutrophil-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, CRP: C-reactive protein, PCT: Procalcitonin, SD: Standard deviation

Similarly, a urine ketone level ≥0.280 mmol/L predicted appendicitis with 59.5% sensitivity and 55.0% specificity (AUC: 0.627; 95% CI: 0.506-0.749; p=0.032) (Figure 2).

Blood ketone positivity was observed in 63.6% (n=42) of appendicitis patients compared to 41.7% (n=20) of non-appendicitis patients, and this difference was statistically significant (p=0.020; Table 2). Furthermore, in the AA subgroup, blood ketone levels showed a significant positive correlation with the length of hospital stay (r=0.428, p=0.013).

When patients were grouped based on symptom duration, those presenting within 24 hours and diagnosed with appendicitis had significantly higher WBC (p=0.013), ANC (p=0.014), and blood ketone levels (p=0.035). Among patients with symptoms lasting more than 24 hours, WBC (p=0.005), ANC (p=0.001), and CRP (p=0.001) levels were significantly higher in the appendicitis group, while serum sodium levels were significantly lower (p=0.046) (Table 3).

Regarding pre-hospital medication use, there was no significant difference in antibiotic or analgesic use between the appendicitis and non-appendicitis groups. However, analgesic use prior to admission was significantly more common in the CA group compared to the AA group (p=0.016).

Discussion

AA is one of the most common surgical emergencies in pediatric emergency departments. Clinicians rely on a combination of history, physical examination, laboratory tests, and imaging to assess the likelihood of appendicitis. However, ongoing diagnostic challenges underscore the need for reliable, objective biomarkers. This study aimed to evaluate the predictive value of leukocyte, neutrophil, lymphocyte, and monocyte counts; CRP, PCT; NLR, LMR; serum sodium; and blood/urine ketone levels in pediatric appendicitis.

Delayed hospital presentation, diagnostic uncertainty, and anatomical variability contribute to an increased incidence of CA in children. While previous studies have reported CA rates ranging from 18.7% to 45.6%,[2,7,12,14,15] we observed a higher rate of 51%. This may be attributable to our hospital's status as a tertiary referral center, where more complex or delayed cases are commonly managed.

Consistent with prior literature, we found that symptom duration significantly influenced disease severity. In our cohort, patients presenting more than 24 hours after symptom onset had a 3.2-fold increased risk of CA. Furthermore, our findings suggest that pre-hospital analgesic use may contribute to diagnostic delay and an increased risk of complications.

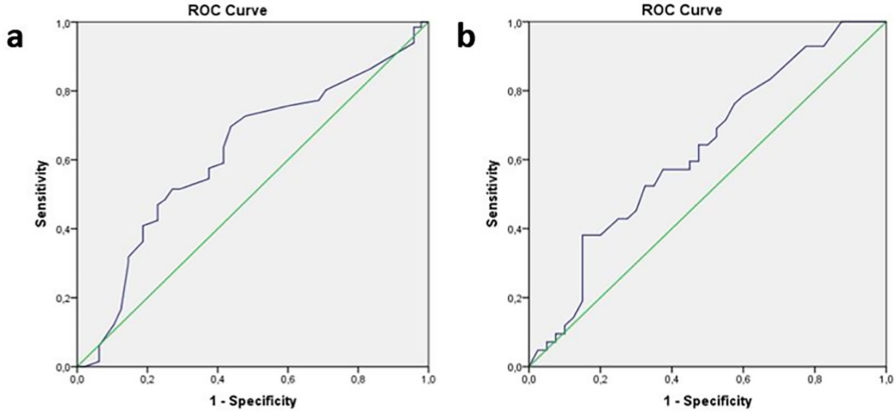

Figure 2. ROC analysis graph of ketone levels between patients with and without appendicitis
a: Blood ketone levels, b: Urine ketone levels, ROC: Receiver operating characteristic

Table 2. Comparison of blood and urine ketone elevation between patients with and without appendicitis according to the cut-off values determined by ROC analysis

		Appendicitis	Non-appendicitis	p-value
Blood ketone n (%)	**Absent**	24 (36.4)	28 (58.3)	**0.020***
	Present	42 (63.6)	20 (41.7)	
Urine ketone n (%)	**Absent**	17 (40.5)	22 (55.0)	0.188
	Present	25 (59.5)	18 (45.0)	

Categorical data is summarized as n (%)
*: p<0.05, ROC: Receiver operating characteristic

Table 3. Comparison of laboratory data between patients with and without appendicitis based on symptom onset time

	First 24 hours			After 24 hours		
	Appendicitis (n=43)	**Non-appendicitis (n=24)**	**p-value**	**Appendicitis (n=57)**	**Non-appendicitis (n=29)**	**p-value**
PAS	7.00 (6.00-8.00)	4.00 (4.00-5.00)	**<0.001***	8.00 (7.00-9.00)	5.00 (4.00-6.00)	**<0.001***
WBC (cells/mm³)	16190.00±4914.05	13233.75±5326.42	**0.025***	15852.81±5305.34	12439.31±5699.12	**0.007***
ANC (cells/mm³)	13516.74±4862.80	10250.42±5443.24	**0.014***	12060.00 (9930.00-15840.00)	9300.00 (4870.00-10590.00)	**0.001***
Lymphocytes (cells/mm³)	1460.00 (980.00-2090.00)	1575.00 (1120.00-2305.00)	0.460	1827.54±818.10	2169.66±812.42	0.070
Monocytes (cells/mm³)	870.00 (740.00-1090.00)	850.00 (695.00-1025.00)	0.628	1220.00 (870.00-1450.00)	940.00 (620.00-1170.00)	**0.014***
Platelets (cells/mm³)	286255.81±74682.53	311750.00±85580.50	0.208	284000.00 (249000.00-340000.00)	260000.00 (210000.00-313000.00)	**0.014***
NLR	8.41 (5.67-15.62)	7.60 (2.07-11.48)	0.082	6.86 (5.21-10.22)	3.65 (2.30-6.33)	**<0.001***
LMR	1.96 (1.09-2.48)	1.95 (1.04-3.12)	0.628	1.47 (1.00-2.04)	2.04 (1.41-3.43)	**0.002***
CRP (mg/L)	11.70 (3.80-32.50)	3.85 (2.00-27.70)	0.092	81.20 (33.60-146.50)	23.30 (2.30-72.80)	**0.001***
PCT (ng/mL)	0.03 (0.02-0.09)	0.05 (0.02-0.14)	0.299	0.11 (0.04-0.43)	0.08 (0.03-0.27)	0.351
Sodium (mEq/L)	137.00 (135.00-139.00)	137.00 (136.00-139.00)	0.640	137.00 (133.00-138.00)	137.00 (136.00-139.00)	**0.046***
Blood ketone (mmol/L)	0.24 (0.18-0.37)	0.18 (0.15-0.25)	**0.035***	0.31 (0.15-0.38)	0.20 (0.17-0.36)	0.233
Urine ketone (mmol/L)	0.36 (0.14-0.48)	0.23 (0.08-0.41)	0.180	0.33 (0.11-0.44)	0.17 (0.10-0.37)	0.173

Categorical data is summarized as n (%), and numerical data is summarized as mean ± SD or median (IQR: 25-75)
*: p<0.05, PAS: Pediatric appendicitis score, WBC: White blood cell, ANC: Absolute neutrophil count, NLR: Neutrophil-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, CRP: C-reactive protein, PCT: Procalcitonin, SD: Standard deviation, IQR: Interquartile range

WBC, ANC, CRP, and PCT

Leukocytosis and a left shift are classical laboratory findings in appendicitis, with elevated WBC and ANC observed in approximately 96% of pediatric cases.[16,17] Numerous studies have demonstrated significantly higher WBC, ANC, and CRP levels in patients with appendicitis, supporting their diagnostic value.[12,14,15] Our results are consistent with these findings, showing elevated levels of WBC, ANC, and CRP, along with pronounced leukocytosis and neutrophilia.

Although PCT is considered a sensitive and specific marker for bacterial infections, its utility in appendicitis remains debated. While some studies report significantly elevated PCT levels in appendicitis,[12,14] our findings-similar to those of Ulusoy et al.[15] did not demonstrate a significant difference between the appendicitis and non-appendicitis groups.

One of the key clinical challenges is predicting complications such as perforation and abscess formation preoperatively. Some studies have shown higher WBC and ANC levels in CA compared to AA,[2,7,12,15] whereas others have not found statistically significant differences.[6,14,18] In our study, while WBC and ANC values did not differ significantly between AA and CA, the prevalence of leukocytosis (WBC >10.000/mm³) was significantly higher in the CA group. According to a meta-analysis by Yu et al.[19], CRP and PCT are better suited to predict CA than AA. In our cohort, CRP was significantly higher in the CA group, whereas PCT showed no significant variation. These findings support the notion that while PCT may have some value in identifying CA, it is less reliable than CRP or WBC in diagnosing appendicitis in general. Thus, routine use of PCT for diagnosis in pediatric appendicitis may not be justified.

We also evaluated biomarker dynamics based on symptom duration. As expected, WBC and ANC were useful for early AA diagnosis. Since CRP is a late-phase reactant, increasing 8-12 hours after symptom onset and peaking between 24-48 hours,[20] it has limited utility early on. However, its sensitivity improves significantly after 24 hours.[21] Our findings confirm that CRP levels were markedly elevated after 24 hours, while PCT levels did not show such time-based variation.

Hematologic Subparameters

Recent research has identified hematologic indices such as NLR and LMR as potential diagnostic tools for appendicitis.[18] Similar to the findings of Tuncer et al.[22], our study showed significantly elevated NLR and monocyte counts, along with lower LMR in patients with appendicitis. Nissen and Tröbs[4] also reported higher NLR and monocyte counts, and reduced LMR in CA cases. However, a recent meta-analysis found insufficient evidence to support the use of LMR specifically in differentiating CA from AA.[23] While NLR and LMR are inexpensive and easily accessible, further prospective studies are needed to establish their diagnostic and prognostic value.

Serum Sodium

Hyponatremia has recently been proposed as a potential biomarker for CA.[2,6,7,18,24] Although Duman et al.[18] found significantly lower sodium levels in patients with appendicitis compared to controls, they observed no difference between AA and CA. In our study, we similarly found no significant difference in sodium levels between appendicitis and non-appendicitis groups or between AA and CA. However, sodium levels tended to decrease with longer symptom duration. This trend may suggest an association with disease severity, although the lack of statistical significance weakens its reliability. Nonetheless, due to its routine availability and low cost, the utility of serum sodium as a predictor of CA warrants further investigation.

Blood and Urine Ketones

The pathophysiology of ketosis in appendicitis likely results from enhanced catabolism, vomiting, fasting, and dehydration. Few studies have explored the diagnostic role of ketone bodies in this context. Song et al.[10] reported that ketonuria may help differentiate AA from right-sided colonic diverticulitis in adults. Chen et al.[11] found a higher frequency of urinary ketone positivity in children with perforated appendicitis compared to those with uncomplicated disease. In a recent study, Arredondo Montero et al.[12] found significantly higher capillary β-OHB levels in children with appendicitis patients compared to those without appendicitis, and also in patients with CA compared to those with uncomplicated appendicitis.

In our study, we measured β-OHB from venous blood and found significantly elevated blood and urine ketone levels in the appendicitis group. However, there was no significant difference between AA and CA groups. Interestingly, elevated blood ketone levels were more prominent in the first 24 hours after symptom onset, possibly reflecting the early metabolic response in pediatric patients. A significant negative correlation between ketone levels and age (r=-0.282, p=0.022) further supports this interpretation.

In children, glycogen stores are depleted more rapidly than in adults-within 8-12 hours (and as little as 4 hours in infants)-resulting in faster onset of ketosis during fasting. Additionally, children have higher metabolic rates and energy requirements. These physiological characteristics may explain the early appearance of ketosis and the inverse correlation between age and ketone levels.[25-27]

To our knowledge, this is the first study to concurrently evaluate both venous blood and urine ketone levels in relation to pediatric appendicitis.

Study Limitations

The strengths of this study include its prospective design and sufficient overall sample size. However, the single-center setting may limit the generalizability of our findings.

The sample size was calculated based on the association between serum sodium and appendicitis, requiring a minimum of 128 patients. With 153 patients enrolled, the study met this threshold. Nonetheless, because ketone measurements were only available for 115 patients, analyses involving ketone levels may have been underpowered.

Another limitation is that ketosis can be seen in various conditions related to fasting, vomiting, dehydration (ketoacidosis, gastroenteritis, etc.) other than appendicitis. Despite this, given that appendicitis is the most common surgical emergency in pediatric emergency departments, we believe that the assessment of ketone levels in this population provides clinically valuable insights.

Further large-scale, prospective, multicenter studies are needed to validate the diagnostic utility of ketone levels and other emerging biomarkers in pediatric appendicitis.

Conclusion

In this study, pediatric patients with appendicitis exhibited significantly elevated levels of CRP, WBC, ANC, and both blood and urine ketones. Notably, blood ketone levels were particularly useful in early presentations, suggesting their potential role as an early diagnostic biomarker. As the time from symptom onset increased, CRP levels rose significantly, and serum sodium levels decreased, highlighting their relevance in later stages of disease progression.

Given the high prevalence and potential morbidity of appendicitis in children, further research is warranted to identify reliable biomarkers that support timely and accurate diagnosis.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine (approval no: 2022/62, date: 07.04.2022).

Informed Consent: Informed consent was obtained from parents or legal guardians prior to participation.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.O.E., A.A., A.T., İ.M., Concept: E.T.B., A.O.E., A.A., A.Ç., Design: E.T.B., A.O.E., Ş.D., A.T., A.Ç., Data Collection or Processing: E.T.B., Ş.D., A.Ç., Analysis or Interpretation: E.T.B., A.A., A.T., A.Ç., Literature Search: E.T.B., A.A., A.Ç., Writing: E.T.B.

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