

## ORIGINAL ARTICLE

## HYPONATREMIA AS A MARKER OF COMPLICATED APPENDICITIS

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**Background:** The most frequent cause of paediatric acute abdomen is acute appendicitis. If acute appendicitis is not treated promptly, one third of cases progress to complicated appendicitis. Complicated appendicitis is associated with significant morbidity and its management protocol differs significantly from that of uncomplicated appendicitis. In this study, we assessed the relationship between serum sodium levels and complicated appendicitis. **Methods:** We conducted a prospective observational study from July to December 2020 at the Department of Neonatal and Paediatric Surgery, The Children Hospital, Pakistan Institute of Medical Sciences, Islamabad, on a sample size of 140 patients who met inclusion and exclusion criteria. For this study, we divided the patients into two groups. Group 1 had uncomplicated appendicitis and Group 2 had complicated appendicitis. These findings were then compared to preoperative serum sodium (Na) levels. **Results:** The median serum sodium level in group 1 (uncomplicated appendicitis) was 137.81 mg/dl, while in group 2 it was 131.35 mg/dl (Complicated Appendicitis). The sensitivity and specificity of serum sodium levels at a cut-off point of less than 135 mg/dl were 84.80% and 89.40%, respectively. **Conclusion:** Hyponatremia is currently thought to be a new marker for differentiating between complicated and uncomplicated appendicitis. It is a low-cost, high-efficiency predictive marker for diagnosing and differentiating complicated appendicitis in children.

**Keywords:** Acute appendicitis; Complicated appendicitis; Hyponatremia; Paediatric; Uncomplicated appendicitis

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## INTRODUCTION

Acute appendicitis is one of the most prevalent surgical emergencies among children, with a higher risk of perforation than in adults. From 0 to 4 years, the incidence rises to 1–2 cases per 10,000 population per year, and from 10–13 years, it increases to 25 cases per 10,000 population per year.<sup>1</sup> Perforation has been reported to occur 20–70% in paediatric acute appendicitis.<sup>2</sup>

Only one-third of children in the paediatric population have the classic presentation of acute appendicitis. Clinical diagnosis of acute appendicitis is difficult for paediatric surgeons due to non-specific symptoms and varied presentations, especially in younger children. According to recent research, a multimodal strategy is quite effective in reducing undue morbidity via perforation and negative appendectomy rates. Clinical evaluation, biochemical indicators, radiographic assessment, and the application of clinical scores are all part of this technique.<sup>3</sup> Despite multiple scoring systems and advancements in diagnostic tests for acute appendicitis, the misdiagnosis rate in children under the age of 12 years ranges from 28 to 55 percent, with the rate being even higher in children under the age

of two years.<sup>3</sup> Thus, uncomplicated appendicitis can advance to complicated appendicitis, which can include gangrene, perforation, intraabdominal abscess, diffuse peritonitis, wound infection, ileus, and adhesion intestinal obstruction. Perforated appendicitis has a significantly higher rate of complications (39%) versus uncomplicated appendicitis (8%), resulting in increased morbidity and a longer hospital stay.<sup>2,4</sup>

Early identification of complicated appendicitis provides for a more effective management approach, which includes parental counselling, surgical or conservative approach, antibiotic use, duration of hospital stays, and treatment cost. Although computed tomography has a high sensitivity and specificity rate for complicated appendicitis, its use has been limited due to high radiation exposure, and the use of magnetic resonance imaging in children is still controversial.<sup>5,6</sup> Age, male gender, symptom duration greater than 24 hours, body temperature greater than 37.5 °C, tachycardia greater than 100bpm, total leukocyte counts greater than  $10 \times 10^3/\text{mm}^3$ , neutrophil greater than 85%, and C reactive protein greater than 50 mg/dl are all clinical and biochemical markers that

affect the prognosis of complicated appendicitis.<sup>7,8</sup> The last three variables are referred to as the "triple screen" for diagnosing complicated appendicitis due to high sensitivity.<sup>8</sup>

Hyponatremia has been linked to necrotizing soft tissue infection and has been found in cases of cholecystitis and perforated colonic pathology. It is now thought to be a novel prognostic factor for complicated appendicitis, although the specific pathophysiology is unknown. Proinflammatory cytokines such as IL-1 and IL-6 are thought to cause a severe inflammatory response that results in hyponatremia due to increased antidiuretic hormone release.<sup>9</sup>

This study was conducted to evaluate hyponatremia at admission as a predictor of complicated appendicitis in children. As in various centers uncomplicated appendicitis is now treated conservatively. This finding will aid clinicians and surgeons in the timely diagnosis and management of severe appendicitis, reducing morbidity.

## MATERIAL AND METHODS

A prospective cross-sectional study was conducted at "The Department of Neonatal and Paediatric Surgery, The Children's Hospital PIMS Islamabad" from July to December 2020. Ethical approval was obtained from Hospital Ethical Committee and informed written consent was taken from parents. Study was conducted on 140 patients sample size. Sample size was calculated by using WHO calculator 1.1 with confidence level (%) of 90%, anticipated population proportion of complicated appendicitis patients having hyponatremia (P) 63 and absolute precision (d) of 7%.<sup>9</sup> Study included basic demographics, duration of symptoms of acute appendicitis, body temperature, biochemical markers included haemoglobin (Hb) level, total leukocytes count (TLC), neutrophil count, C reactive protein (CRP), serum sodium (Na) level and intraoperative findings.

Patients of both genders, younger than 14 years, presented with signs and symptoms of acute appendicitis, confirmed by intraoperative findings were included in study.

Exclusion criteria comprised of patients with chronic metabolic or endocrine disorders, a history of abdominal surgery, other causes of abdominal pain, and a negative appendectomy.

True positives identified based on the correlation of serum sodium (Na) and complicated appendicitis included serum sodium levels less than 135 mg/dl preoperatively and complicated appendicitis in perioperative findings. Perioperative findings for complicated appendicitis included appendicular abscess, appendicular tumour, perforated appendix, and phlegmonous appendix.

Patients presented with suspected appendicitis were confirmed by detailed history, physical examination, biochemical markers and ultrasonography. Alvarado Score was calculated in each patient. After resuscitation, performed open appendectomy under General Anaesthesia in diagnosed patients of acute appendicitis and intraoperative findings were noted. Patients were divided into two groups based on operative findings. Group 1 had acutely inflamed appendix without complication and Group 2 had Complicated Appendix, then we correlated perioperative findings with serum sodium (Na) level in each patient. Figure 1 showing management strategy of Acute Appendicitis in our setup.

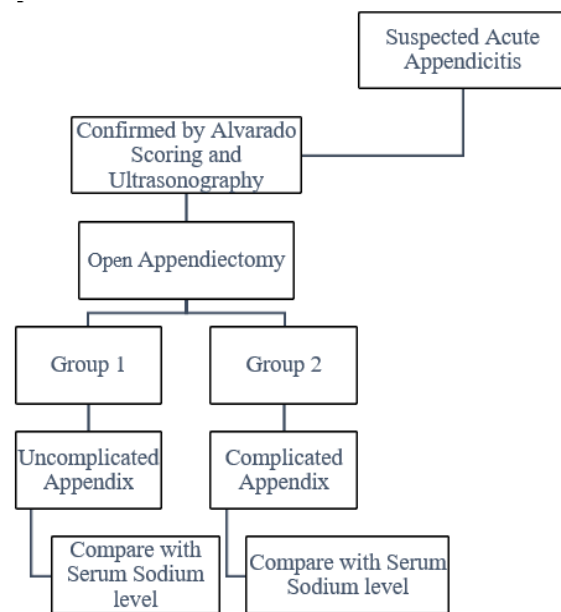


Figure-1: Flowsheet showing management of Appendicitis

Data was analyzed using SPSS version 25.0. Frequencies were calculated for categorical variables like gender. Mean and standard deviation were calculated for continuous variables like age, symptoms of duration, temperature, haemoglobin level, total leukocyte count, neutrophil, C reactive protein and serum sodium. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for serum sodium in complicated and uncomplicated appendicitis.

Chi square test was applied to qualitative variables for comparison, while the independent sample *t*-test was applied to all quantitative variables. The *p* value of  $\leq 0.05$  was considered significant.

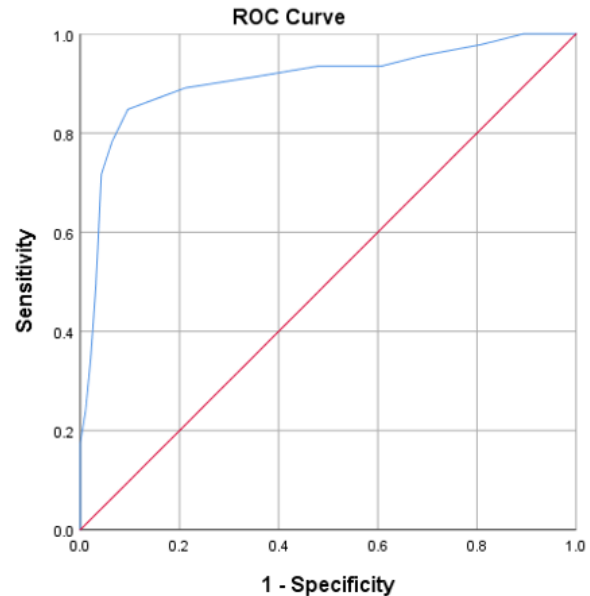
**RESULTS**

A total of 140 patients, 97 (69.3%) male and 43 (30.7%) female, were evaluated for serum sodium (Na) levels in acute appendicitis. The male-female ratio was 2:1. The average age was 08.42±2.76 years (range 02 to 12 years). Out of 140 patients, 94 (67.1%) had uncomplicated appendicitis and 46 (32.9%) had complicated appendicitis, as confirmed by intraoperative findings. Details of patient’s data included in study is shown in Table-I

There was no statistically significant difference in age (0.58) and gender (0.73) between the two groups. Statistically significant differences were noted between two groups in the duration of symptoms (0<0.001), body temperature (<0.001), total leukocyte count (<0.001), neutrophil (0.001), C-reactive protein (<0.001) and serum sodium (Na) level (<0.001). In complicated appendicitis, the median serum sodium (Na) level was 131.35 mg/dl, while in uncomplicated appendicitis, it was 137.81 mg/dl. The area under the curve of serum sodium level in the ROC curve is 90.6 percent in complicated appendicitis with hyponatremia as shown in Figure-2.

Cutoff value of Serum Sodium (Na) less than 135mmol showed sensitivity 84.80% and specificity 89.40%. The positive predictive value was 79.59% and

negative predictive value was 92.31% were calculated by 2x2 table as shown in Table-2



Diagonal segments are produced by ties.

**Figure-2: ROC Curve for serum sodium level as a predictor for complicated appendicitis**

**Table-1: Summary of Results**

	Complicated Appendicitis	Uncomplicated Appendicitis	P value
Age	7.79 years	8.74 years	0.58
Male	31	66	0.73
Female	15	28	0.73
Symptoms duration(hours)	61.28 hours	20.13 hours	<0.001
Temperature	38.98°C	37.62 C	<0.001
TLC	20.69x10 <sup>3</sup> /mm <sup>3</sup>	12.91x10 <sup>3</sup> /mm <sup>3</sup>	<0.001
Neutrophil	83%	75%	0.001
Haemoglobin	10.83 mg/dl	11.95 mg/dl	<0.001
CRP	63.57	24.63	<0.001
Serum Na	131.35	137.81	<0.001

**Table-2: 2x2 table for Serum Sodium (Na)**

Serum sodium (Na)	Complicated appendicitis	Uncomplicated appendicitis
<135 mg/dl	39 (84.78%)	10 (10.6%)
≥135 mg/dl	7 (15.2%)	84 (89.40%)

**DISCUSSION**

Acute appendicitis is one of the most prevalent non traumatic paediatric surgical emergencies and diagnosed in 7– 8% children presented with acute abdominal pain.<sup>10</sup> Different scoring systems (Alvarado, RIPASA and Paediatric Appendicitis Score) and radiological investigations has been introduced to diagnose acute appendicitis. Despite this, atypical symptoms, a difficult physical examination, and a communication barrier with children are the most common causes of misdiagnosis. It can progress from uncomplicated

appendicitis to complicated appendicitis. Incidence of complicated appendicitis is 30% and associated with high morbidity rate.<sup>11</sup> It is critical for the paediatric surgeon to forecast the probability of difficult appendicitis during the preoperative period in order to establish therapeutic interventions and inform parents about the expected post-operative course, possible morbidities, and duration of hospital stay. Patients with complicated appendicitis have a longer hospital stay, a higher rate of complications, and a higher treatment cost. Early diagnosis and treatment

are critical to reducing complications subsequent to complicated appendicitis.<sup>3</sup>

The duration of symptoms greater than 24 hours and body temperature greater than 38.5 °C are most commonly described clinical factors for complicated appendicitis. Bickell *et al.* reported that the risk of complicated appendicitis was significantly lower in patients presenting within the first 36 hours, and the risk increased by 5% every 12 hours after that.<sup>12</sup> Pham *et al.* found a significant difference in the duration of symptoms comparing complicated appendicitis (48-72 hours) and noncomplicated appendicitis (less than 48 hours).<sup>9</sup> According to Pogorelic *et al.*, the duration of symptoms for perforated and nonperforated appendicitis was 60.27 hours and 26.84 hours, respectively.<sup>13</sup> In our study, there was a significant difference (0.001) between complicated (61.28 hours) and uncomplicated appendicitis (20.13 hours). Avanesov *et al.* found that body temperature difference between complicated and uncomplicated appendicitis was 36.7 °C and 37.2 °C respectively.<sup>14</sup> The average body temperature of complicated appendicitis patients in our study was 38.98 °C.

Elevated total leukocyte count and CRP levels are also known predictors of complicated appendicitis. Elevated CRP and total leukocyte count levels are associated with an increased likelihood of complicated appendicitis. Yang *et al.* found that a combination of elevated C-reactive protein and leucocytosis or neutrophilia is associated with a higher risk of complicated appendicitis.<sup>15</sup> C-reactive protein less than 40 mg/l has an 80% probability of uncomplicated appendicitis.<sup>16</sup> Zani *et al.* found a significant difference in CRP (0.001) and total leukocyte count (0.001) between complicated and uncomplicated appendicitis as compare to our study, a significant difference in CRP (<0.001) and total leukocyte count (<0.001) had been noted in both groups.<sup>16</sup>

We conducted a prospective study on hyponatremia as a marker of complicated appendicitis. Hyponatremia is a novel and specific predictor of complicated appendicitis. Lindestam *et al.* discovered that in complicated appendicitis, the serum sodium concentration was significantly lower than in uncomplicated appendicitis. The sensitivity and specificity of  $\leq 135$  mg/dl serum sodium levels are 94.7% and 88.5%, respectively. Serum sodium with a cutoff value of  $\leq 136$  mg/dl has a sensitivity and specificity of 82 percent and 87 percent, respectively. He reported a 93% area under the curve for hyponatremia level in complicated appendicitis and, found that hyponatremia had a 15-fold increased risk of perforated appendicitis.<sup>17</sup> Pham *et al.* reported that the average serum sodium level in complicated

appendicitis was 134 mg/dl, as compared to uncomplicated appendicitis, which had 137 mg/dl.<sup>13</sup> In our study, found the mean serum sodium level in complicated appendicitis was 131.35 mg/dl. Sensitivity and specificity of serum sodium level at 135 mg/dl cutoff point were 84.80% and 89.40%, respectively, with 90.6 percent AUC.

After duration of symptoms, serum sodium (Na) level has been recently considered the second strongest independent predictor marker of complicated appendicitis in children.<sup>13</sup> In addition to other clinical, radiological, and laboratory parameters, sodium concentrations of  $\leq 135$  mg/dl may aid the clinician in making a decision for management of complicated appendicitis.

## CONCLUSION

Low serum sodium levels are a strong predictor marker and a newly defined diagnostic tool as a supplement for diagnosing complicated appendicitis. It can aid in the diagnosis of complicated appendicitis because to its high efficacy, strong relevance, and ease of accessibility at the time of admission.

### Conflict of interest

None

## AUTHORS' CONTRIBUTION

MUQ: Concept of article, data collection, data analysis and original draft preparation. AI: Data collection. MH: Writing and proof reading. MUN: Conceptualization. AA: Data analysis. MAC: Supervision. SB: Methodology

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