

Is Hyponatremia a Predictor for Perforated Appendicitis in Children?

Hiponatremi Çocuklarda Perfore Apandisit için Prediktör mü?

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Abstract

Introduction: Acute appendicitis (AA) is a leading cause morbidity and mortality in childhood. Unfortunately AA can be difficult to distinguish from other clinical conditions during the early course of the disease. Biomarkers are molecular indicators of a disease process, diagnosis, prognosis and can be used to monitor the effects of disease management. We aimed to determine which of the demographic, clinical or laboratory data is more predictive for complicated AA.

Materials and Methods: A hundred forty five consecutive patients aged 1 month to 18 years diagnosed with AA were retrospectively analyzed. Age, gender, body temperature (°C), laboratory data and symptom duration (days) of the patients were recorded.

Results: A total of 145 children with AA, 38 in group 1 and 107 in group 2, were included in the study. Group 1 was perforated appendicitis and group 2 was non-perforated appendicitis. Plasma sodium value was lower in group 1 than group 2, and C-reactive protein (CRP) values were significantly lower in group 2 compared to group 1.

Conclusion: Laboratory values can guess complicated appendicitis in children with appendicitis. CRP level and presence of hyponatremia may be more predictive than white blood cell count for the the diagnosis of perforated appendicitis.

Öz

Giriş: Akut apandisit (AA) çocukluk çağında önde gelen morbidite ve mortalite nedenidir. Ne yazık ki, AA hastalığın erken seyri sırasında diğer klinik durumlardan ayırt edilmesi zor olabilir. Biyobelirteçler, bir hastalık sürecinin, teşhisinin, prognozunun moleküler göstergeleridir ve hastalık yönetiminin etkilerini izlemek için kullanılabilir. Komplike AA için demografik, klinik veya laboratuvar verilerinden hangisinin daha prediktif olduğunu belirlemeyi amaçladık.

Gereç ve Yöntem: AA tanısı alan 1 ay-18 yaş arası ardışık 145 hasta retrospektif olarak incelendi. Hastalara ait yaş, cinsiyet, vücut ısısı (°C), laboratuvar verileri ve semptomların süresi (günler) kaydedildi.

Bulgular: Grup 1'de 38, grup 2'de 107'si olmak üzere 145 AA tanısı alan çocuk çalışmaya dahil edildi. Grup 1 perfore apandisit ve grup 2 non-perfore apandisit idi. Plazma sodyum değeri grup 1'de grup 2'ye göre daha düşüktü ve C-reaktif protein (CRP) değerleri grup 2'de grup 1'e göre anlamlı derecede düşüktü.

Sonuç: Apandisitli çocuklarda laboratuvar değerleri komplike apandisitleri tahmin edebilir. CRP düzeyi ve hiponatreminin varlığı perfore apandisit tanısında lökosit sayısından daha belirleyici olabilir.

Keywords

Acute appendicitis, C-reactive protein, hyponatremia, perfore appendicitis

Anahtar kelimeler

Akut apandisit, C-reaktif protein, hiponatremi, perfore apandisit

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Introduction

Acute appendicitis (AA) is the most common reason for emergency surgery in children (1). Despite advances in diagnosis and treatment, it is associated with significant morbidity (10%) and mortality (1-5%) (2). Perforation is an important factor for morbidity in patients with AA and associated with increased frequency of postoperative complications (3). Delayed diagnosis and treatment increase the risk of perforation, abscess, peritonitis and partial bowel obstruction. Laboratory markers can be used to predict perforated appendicitis. C-reactive protein (CRP), white blood cell (WBC) and absolute neutrophil counts are markers that are commonly used to differentiate perforation of appendicitis (4). Recent studies have shown that hyponatremia is associated with inflammatory events such as pneumonia, acute respiratory distress syndrome, meningitis and necrotizing soft tissue infections. However, studies examining the relationship between hyponatremia and AA are limited (5,6).

Our primary objective was to investigate the clinical significance of preoperative hyponatremia and to assess as a predictor of the perforated AA. Another objective was to identify the differences regarding age, gender, duration of symptoms, WBC count and CRP levels among both groups.

Materials and Methods

Study population

In this retrospective single-center study, we evaluated all (n=145) patients under 18 years of age with intraoperative diagnosed appendicitis who underwent appendectomy at our institution between June 2018 and June 2019. The study was approved by our institutional review board and the ethical committee (approval number: E-20/12-50).

Demographic and clinical information were retrospectively obtained from all subjects with AA. Demographic information included patient's age and gender. Clinical data included body temperature (as measured in the pediatric emergency room), duration of symptoms, laboratory data (WBC count, CRP and sodium levels) and outcome. Exclusion criteria were missing laboratory values, concomitant chronic disease, history of secondary or elective

appendectomy. The collected data were compiled in an electronic database and mean values and standard deviation (SD) for numeric items were calculated. Patients were divided into two groups as perforated and non-perforated appendicitis according to their surgical reports and pathology results. Age, gender, serum sodium levels, WBC count and CRP were compared between the two groups.

Statistical Analysis

Clinicopathological characteristics were compared between the two groups using Student's t-test. Parametric data were mean \pm SD, categorical data were expressed as frequency (n) and percentage (%). The sensitivity and specificity in the diagnosis of acute perforated appendicitis with WBC count, CRP and serum sodium levels were evaluated with receiver operating characteristic (ROC) analysis. ROC curve analysis was performed to assess the best cutoff for the prediction of perforated AA and values for area under the curve (AUC). Multivariate analysis was carried out by binomial logistic analyses, with adjustments for variables significant in univariate analysis. Statistical significance was defined as $p < 0.05$.

Results

A total of 145 patients with appendicitis were included in the study. The mean age of the patients was 11 ± 3.6 (minimum: 3-maximum: 17.5) years, and 92 (64.3%) of the patients were male. The mean WBC was 14,400/IL (range: 4,600-36,400/IL), mean CRP level was 68 (range: 0-342) mg/L and mean serum sodium level was 136 (range: 128-141) mEq/L. The demographic and laboratory data of the patients are shown in Table 1. All patients were hospitalized and none of them died.

Thirty-eight patients (26.2%) had perforated appendicitis. No difference was found between patients with perforated and non-perforated appendicitis in terms of gender, age and body temperature. However, the duration of symptoms was longer in patients with perforated appendicitis ($p < 0.001$).

There was a significant difference between the perforated appendicitis group and the non-perforated appendicitis group in terms of CRP level and plasma sodium levels ($p < 0.001$, $p < 0.001$ respectively). No significant relationship was found between acute perforated appendicitis and WBC count ($p = 0.74$).

Table 1. The demographic and laboratory data of the patients

Demographic and laboratory data (mean \pm SD)	Perforated group (n=38)	Non-perforated group (n=107)	p-value
Age (years)	10.8 \pm 3.9	11.1 \pm 3.6	0.70
Gender (male) n (%)	25 (65)	67 (62%)	0.33
Body temperature ($^{\circ}$ C)	36.7 \pm 0.8	36.6 \pm 0.6	0.23
Semptom duration(day)	2.8 \pm 2.6	1.5 \pm 1.8	<0.001
WBC ($\times 10^9$ /L)	15.8 \pm 5.3	13.9 \pm 5.2	0.74
CRP (mg/L)	139 \pm 94	43 \pm 49	<0.001
Plasma sodium (mEq/L)	134.3 \pm 3.2	136.6 \pm 2.1	<0.001

SD: Standard deviation, WBC: White blood cell, CRP: C-reaktif protein

Most sensitive association with acute perforated appendicitis in receiver ROC analysis was determined by CRP (AUC: 0.814) and serum sodium value (AUC: 0.716). Figure 1 shows CRP level as a predictor of acute perforated appendicitis. Using the Youden index we established the following cutoff points: serum CRP of 89 mg/L, serum sodium value ≤ 135 mEq/L. CRP value above 89 mg/L had 71.0% sensitivity and 84.1% specificity. For sodium value ≤ 135 mEq/L, sensitivity was 57.9% and specificity was 71.0. The ROC for plasma sodium levels considered as a predictor for perforated AA is shown in Figure 2.

Plasma sodium levels were found significantly lower in patients with perforated appendicitis than non-perforated group. The median (IQR) value is 135 (132-138) mEq/L in the perforated group and 136 (133-139) mEq/L in the non-perforated group. Sodium values of the two groups are shown in Figure 3.

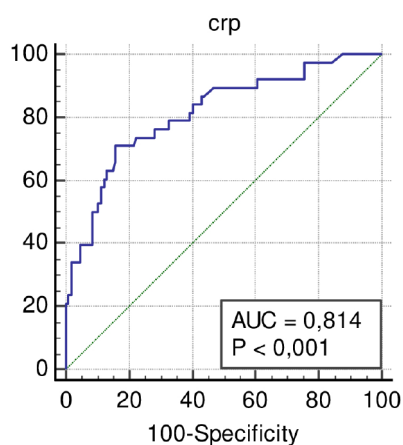


Figure 1. C-reactive protein as a predictor of perforated appendicitis. Area under the curve (AUC) is area under the curve; dashed line is the line of no predictive value, that is, AUC=0.5.

CRP: C-reactive protein

Discussion

In this study, 145 pediatric patients were evaluated diagnosed with AA. Sodium levels were significantly lower and the CRP levels were higher in patients diagnosed with perforated appendicitis. WBC count did not differ significantly between simple and perforated appendicitis.

Young children can not explain their pain symptoms like an adolescent or adult. Therefore a significant delay may occur in assessment, diagnosis and treatment. Perforation, abscess and peritonitis are still common in children with appendicitis. Diagnosing perforated appendicitis presents with some difficulties, as children often do not present with the classic presentation of appendicitis (7). In clinical studies investigating complications in children with appendicitis, the mean age in complicated appendicitis was found to be significantly lower than those with uncomplicated

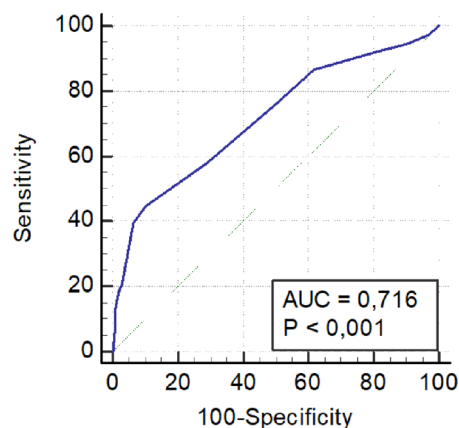


Figure 2. Receiver operating characteristic curve for plasma sodium concentration as a predictor of perforated AA. Area under the curve (AUC) is area under the curve; dashed line is the line of no predictive value, that is, AUC=0.5.

AA: Acute appendicitis

appendicitis (8-10). In our study, age of the patients was not found to be associated with perforation. This may be due to differences in the number of patients included in the study and differences in perforated non-perforated appendicitis rates.

Univariate analysis demonstrated that patients with perforated appendicitis had a longer duration of symptoms. However, there is no common consensus in the pediatric literature regarding for which time frame there is a significant increase in risk for perforated appendicitis (11-13).

We can interpret that objective laboratory parameters are needed for diagnosis. However, no parameter can show perforation in a satisfactory way. The importance of laboratory data in the diagnosis of acute perforated appendicitis is controversial. In a previous study, it was reported that WBC count did not differ in patients diagnosed with complicated and uncomplicated AA (9). Similarly, in our study, WBC count did not help distinguish the two groups. Although it is not an indicator alone, there is an increased number of WBC count in complicated appendicitis cases (14). CRP is an acute inflammatory protein and has been used as a marker of acute infections. In our study, increased CRP value was found to be sensitive in predicting perforated appendicitis, similar to some studies (11,15,16).

Hyponatremia is the most common electrolyte disorder in clinical medicine and may be seen in many inflammatory diseases such as Kawasaki

disease, sigmoid diverticulitis and AA. In AA hyponatremia develops due to factors causing non-osmotic release of antidiuretic hormone such as, pain, hypovolemia, and nausea (17-19). Serradilla et al. (20) found that preoperative low serum sodium levels were associated with intraabdominal abscess in AA. In Sweden, a study in which 80 pediatric appendicitis patients were evaluated, serum sodium level was found to be significantly lower in patients with complicated appendicitis compared to simple appendicitis (21). Pogorelić et al. (22) evaluated 184 pediatric appendicitis patients and when the cut-off value for plasma sodium was 135, AUC to be 0.983 in predicting perforated appendicitis. In our study, serum sodium levels were significantly lower in patients with perforated appendicitis, and the best cut-off value for predicting perforated appendicitis was 135 mmol/L and AUC was 0.716. Our study was generally compatible with the literature.

Serum sodium level, which is routinely checked in patients with suspected appendicitis, is also low-cost, and can be a good predictor of perforated appendicitis cases. Early detection of hyponatremia at the time of presentation has been shown to be associated with complications, and in the light of this information, it has been emphasized that it can be an early predictor in terms of operation timing.

Conclusion

Perforated appendicitis is not uncommon in the childhood age group. Our study shows that plasma sodium levels and CRP at the time of admission may be useful in predicting perforated appendicitis. Hyponatremia and elevation of CRP may be more predictive in cases with perforated appendicitis than WBC count, age or body temperature.

Ethics

Ethics Committee Approval: The study was approved by our institutional review board and the ethical committee (approval number: E-20/12-50).

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

Financial Disclosure: The authors declared that this study received no financial support.

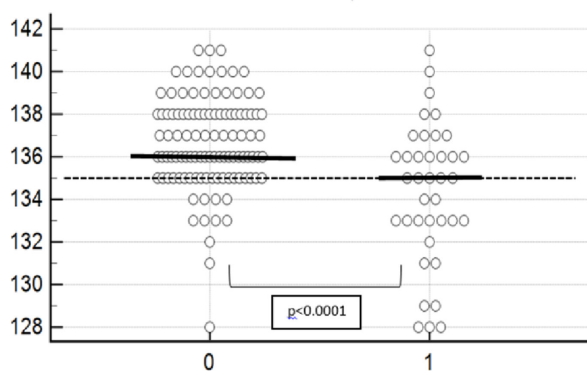


Figure 3. In the vertical column of the graph, serum sodium concentrations are indicated in mmol/L at emergency admission. Plasma sodium levels of patients with perforated and non-perforated appendicitis (0: non-perforated appendicitis, 1: perforated appendicitis) straight line shows median value. Dashed line corresponds to the chosen value for dichotomization of data. The groups were compared using the non-parametric Mann-Whitney U test.

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