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## Diagnostic Value of Sodium, White Blood Cell, Neutrophil Levels; White Blood Cell/Sodium and Neutrophil/Sodium Ratios in Appendicitis in Pediatric Patients

Pediyatrik Yaş Grubu Apandisit Hastalığında Sodyum, Beyaz Kan Hücresi, Nötrofil Düzeyleri; Beyaz Küre/Sodyum ve Nötrofil/Sodyum Oranlarının Tanısal Değeri

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### ABSTRACT

**Objective:** Acute appendicitis is one of the most common causes of abdominal pain requiring surgical intervention in children. Although clinical and imaging modalities play a central role in disease diagnosis, laboratory markers, such as white blood cell (WBC) count, neutrophil count, and electrolyte disturbances, particularly sodium levels, have been explored as potential indicators of disease severity. This study aimed to evaluate the relationship between serum sodium levels, WBC and neutrophil counts, and their respective ratios with the diagnosis and severity of appendicitis.

**Methods:** This retrospective analysis included 176 pediatric patients who underwent appendectomy. Patients were divided into three groups based on pathological findings: Group 1 (non-appendicitis, n=59), group 2 (acute appendicitis, n=82), and group 3 (perforated appendicitis, n=35). WBC, neutrophil, and sodium levels were recorded. ANOVA and post-hoc Tukey's tests were used to assess differences between groups. A logistic regression model was employed to evaluate the combined ability of WBC, neutrophil, and sodium levels to distinguish group 1 from groups 2 and 3, and the model's performance was evaluated using the area under the ROC curve (AUC).

**Results:** Significant differences were observed between group 1 and groups 2 and 3 regarding WBC ( $p<0.001$ ), neutrophil ( $p<0.001$ ), and sodium levels ( $p<0.001$ ). Group 3 had the highest WBC count ( $17,123\pm4,491$  cells/ $\mu$ L) and the lowest sodium levels ( $132.5\pm1.4$  mEq/L), whereas group 1 had the lowest WBC count ( $10,660\pm3,804$  cells/ $\mu$ L) and the highest sodium levels ( $137.5\pm2.6$  mEq/L). Logistic regression analysis of the combined WBC, neutrophil, and sodium values obtained an AUC of 0.703, indicating moderate diagnostic utility.

### Öz

**Amaç:** Akut apandisit, çocuklarda cerrahi müdahale gerektiren en yaygın karın ağrısı nedenlerinden biridir. Tanıda klinik değerlendirme ve görüntüleme yöntemleri önemli rol oynasa da, beyaz kan hücresi (WBC) sayısı, nötrofil sayısı ve özellikle sodyum seviyeleri gibi laboratuvar belirteçleri hastalığın şiddetini gösterebilecek potansiyel işaretler olarak araştırılmıştır. Bu çalışmada, serum sodyum seviyeleri, WBC ve nötrofil sayıları ile bunların oranlarının apandisit tanısı ve şiddeti ile ilişkisi değerlendirilmektedir.

**Yöntemler:** Apandektomi geçiren 176 pediyatrik hasta üzerinde retrospektif bir analiz yapılmıştır. Hastalar patolojik bulgulara göre üç gruba ayrıldı: Grup 1 (apandisit olmayan, n=59), grup 2 (akut apandisit, n=82) ve grup 3 (perfore apandisit, n=35). WBC sayısı, nötrofil sayısı ve sodyum seviyeleri kaydedildi. Gruplar arasındaki farkları değerlendirmek için tek yönlü ANOVA ve post-hoc Tukey testleri kullanıldı. Grup 1 ile grup 2 ve 3'ü ayırt etmek için WBC, nötrofil ve sodyum seviyelerinin birlikte değerlendirildiği lojistik regresyon modeli kullanıldı ve modelin performansı ROC eğrisi altındaki alan (AUC) ile değerlendirildi.

**Bulgular:** WBC ( $p<0,001$ ), nötrofil ( $p<0,001$ ) ve sodyum seviyeleri ( $p<0,001$ ) açısından grup 1 ile grup 2 ve 3 arasında anlamlı farklar gözlemlendi. Grup 3, en yüksek WBC sayısına ( $17.123\pm4.491$  hücre/ $\mu$ L) ve en düşük sodyum seviyesine ( $132.5\pm1.4$  mEq/L) sahipken, grup 1 en düşük WBC sayısına ( $10.660\pm3.804$  hücre/ $\mu$ L) ve en yüksek sodyum seviyesine ( $137.5\pm2.6$  mEq/L) sahipti. WBC, nötrofil ve sodyum değerlerinin birlikte değerlendirildiği lojistik regresyon analizi, AUC'nin 0,703 olduğunu ve orta düzeyde tanısal fayda sağladığını gösterdi.

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**Conclusion:** This study demonstrated that WBC count, neutrophil count, and sodium level, as well as their ratios, can aid in diagnosing appendicitis in pediatric patients. Although sodium levels were significantly lower in patients with appendicitis, no significant difference was found between acute and perforated appendicitis. The WBC/sodium and neutrophil/sodium ratios could be valuable in clinical practice, especially for distinguishing between appendicitis and non-appendicitis cases. Further research is warranted to explore their utility in larger populations.

**Keywords:** Acute appendicitis, sodium, white blood cell count, neutrophil, hyponatremia

**Sonuç:** Bu çalışma, WBC sayısı, nötrofil sayısı ve sodyum seviyeleri ile bu değerlerin oranlarının, pediatrik hastalarda apandisit tanısında yararlı olabileceğini göstermektedir. Sodyum seviyeleri apandisit vakalarında anlamlı derecede düşük olmasına rağmen, akut ve perforate apandisit arasında istatistiksel olarak anlamlı bir fark bulunamamıştır. WBC/sodyum ve nötrofil/sodyum oranları, özellikle apandisit ve apandisit olmayan vakaların ayırt edilmesinde klinik uygulamada değerli olabilir. Daha geniş popülasyonlarda bu belirteçlerin faydasını incelemek için daha fazla araştırmaya ihtiyaç vardır.

**Anahtar Sözcükler:** Akut apandisit, sodyum, beyaz küre sayısı, nötrofil, hiponatremi

## INTRODUCTION

Acute appendicitis is one of the most common causes of abdominal pain requiring surgical intervention, particularly in pediatric and adult populations (1). Although modern diagnostic imaging techniques, such as ultrasound and computed tomography (CT), have improved the early detection of appendicitis, accurately assessing disease severity and predicting complications remains a challenge (2).

In recent years, electrolyte disturbances, particularly hyponatremia, have been proposed as potential markers of inflammation and systemic stress in various surgical conditions (3). Sodium, a key electrolyte for maintaining cellular homeostasis and fluid balance, is frequently affected in acute inflammatory processes. Disruption of this mechanism may reflect systemic inflammation and fluid shifts that occur in response to severe infections or tissue injury (4).

Several studies have highlighted the association between hyponatremia and severe appendicitis, suggesting that lower sodium levels are associated with higher rates of perforation, abscess formation, and postoperative complications (5). In particular, hyponatremia has been proposed as a surrogate marker for more advanced disease, potentially aiding clinicians in identifying patients at greater risk for poor outcomes (6,7).

Nevertheless, the clinical utility of hyponatremia as a prognostic marker in appendicitis remains controversial. While some studies support its association with complicated appendicitis, other studies have found no significant relationship between sodium levels and disease severity, emphasizing the need for further investigation (8,9). Given these conflicting findings, exploring the potential role of sodium disturbances in predicting appendicitis outcomes in a more comprehensive and systematic manner is crucial.

The aim of this study was to evaluate the relationship between serum sodium levels, WBC and neutrophil counts, WBC/sodium ratio, and appendicitis.

## MATERIALS AND METHODS

This retrospective study, initiated after receiving approval from Gazi University Clinical Research Ethics Committee (approval number: 514, date: 27.06.2022), included 176 pediatric patients who underwent appendectomy due to appendicitis and underwent complete blood counts and biochemistry tests between 2019 and 2021. Patients were divided into three groups based on pathological findings: non-appendicitis (group 1), acute appendicitis (group 2), and perforated appendicitis (group 3). Patient data, including sex, age (in months), white blood cell count (WBC), neutrophil count,

sodium levels, WBC/sodium ratio, neutrophil/sodium ratio, and pathological results, were collected from hospital records.

Blood samples were collected preoperatively from all patients. WBC and neutrophil counts were measured in units of cells per microliter (cells/ $\mu$ L) using an automated hematology analyzer. Sodium levels were measured in milliequivalents per liter (mEq/L) using standard electrolyte panels.

### Statistical Analysis

Data were analyzed using SPSS Version 22.0 for Windows (IBM Corp, Armonk, NY). Continuous variables, such as WBC count, neutrophil count, sodium level, WBC/sodium ratio, and neutrophil/sodium ratio, were presented as mean  $\pm$  standard deviation. Normality of data was assessed using the Shapiro-Wilk test. Because the data were normally distributed ( $p > 0.05$  for all variables), one-way analysis of variance was used to compare continuous variables between the pathology groups. A post-hoc analysis was performed using Tukey's test to identify specific group differences. Additionally, a logistic regression model was used to assess whether WBC, neutrophil, and sodium levels, when considered together, could distinguish between group 1 and groups 2 and 3. The model performance was evaluated using the area under the receiver operating characteristic curve (AUC). A  $p$ -value 0.05 was considered statistically significant.

## RESULTS

A total of 176 pediatric patients were included in the study. The mean age of the patients was  $135.6 \pm 47.8$  months, with 43.2% ( $n=76$ ) being female and 56.8% ( $n=100$ ) being male. Based on the pathological results, 59 patients (33.5%) were classified as having non-appendicitis (group 1), 82 patients (46.6%) as having acute appendicitis (group 2), and 35 patients (19.9%) as having perforated appendicitis (group 3).

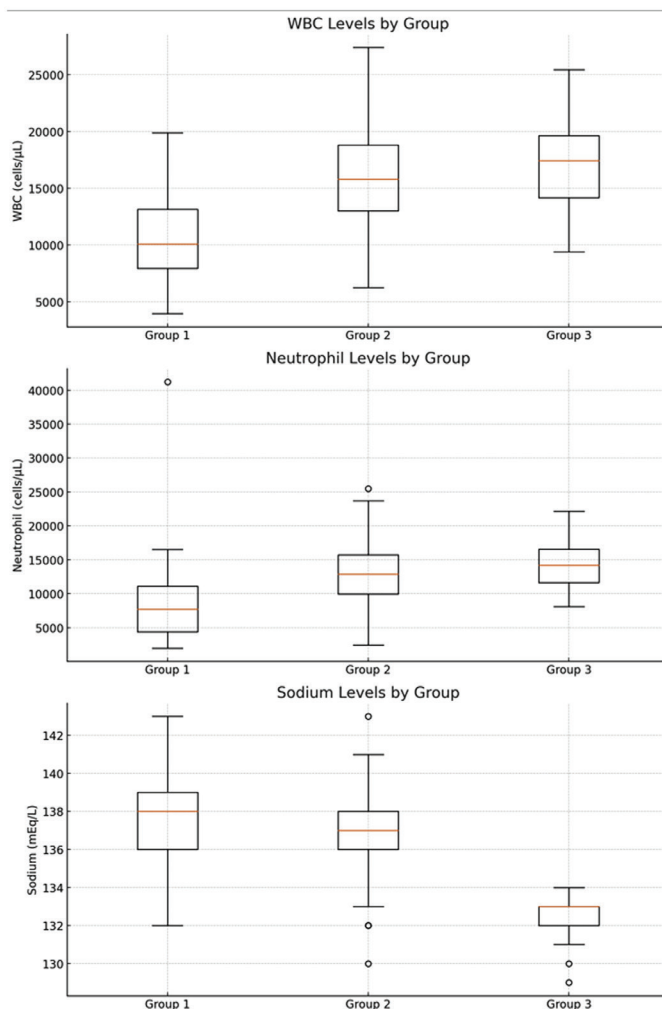
A significant difference was found in terms of WBC count between group 1 (non-appendicitis), group 2 (acute appendicitis), and group 3 (perforated appendicitis) ( $p < 0.001$ ). Group 3 had the highest WBC count ( $17,123 \pm 4,491$  cells/ $\mu$ L), whereas group 1 had the lowest WBC count ( $10,660 \pm 3,804$  cells/ $\mu$ L). No significant difference was found between group 2 ( $15,914 \pm 4,451$  cells/ $\mu$ L) and group 3 (Table 1, Figure 1).

Similarly, significant differences were observed in terms of neutrophil counts between groups 1, 2 and 3 ( $p < 0.001$ ). Group 3 had the highest neutrophil count ( $14,581 \pm 4,054$  cells/ $\mu$ L), whereas group 1 had the lowest ( $8,469 \pm 5,998$  cells/ $\mu$ L). No significant difference was

**Table 1.** Patient characteristics and laboratory findings by groups

Variable	Group 1 (non-appendicitis)	Group 2 (acute appendicitis)	Group 3 (perforated appendicitis)	p
WBC (cells/ $\mu$ L)	10,660 $\pm$ 3,804	15,914 $\pm$ 4,451	17,123 $\pm$ 4,491	<0.001
Neutrophil (cells/ $\mu$ L)	8,469 $\pm$ 5,998	13,046 $\pm$ 4,375	14,581 $\pm$ 4,054	<0.001
Sodium (mEq/L)	137.5 $\pm$ 2.6	137.0 $\pm$ 2.3	132.5 $\pm$ 1.4	<0.001
WBC/sodium ratio	7,767 $\pm$ 2,804	11,500 $\pm$ 3,471	12,929 $\pm$ 3,434	<0.001
Neutrophil/sodium ratio	5,690 $\pm$ 2,951	9,535 $\pm$ 3,229	11,011 $\pm$ 3,105	<0.001

WBC: White blood cell.



**Figure 1.** Box plot illustrating the distribution of white blood cell, neutrophil, and sodium levels by group.

WBC: White blood cell.

found between group 2 (13,046 $\pm$ 4,375 cells/ $\mu$ L) and group 3 (Table 1, Figure 1).

Both group 2, 3 had significantly lower sodium levels than group 1 ( $p$ <0.001). Group 3 had the lowest sodium level (132.5 $\pm$ 1.4 mEq/L), whereas group 1 had the highest (137.5 $\pm$ 2.6 mEq/L). No significant difference was observed between group 2 (137.0 $\pm$ 2.3 mEq/L) and group 3 (Table 1, Figure 1).

When we evaluated the WBC/sodium ratio, significant differences were found between groups 1, 2, and 3 ( $p$ <0.001). Group 3 had the highest WBC/sodium ratio (12,929 $\pm$ 3,434), whereas group 1 had the lowest (7,767 $\pm$ 2,804). No significant difference was found between group 2 (11,500 $\pm$ 3,471) and group 3. Similarly, when we looked at the neutrophil/sodium ratio, group 3 had the highest neutrophil/sodium ratio (11,011 $\pm$ 3,105), and group 1 had the lowest (5,690 $\pm$ 2,951) ( $p$ <0.001). No significant difference was found between group 2 (9,535 $\pm$ 3,229) and group 3 (Table 1).

When WBC, neutrophil, and sodium levels were evaluated together using a logistic regression model, the AUC was 0.703. This indicates a moderate ability to distinguish group 1 from groups 2 and 3 when these parameters are used in combination.

## DISCUSSION

Acute appendicitis is one of the most common surgical causes of abdominal pain in children and often requires urgent surgical intervention. If untreated, appendicitis can lead to complications, such as perforation, peritonitis, and sepsis, which can significantly increase morbidity and mortality rates. Thus, early and accurate diagnosis is essential. However, diagnosing appendicitis in children is more challenging than in adults, as children may have difficulty expressing their symptoms clearly, and the clinical presentation can overlap with other pediatric conditions. In particular, younger children may present with non-specific symptoms, such as nausea, vomiting, anorexia, and diffuse abdominal pain, which can delay diagnosis and increase the risk of perforation. The diagnostic process often involves a combination of clinical evaluation, laboratory testing, and imaging. Clinical signs such as tenderness at McBurney's point, right lower-quadrant pain, and guarding may suggest appendicitis. Laboratory findings frequently include leukocytosis and elevated C-reactive protein although these markers are not always specific to appendicitis. Imaging studies, including ultrasonography (US) and CT, play a key role in diagnosis. However, because of concerns about radiation exposure, the use of CT in children is approached with caution, and US is often preferred as the first-line imaging modality (10-14).

Diagnosis of this condition remains a significant clinical challenge, especially in young children, because of its atypical presentation and overlap of symptoms with other gastrointestinal conditions. In response to this challenge, several diagnostic scoring systems have been developed, including the Alvarado score and Pediatric Appendicitis score. In addition, sodium levels can be used as a marker of appendicitis severity (15).

This study highlights the difficulty of diagnosing acute appendicitis in children and demonstrates that WBC, neutrophil, and sodium levels may serve as important biomarkers for assessing the severity of appendicitis. The results indicate that patients with non-perforated appendicitis (group 2) and perforated appendicitis (group 3) had significantly higher WBC and neutrophil counts compared to non-appendicitis patients (group 1). These findings are consistent with those of Nissen and Tröbs (16), who reported that elevated WBC and neutrophil counts support the diagnosis of appendicitis.

Hyponatremia has gained increasing attention as a potential biochemical marker of disease severity in the differential diagnosis of acute and complicated appendicitis. Numerous publications have increasingly been published in recent years supporting sodium as a significant differentiating biochemical marker (8,17,18). Although sodium levels were lower in complicated appendicitis, the findings of this study revealed no statistically significant difference between acute appendicitis and complicated appendicitis in terms of sodium levels. Nonetheless, a significant difference was found between patients with and without appendicitis. In our study, patients with perforated appendicitis (group 3) had the lowest sodium levels ( $132.5 \pm 1.4$  mEq/L), which was significantly lower than those in the non-appendicitis group (group 1), who had the highest sodium levels ( $137.5 \pm 2.6$  mEq/L).

## CONCLUSION

Considering that the WBC/sodium and neutrophil/sodium ratios significantly differ in the diagnosis of appendicitis, it can be concluded that these ratios should be considered in clinical practice. Although the WBC/sodium and neutrophil/sodium ratios were higher in the perforated appendicitis group than in the acute appendicitis group, no statistically significant difference was found. In conclusion, the present study indicates that WBC, neutrophil, and sodium levels are important biomarkers for the diagnosis of appendicitis in children. Early diagnosis of acute appendicitis and the presence of conditions leading to perforation is critical to prevent complications.

## Ethics

**Ethics Committee Approval:** The study protocol was approved by the Gazi University Clinical Research Ethics Committee (approval number: 514, date: 27.06.2022).

**Informed Consent:** Retrospective study.

## Authorship Contributions

Concept: C.K., Design: G.A., Supervision: R.K., Z.T., Resources: K.S., Materials: A.K., Data Collection or Processing: F.N.A.U., L.N.T., Analysis or Interpretation: C.K., Literature Search: G.A., Writing: G.A., C.K., Critical Review: R.K., Z.T., K.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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