Medical Principles and Practice

Original Paper

Med Princ Pract 2024;33:347–354
DOI: 10.1159/000538778

Received: December 11, 2023
Accepted: April 8, 2024
Published online: April 9, 2024

The Predictive Value of Plasma Sodium and Other Laboratory Parameters in Determining Complicating Appendicitis in Children

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Highlights of the Study

- Finding reliable preoperative predictors of complicated acute appendicitis (AA) has been a challenging diagnostic problem in emergency departments worldwide.
- We identified mild hyponatremia and elevated levels of C-reactive protein and white blood cells as potential markers for distinguishing between complicated and uncomplicated pediatric AA.
- Our study may have implications for surgical approaches in complicated disease and conservative approaches in uncomplicated disease.
- Routine blood tests can help emergency physicians discriminate between complicated and uncomplicated AA.

Keywords

Complicated appendicitis · Laboratory parameters · Hyponatremia · Children

Abstract

Objective: Finding a reliable preoperative predictor of complicated acute appendicitis (AA) has been a challenging diagnostic problem. The present study aimed to identify potential factors that may predict complicated AA in the pediatric emergency department (ED) based on routine, widely available laboratory tests on admission to the ED, including plasma sodium concentration. ***Methods:*** We retrospectively reviewed clinical and laboratory data of pediatric patients with AA who underwent emergency surgery at our department between January 2020 and December 2022. The patients were divided into two groups: histopathologically proven complicated AA (n = 80) and noncomplicated AA (n = 155). ***Results:*** Complicated AA was associated with reduced plasma sodium and chloride concentrations ($p < 0.001$, both), decreased values of lymphocytes ($p = 0.002$), elevated C-reactive protein (CRP) ($p < 0.001$), and elevated values of white blood cells (WBC) and neutrophils ($p = 0.012$ and 0.001, respectively). In binomial logistic regression, increased levels of CRP and WBC and decreased levels of sodium were predictors of complicated AA. The area under the receiver operating characteristic curve was 0.825 (95% confidence interval: 0.764, 0.886). ***Conclusion:*** We identified mild hyponatremia and elevated CRP and WBC values as potential markers for distinguishing complicated

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from uncomplicated pediatric AA with implications for surgical approaches for treating complicated AA and conservative approaches for treating uncomplicated AA.

Introduction

Although acute appendicitis (AA) can develop at any age, it most commonly occurs in the second decade of life, with an annual rate of 23.3 cases per 10,000 [1]. However, the diagnosis of AA remains challenging, and some controversies regarding its management are still present in different settings and practices worldwide, especially for the pediatric population. Consequently, the rate of appendiceal perforation is still high in children aged under <5 years and varies from 47 to 100%, depending on age with significantly higher perforation rates in younger age-groups (100%, <1 year; 100%, 1–2 y; 83.3%, 2–3 y; 71.4%, 3–4 y; 78.6%, 4–5 y, and 47.3%, 5 y) [2]. As managing complicated AA requires urgent intervention and intravenous broad-spectrum antibiotics, it is crucial to establish its timely diagnosis through clinical examination, different clinical and imaging scoring systems, and laboratory biomarkers [2–7]. Otherwise, a delay in diagnosis can cause perforation, peritonitis, sepsis, and extended hospital stays.

In recent years, finding a reliable preoperative predictor of complicated AA has emerged as a prominent topic in clinical research, potentially improving diagnostic accuracy without invasive surgery or ionizing radiation. Among several laboratory parameters evaluated, measurement of serum sodium has been proposed as a valuable indicator to help delineate uncomplicated AA from complicated AA. Recent studies have investigated the possible association between preoperative hyponatremia (serum sodium level <135 mEq/L) and complicated AA in both pediatric and adult populations [8–12]. However, the results are contradictory as several authors have found a positive association between preoperative hyponatremia and complicated appendicitis [8–13], while others have reported an insignificant association [14–16].

The primary aim of the present study was to identify reliable predictors of complicated AA in the pediatric emergency department (ED) based on routine, widely available laboratory tests. Our secondary aim included the potential association between pre-appendectomy hyponatremia with higher detection rates of complicated AA in the pediatric population of different ages. We hypothesized that preoperative values of serum sodium in children with suspected AA would be helpful in the early differentiation between complicated AA and uncomplicated appendicitis and more prompt treatment.

Materials and Methods

Study Design and Period

We conducted a retrospective chart review of 264 consecutive pediatric patients (<18 years old) who had undergone appendectomy (open or laparoscopic) due to AA (International Classification of Diseases Tenth Revision, code K35). The study was performed at the Clinical Center University of Sarajevo in Sarajevo, Bosnia and Herzegovina, between January 2020 and December 2022. All surgeries were performed as emergency procedures. Open appendectomies were performed through a muscle-splitting incision in the right lower quadrant of the abdomen, while laparoscopic appendectomies were performed using the three-port technique.

Population

Patients were included if they had received a histopathologic diagnosis of AA. All patients with negative (23/264, 8.7%) or interval appendectomies (1/264, 0.4%) were excluded from the study. Patients with missing or incomplete medical records were also excluded (5/264, 1.9%). Finally, 235 patients were selected for analysis.

Diagnostic Approach and Interventions

Based on intraoperative macroscopic appearance and postoperative histopathology, patients were divided into two groups: those with simple AA (uncomplicated appendicitis group) and those with complicated AA (complicated appendicitis group). Uncomplicated AA was defined as simple (catarrhal and phlegmonous) or gangrenous without perforation, similar to American Association for the Surgery of Trauma (AAST) grades I and II [17]. AA with perforation or abscess formation was defined as complicated AA (AAST grades III– V) [17]. Histopathologically, catarrhal AA was defined as the enlargement of lymphoid follicles in the appendiceal mucosa, and phlegmonous AA was defined as the presence of neutrophils in all appendiceal layers [18]. Gangrenous AA was defined as neutrophil infiltration with smooth muscle layer necrosis, and perforated AA was defined as necrosis and perforation in all layers [18]. From a surgeon's perspective, perforated AA was defined as a visual hole in the appendix, gross contamination in the abdomen during appendectomy, or the presence of an extraluminal appendicolith in the abdominal cavity.

The patients were categorized into five groups according to age: infancy (>28 days–<1 year), toddlerhood (1–2 years), early childhood (3–5 years), middle childhood (6–11 years), and early adolescence (12–18 years) as per the Eunice Kennedy Shriver National Institute of Child Health and Human Development in the USA [19]. These subgroups were further subdivided into those with hyponatremia and eunatremia in the immediate preoperative setting. Hyponatremia was defined as a sodium level <135 mmol/L and further classified into three categories by its severity: mild hyponatremia (130–134 mmol/L), moderate hyponatremia (125–129 mmol/L), and severe hyponatremia (<125 mmol/L) [20]. Eunatremia was defined as a sodium level between 135 and 145 mmol/L [20].

A C-reactive protein (CRP) level >10 mg/dL was considered high [21]. Hyperbilirubinemia was defined as a TBIL level of >20 μmol/L. A total white blood cell (WBC) count was considered elevated according to the age-groups and cutoff values defined by the pediatric complete blood count (CBC) reference values (LTR10211) [22]. Neutrophilia was defined as a percentage of neutrophils >70% [10]. Reference values for erythrocyte count, hemoglobin quantity, hematocrit, and other erythrocyte parameters including mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and red blood cell distribution width were determined based on the pediatric CBC reference values (LTR10211) [22].

The length of postoperative hospital stay was counted as days from surgery until discharge. All medical records were de-identified and anonymized for the current study. All modifications and analyses were performed via programming, a new database was created, and no changes were made to the original database.

Statistical Analysis

The normality of data distribution and the presence of outliers were evaluated visually by analyzing histograms, Q-Q, and boxplot graphs and numerically by calculating z-values for skewness and kurtosis and application of the Kolmogorov-Smirnov test. For comparison of parameters between uncomplicated and complicated AA groups, an independent samples Student's *t* test was used for the analysis of variables that had a normal distribution with no outliers, while Mann-Whitney U test was used for other numeric variables. The χ^2 test for homogeneity was used to analyze differences in proportions of categorical variables. Binomial logistic regression was used to create a model for predicting patients' classification into complicated or uncomplicated AA. Neutrophils, lymphocyte levels, and concentrations of calcium, chloride, and total bilirubin were not included in the model due to the large proportion of missing data for those variables. Age, sex, CRP, WBC, and sodium levels were included in the model. The linearity of continuous variables concerning dependent variable logit transformation was evaluated by the Box-Tidwell procedure. Multicollinearity was tested by linear regression. The odds ratio and 95% confidence interval (CI) were used for the presentation of outcome predictors. The receiver operating characteristic curve was prepared and analyzed. All tests were two-tailed, with a p value <0.05 considered statistically significant. Statistical Package for Social Sciences (SPSS) program version 23.0 and R Statistical Software (Foundation for Statistical Computing, Vienna, Austria) version 4.3.2 were used for the analysis.

Results

The demographic and laboratory findings of the entire cohort are shown in Table 1. Of the 235 pediatric patients with confirmed AA, 155/235 (66%) had uncomplicated AA and 80/235 (34%) patients presented with complicated AA (Fig. 1).

Sodium and chloride levels were significantly lower in complicated than in uncomplicated AA ($p < 0.001$; 95% CI, 0.968, 3.005). A significantly higher proportion of patients with mild hyponatremia was found in complicated compared with uncomplicated AA ($p < 0.001$). The significance was evident in all three major age-groups (Table 1; Fig. 2). There were no patients with moderate or severe hyponatremia.

Total bilirubin median concentration was 13.1 μmol/L (interquartile range [IQR] 8.8–17.5) in uncomplicated and 16.2 μmol/L (IQR 14.2–34.8) in complicated AA ($p = 0.055$). CRP concentration was higher in complicated than in uncomplicated AA ($p < 0.001$) (Table 1). Also, the higher WBC level was found in the complicated (mean: 16.5 ± SD 5.6 × 10^9/L) than in uncomplicated AA (mean: 14.6 ± SD 5.0 × 10^9/L) ($p = 0.012$, 95% CI, −3.4, −0.4) (Table 1). Neutrophils were significantly higher in the complicated AA (mean 83% ± SD 8%) than in uncomplicated AA (mean 76% ± SD 15%) ($p = 0.001$). Significantly lower lymphocyte values were found in the complicated AA compared with the uncomplicated AA (median 8% vs. 11%, IQR 5–12%, and 7–18%, respectively) ($p = 0.002$). However, no significant difference was observed in NLR between the groups (Table 1).

We performed binomial logistic regression to explore predictors of the classification of patients into complicated or uncomplicated AA. The model included age, sex, CRP, WBC, and sodium. All continuous variables had a linear relation to the dependent variable logit. Eight standardized residuals with a value greater than 2.5 SD were included in the analysis. The model was statistically significant ($\chi^2(4) = 78.29$, $p < 0.001$). The model explained 40.3% (Nagelkerke R^2) of the variance in classification into complicated or uncomplicated AA and correctly classified 80.3% of cases. Of the five predictors, CRP, WBC, and sodium were statistically significant (Table 2). The area under the receiver operating characteristic curve was 0.825 (95% CI, 0.764, 0.886), corresponding to excellent discrimination (Fig. 3). Increased levels of CRP and WBC and decreased levels of sodium were predictors of complicated AA in our study.

Discussion

In the current study, we explored the predictive utility of routine laboratory tests to discriminate between complicated and noncomplicated AA in pediatric emergency settings. We found an association

Table 1. The demographic and laboratory data of patients included in the study

Parameter	All patients (n = 235)	Uncomplicated AA (n = 155)	Complicated AA (n = 80)	p values
Age, mean±SD, years	11±4	12±4	11±4	0.135
Age categories, n (%)				**0.013**
Infancy (>28 days–<1 year)	0 (0)	0 (0)	0 (0)	
Toddlerhood (1–2 years)	1 (0.5)	1 (0.6)	0 (0)	
Early childhood (3–5 years)	20 (8.5)	7 (4.5)	13 (16.3)	
Middle childhood (6–11 years)	111 (47.2)	77 (49.7)	34 (42.5)	
Early adolescence (12–18 years)	103 (43.8)	70 (45.2)	33 (41.3)	
Sex, male, n (%)	157 (67)	106 (68)	51 (64)	0.474
Weight, mean±SD, kg	46±19	46±18	45±21	0.321
Height, mean±SD, cm	154±21	155±21	152±22	0.189
CRP, median (IQR), mg/L	39 (16–66)	31 (12–51)	63 (38–137)	<**0.001**
Erythrocytes, median (IQR), ×10^9/L	4.8 (4.6–5.1)	4.8 (4.6–5.1)	4.8 (4.6–5.1)	0.372
Hemoglobin, mean±SD, g/L	136±13	136±13	136±14	0.596
Hematocrit, mean±SD, %	0.39±0.04	0.39±0.04	0.39±0.04	0.610
MCV, mean±SD, fL	80±7	81±5	79±9	0.074
MCH, mean±SD, pg	28±2	28±2	28±2	0.613
MCHC, median (IQR), g/L	346 (332–361)	346 (331–361)	346 (332–363)	0.510
RDW, mean±SD, %	13±1	13±1	13±2	0.582
WBC, mean±SD, ×10^9/L	15.2±5.3	14.6±5.0	16.5±5.6	**0.012**
Neutrophils, mean±SD, %	79±13	76±15	83±8	**0.001**
Lymphocytes, median (IQR), %	10 (6–16)	11 (7–18)	8 (5–12)	**0.002**
NLR, median (IQR)	8 (4–13)	6 (4–11)	10 (6–14)	0.178
Thrombocytes, mean±SD, ×10^9/L	284±78	279±65	295±97	0.488
MPV, mean±SD, fL	7.2±1.1	7.2±0.9	7.3±1.5	0.964
Potassium, mean±SD, mmol/L	4.2±0.3	4.2±0.3	4.2±0.4	0.656
Sodium, median (IQR), mmol/L	137 (135–139)	138 (136–139)	135 (134–138)	<**0.001**
Mild hyponatremia, n (%)	46 (20)	11 (7)	35 (44)	<**0.001**
Calcium, mean±SD, mmol/L	2.5±0.1	2.5±0.1	2.4±0.1	0.241
Chloride, mean±SD, mmol/L	101±3	101±3	100±3	<**0.001**
Bilirubin total, median (IQR), μmol/L	14.3 (10.5–19.0)	13.1 (8.8–17.5)	16.2 (14.2–34.8)	0.055

Only significant p values are bolded. IQR, interquartile range; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; MPV, mean platelet volume; NLR, neutrophils-lymphocytes ratio; RDW, red blood cell distribution width; SD, standard deviation; WBC, white blood cells.

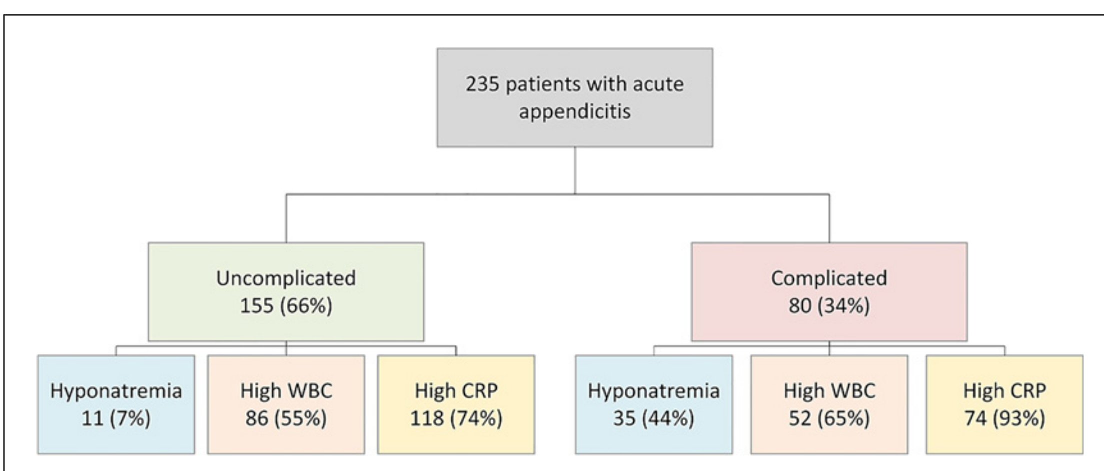

Fig. 1. A flow diagram of the study.

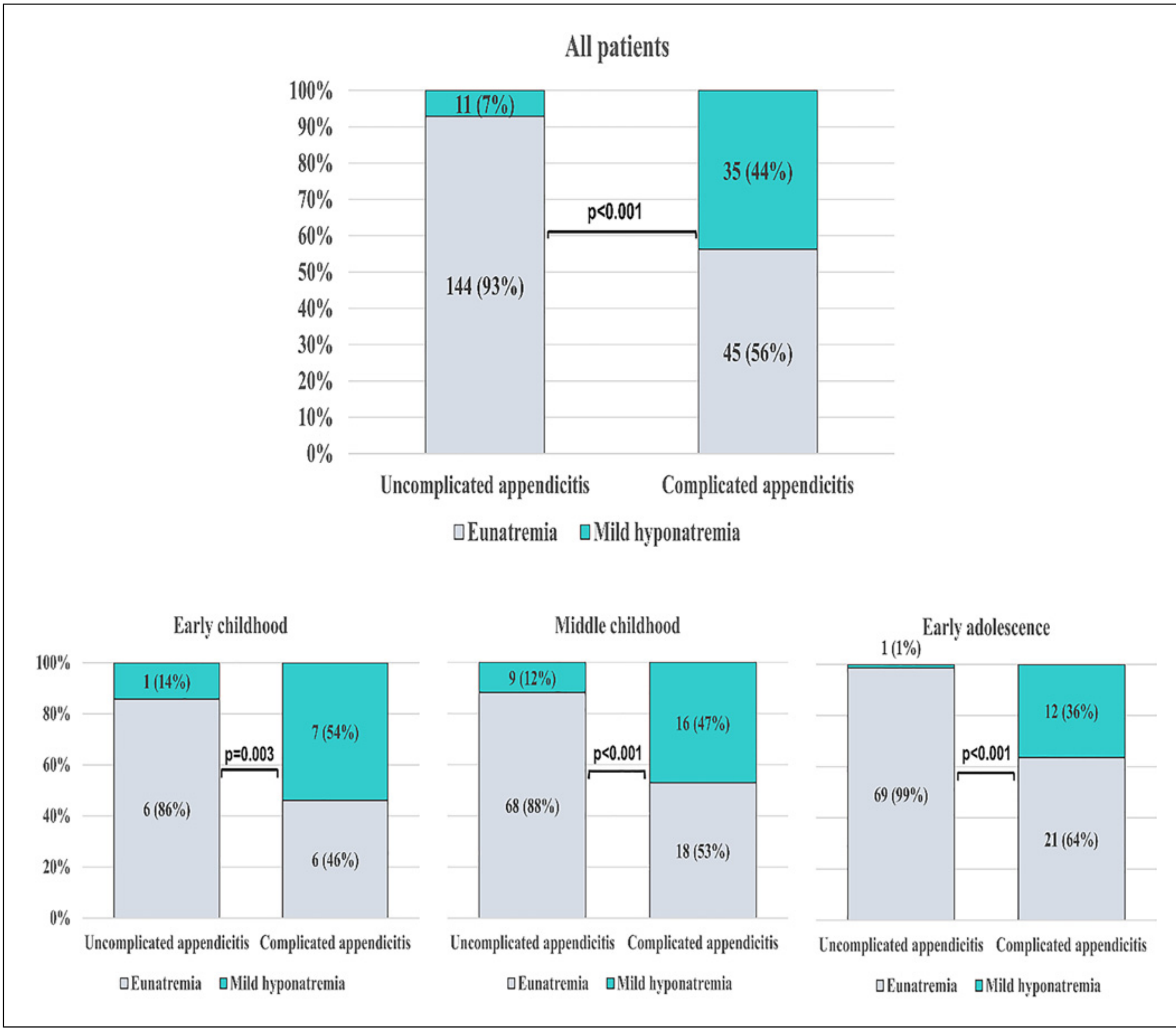

Fig. 2. Percentage and number of patients with uncomplicated and complicated AA having eunatremia or mild hyponatremia.

Table 2. Logistic regression predicting the likelihood of complicated AA based on age, sex, white blood cells (WBC), C-reactive protein (CRP), and sodium

Parameter	B	SE	Wald	df	Sig	Exp(B)	95% CI for Exp(B)	
							lower	upper
Sex	0.135	0.364	0.137	1	0.712	1.144	0.561	2.335
Age	0.025	0.047	0.291	1	0.590	1.026	0.935	1.125
CRP	0.017	0.003	23.329	1	0.000	1.017	1.010	1.024
WBC	0.083	0.036	5.267	1	0.022	1.087	1.012	1.167
Sodium	−0.331	0.071	21.466	1	0.000	0.718	0.625	0.826
Constant	41.794	9.589	18.998	1	0.000	4.415E+18		

SE, standard error; CI, confidence interval; CRP, C-reactive protein; WBC, white blood cells.

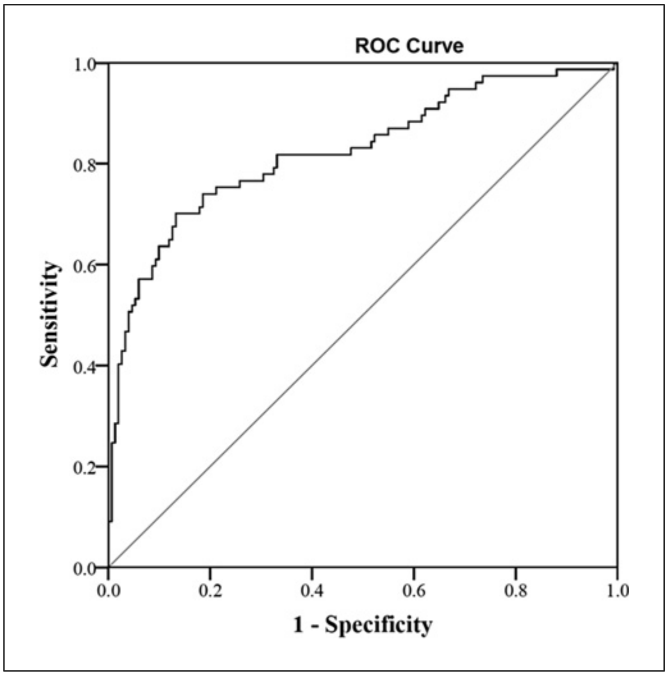

Fig. 3. ROC curve for binomial logistic regression model. ROC, receiver operating characteristic.

between preoperative hyponatremia and complicated AA. This finding could help emergency physicians, pediatricians, and pediatric surgeons resolve their diagnostic dilemmas in case of suspected complicated AA more quickly. The significance of this association lies in the fact that the serum sodium level is routinely tested in all children presenting to the ED with suspected AA. The ability to predict complicated AA already at the initial evaluation of a pediatric patient in the ED could substantially reduce associated morbidity and the costs of additional diagnostic tests.

Several researchers have studied predictors of complicated AA, including CRP, leukocytosis, the length of symptoms, and fever, to assess the need for surgery [18, 23–25]. However, the results of these studies were controversial and difficult to apply in clinical practice. The first study that reported hyponatremia as an independent predictor of complicated AA in children (n = 392) was published in 2016 when Pham et al. [26] found hyponatremia in 63% of children with complicated AA and only 33% of those with uncomplicated AA. This finding has been confirmed by several recent studies [9–11, 13, 27]. Systematic reviews [11, 13] and meta-analysis [13] confirmed these observations and found that hyponatremia corresponded to complicated AA in the pediatric population [11, 13]. However, several studies reporting no statistically significant association between hyponatremia and complicated AA in the pediatric population have also been published [16, 28]. Such contradictory findings are probably due to inconsistencies in the definition of complicated AA, making comparisons difficult. The present study used the classification of complicated/uncomplicated AA based on the AAST grading system [17]. Furthermore, the design of the previous studies varied; some were retrospective [9, 16, 28], while others were prospective [10, 27]. The definition of hyponatremia was also inconsistent, which could further affect the interpretation of data.

Serum levels of sodium affect the cellular volume and determine tonicity, thus regulating fluid distribution among different body compartments [29]. Hyponatremia is the most common electrolyte abnormality encountered in hospitalized patients, either as a complication of an underlying acute illness or as a consequence of therapeutic interventions [30]. In the pediatric population, hyponatremia is associated with poor overall outcomes [31] in the case of central nervous system disorders, gastrointestinal disorders, and sepsis [32]. Although the exact mechanism responsible for the development of hyponatremia in severe infectious processes, including complicated AA, is not completely clear, the immuno-neuroendocrine pathway is believed to be behind it [33]. Swart et al. pointed out the important role of interleukin 6, whose value increases during inflammation and mediates the cascade of non-osmotic secretion of vasopressin (antidiuretic hormone) with resulting hyponatremia [33].

Although appendectomy remains the standard of care in the treatment of AA at our institution, the results of the present study related to different levels of sodium in uncomplicated and complicated AA could contribute to our additional rate of adoption of non-operative management by early prediction of patients with uncomplicated AA who would potentially benefit from this treatment modality. On the other hand, early prediction of complicated AA would enable more prompt treatment and reduce the morbidity rate, stay in the hospital, and the exposure to unnecessary preoperative diagnostic procedures. The usefulness of hyponatremia as a promising marker for predicting the severity of AA is strengthened if changes in the values of other preoperative laboratory tests, especially inflammatory parameters, are observed. A retrospective cohort study of 841 adult patients who underwent emergency appendectomy emphasized the importance of basic laboratory parameters such as CBC parameters and CRP and found CRP to be a good independent predictor of complicated AA [34]. Although in adult patients, these basic laboratory parameters can be affected by various diseases (chronic, inflammatory, neoplastic, hematologic, and allergic) and drugs and therefore be less reliable indicators of complicated AA [35]. We believe that the use of basic preoperative biochemical laboratory parameters in determining complicated or uncomplicated AA in children can have an increased diagnostic value in achieving this goal, which was observed in our study.

This study has some limitations. First, this study was retrospective, lacking the validation of prospective studies. Second, this study was a single-center study, and hence, further research on larger samples is needed to identify a stronger association of hypothermia with complicated AA in children. Finally, there was a lack of certain laboratory tests for some patients, which could have led to a potential misinterpretation of the analyzed data.

Conclusions

Our study supports previous observations that preoperative hyponatremia along with elevated CRP and WBC levels could reliably predict complicated AA in pediatric patients. Further prospective and large-scale studies should confirm these observations.

Acknowledgment

Qatar National Library (QNL) covered the article-processing fee of the manuscript.

Statement of Ethics

Ethical approval for this study was obtained by the local Institutional Review Board (Ethical Committee of the Clinical Center, University of Sarajevo, Number: 51-30-5-13298). The requirement for informed consent was waived due to the retrospective nature of the study.

Conflict of Interest Statement

Una Glamoclija is an employee of the Bosnalijek d.d., Sarajevo, Bosnia and Herzegovina. The other authors declare no conflict of interest.

Funding Sources

This study did not receive any funding.

Author Contributions

Zlatan Zvizdic and Semir Vranic conceived and designed the study. Una Glamoclija performed the statistical analysis. Asmir Jonuzi and Zlatan Zvizdic treated the patients and reviewed all the clinical records. Semir Vranic performed histopathologic analysis. All the authors read and approved the final manuscript.

Data Availability Statement

The datasets used in the study can be made available from the corresponding author upon reasonable request.

References

1 Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol. 1990;132(5):910–25. https://doi.org/10.1093/oxfordjournals.aje.a115734.

2 Pogorelic Z, Domjanovic J, Jukic M, Poklepovic Pericic T. Acute appendicitis in children younger than five years of age: diagnostic challenge for pediatric surgeons. Surg Infect. 2020;21(3):239–45. https://doi.org/10.1089/sur.2019.175.

3 Podda M, Pisanu A, Sartelli M, Coccolini F, Damaskos D, Augustin G, et al. Diagnosis of acute appendicitis based on clinical scores: is it a myth or reality? Acta Biomed. 2021;92(4):e2021231. https://doi.org/10.23750/abm.v92i4.11666.

4 Zvizdic Z, Golos AD, Milisic E, Jonuzi A, Zvizdic D, Glamoclija U, et al. The predictors of perforated appendicitis in the pediatric emergency department: a retrospective observational cohort study. Am J Emerg Med. 2021;49:249–52. https://doi.org/10.1016/j.ajem.2021.06.028.

5 Haider Kazmi SJ, Tabassum S, Asghar MS, Siddiqui MA, Avinash YF, Yasmin F, et al. Role of inflammatory and hematological markers in predicting the complicated and perforated acute appendicitis in pediatric population: a cohort study. Ann Med Surg. 2022;76:103524. https://doi.org/10.1016/j.amsu.2022.103524.

6 Singh A, Pogorelic Z, Agrawal A, Munoz CML, Kainth D, Verma A, et al. Utility of ischemia-modified albumin as a biomarker for acute appendicitis: a systematic review and meta-analysis. J Clin Med. 2023;12(17):5486. https://doi.org/10.3390/jcm12175486.

7 Tintor G, Jukic M, Supe-Domic D, Jeroncic A, Pogorelic Z. Diagnostic utility of serum leucine-rich α-2-glycoprotein 1 for acute appendicitis in children. J Clin Med. 2023;12(7):2455. https://doi.org/10.3390/jcm12072455.

8 Poston LM, Leavitt T, Pope S, Hill H, Tollinche LE, Kaelber DC, et al. Pre-appendectomy hyponatremia is associated with increased rates of complicated appendicitis. Surg Open Sci. 2023;13:88–93. https://doi.org/10.1016/j.sopen.2023.05.001.

9 Walsh A, Lala S, Wells C, Upadhyay V. Hyponatremia an indicator of complicated appendicitis in children: starship experience. ANZ J Surg. 2022;92(4):747–52. https://doi.org/10.1111/ans.17425.

10 Pogorelic Z, Luksic B, Nincevic S, Luksic B, Polasek O. Hyponatremia as a predictor of perforated acute appendicitis in pediatric population: a prospective study. J Pediatr Surg. 2021;56(10):1816–21. https://doi.org/10.1016/j.jpedsurg.2020.09.066.

11 Giannis D, Matenoglou E, Moris D. Hyponatremia as a marker of complicated appendicitis: a systematic review. Surgeon. 2020;18(5):295–304. https://doi.org/10.1016/j.surge.2020.01.002.
12 Kim DY, Nassiri N, de Virgilio C, Ferebee MP, Kaji AH, Hamilton CE, et al. Association between hyponatremia and complicated appendicitis. JAMA Surg. 2015;150(9):911–2. https://doi.org/10.1001/jamasurg.2015.1258.
13 Anand S, Krishnan N, Birley JR, Tintor G, Bajpai M, Pogorelic Z. Hyponatremia-A new diagnostic marker for complicated acute appendicitis in children: a systematic review and meta-analysis. Children. 2022;9(7):1070. https://doi.org/10.3390/children9071070.
14 Wu HC, Yan MT, Lu KC, Chu P, Lin SH, Yu JC, et al. Clinical manifestations of acute appendicitis in hemodialysis patients. Surg Today. 2013;43(9):977–83. https://doi.org/10.1007/s00595-012-0349-8.
15 Kaser SA, Furler R, Evequoz DC, Maurer CA. Hyponatremia is a specific marker of perforation in sigmoid diverticulitis or appendicitis in patients older than 50 years. Gastroenterol Res Pract. 2013;2013:462891. https://doi.org/10.1155/2013/462891.
16 Besli GE, Cetin M, Ulukaya Durakbasa C, Ozkanli S. Predictive value of serum sodium level in determining complicated appendicitis risk in children. Haydarpasa Numune Med J. 2019;59:35–40. https://doi.org/10.14744/hnhj.2019.16013.
17 Tominaga GT, Staudenmayer KL, Shafi S, Schuster KM, Savage SA, Ross S, et al. The American Association for the Surgery of Trauma grading scale for 16 emergency general surgery conditions: disease-specific criteria characterizing anatomic severity grading. J Trauma Acute Care Surg. 2016;81(3):593–602. https://doi.org/10.1097/TA.0000000000001127.
18 Imaoka Y, Itamoto T, Takakura Y, Suzuki T, Ikeda S, Urushihara T. Validity of predictive factors of acute complicated appendicitis. World J Emerg Surg. 2016;11:48. https://doi.org/10.1186/s13017-016-0107-0.
19 NICHD. Pediatric terminology; p. c2023. [cited November 12, 2023]. Available from: http://bioportal.bioontology.org/ontologies/45989?p=terms.
20 Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Intensive Care Med. 2014;40(3):320–31. https://doi.org/10.1007/s00134-014-3210-2.
21 Schlenz H, Intemann T, Wolters M, Gonzalez-Gil EM, Nappo A, Fraterman A, et al. C-reactive protein reference percentiles among pre-adolescent children in Europe based on the IDEFICS study population. Int J Obes. 2014;38(Suppl 2):S26–31. https://doi.org/10.1038/ijo.2014.132.
22 Pediatric CBC reference values (LTR10211). [cited November 9, 2023]. Available from: https://www.dynalife.ca/portals/0/pdf/Lab%20procedure%20or%20protocol/Pediatric%20CBC%20reference%20values.pdf.
23 Dayawansa NH, Segan JDS, Yao HHI, Chong HI, Sitzler PJ. Incidence of normal white cell count and C-reactive protein in adults with acute appendicitis. ANZ J Surg. 2018;88(6):E539–43. https://doi.org/10.1111/ans.13760.
24 Beltran MA, Almonacid J, Vicencio A, Gutierrez J, Cruces KS, Cumsille MA. Predictive value of white blood cell count and C-reactive protein in children with appendicitis. J Pediatr Surg. 2007;42(7):1208–14. https://doi.org/10.1016/j.jpedsurg.2007.02.010.
25 Hansson LE, Laurell H, Gunnarsson U. Impact of time in the development of acute appendicitis. Dig Surg. 2008;25(5):394–9. https://doi.org/10.1159/000180451.
26 Pham XBD, Sullins VF, Kim DY, Range B, Kaji AH, de Virgilio CM, et al. Factors predictive of complicated appendicitis in children. J Surg Res. 2016;206(1):62–6. https://doi.org/10.1016/j.jss.2016.07.023.
27 Lindestam U, Almstrom M, Jacks J, Malmquist P, Lonnqvist PA, Jensen BL, et al. Low plasma sodium concentration predicts perforated acute appendicitis in children: a prospective diagnostic accuracy study. Eur J Pediatr Surg. 2020;30(4):350–6. https://doi.org/10.1055/s-0039-1687870.
28 Duman L, Karaibrahimoglu A, Buyukyavuz BI, Savas MC. Diagnostic value of monocyte-to-lymphocyte ratio against other biomarkers in children with appendicitis. Pediatr Emerg Care. 2022;38(2):e739–42. https://doi.org/10.1097/PEC.0000000000002347.
29 Pintaldi S, Zago A, Pizzolon C, Magni E, Cozzi G, Andrade S, et al. Children with mild hyponatremia at the emergency department are at higher risk of hospitalization. BMC Pediatr. 2023;23(1):318. https://doi.org/10.1186/s12887-023-04109-8.
30 Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. Am J Med. 2006;119(7 Suppl 1):S30–5. https://doi.org/10.1016/j.amjmed.2006.05.005.
31 Elliman MG, Vongxay O, Soumphonphakdy B, Gray A. Hyponatraemia in a Lao paediatric intensive care unit: prevalence, associations and intravenous fluid use. J Paediatr Child Health. 2019;55(6):695–700. https://doi.org/10.1111/jpc.14278.
32 Al-Sofyani KA. Prevalence and clinical significance of hyponatremia in pediatric intensive care. J Pediatr Intensive Care. 2019;8(3):130–7. https://doi.org/10.1055/s-0038-1676635.
33 Swart RM, Hoorn EJ, Betjes MG, Zietse R. Hyponatremia and inflammation: the emerging role of interleukin-6 in osmoregulation. Nephron Physiol. 2011;118(2):45–51. https://doi.org/10.1159/000322238.
34 Ribeiro AM, Romero I, Pereira CC, Soares F, Goncalves A, Costa S, et al. Inflammatory parameters as predictive factors for complicated appendicitis: a retrospective cohort study. Ann Med Surg. 2022;74:103266. https://doi.org/10.1016/j.amsu.2022.103266.
35 Peksoz R, Bayar B. The role of complete blood count parameters in diagnosing acute appendicitis and measuring the severity of inflammation. Ulus Travma Acil Cerrahi Derg. 2021;27(6):654–61. https://doi.org/10.14744/tjtes.2020.69195.