



## Preoperative Hyponatraemia As A Touchstone For Complicated Appendicitis – A Retrospective Study

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### Abstract

#### Introduction:

The most prevalent surgical emergency is acute appendicitis. Early identification of patients with complex Appendicitis leads to better results and prompt surgical management. The current research examined the relationship between the degree of acute appendicitis and the existence of preoperative hyponatremia

#### Materials And Procedures:

We revisited the medical records of adult patients operated on for acute appendicitis in a span of six years. Hyponatremia was described as serum sodium level of  $\leq 135$  mEq/L.

patients were categorized into those with complicated and non-complicated.

appendicitis based on histopathology reports and/or operative findings.

#### Results:

150 cases were found and incorporated in this research.

Complicated appendicitis appears more often in older and female patients.

Significantly higher frequency of hyponatremia was identified in individuals with complicated appendicitis ( $p < 0.001$ ), and in cases having perforation were more likely than those without ( $p = 0.045$ ).

#### Conclusions

The current investigation showed that low preoperative sodium levels are linked to complicated appendicitis.

Serum sodium levels is a routine, inexpensive laboratory test, which could serve as a supplementary marker to help surgeons detect gangrenous or perforated severe appendicitis.

**Keywords:** NIL

### Introduction

The most frequent cause of acute abdominal pain and the most frequent reason for emergency abdominal surgery worldwide is acute appendicitis. According to the estimates, 7-8% of the general population in the West will undergo an emergency appendectomy at some point in their lives. However, the recent developments in diagnosis and therapy have not

resulted in a discernible decrease in morbidity or mortality. Most of the time, patients have straightforward, noncomplicated appendicitis (NCA). Patients with complicated appendicitis (CA) have much worse postoperative outcomes, including higher rates of morbidity, longer recovery times, and higher hospital expenses [1,2].

The presence of a perforated or gangrenous appendix defines the CA group's classification of patients with acute appendicitis. Twenty to thirty percent of cases can result in a perforation; however, rates are higher in older adults and children. Perforation rates are even higher, especially in children under the age of five, ranging from 100% in children under the age of one year to 47.7% in children five years old. In California, early surgery is linked to fewer postoperative complications, but late surgery entails higher costs and longer hospital stays. [3,4]

While it is obvious that patients with diffuse peritonitis and appendiceal perforations require immediate surgery, it can be challenging to determine which patients also require an appendectomy. Decisions about when to perform CA procedures may be impacted by early diagnosis of patients.

both the appropriateness of nonoperative management and the surgery. Several scoring systems, including the Appendicitis Inflammatory Response Score (AIR), the Pediatric Appendicitis Score (PAS), and the Alvarado, have been developed to evaluate patients suffering from acute appendicitis. It has been demonstrated that none of these scoring systems can accurately predict the presence of CA in the adult population, underscoring the need for more easily utilized, highly specific markers in emergency clinical settings. [4,5]

Numerous studies have introduced a range of laboratory (C-reactive protein, leukocytosis, neutrophil count, delta neutrophil index, neutrophil/lymphocyte ratio, erythrocyte sedimentation ratio, and bilirubin) and demographic (age, gender, and comorbidities) parameters to be associated with CA in an effort to improve detection. Serum sodium levels less than 135 mEq/L, or hyponatremia, are linked to higher rates of perioperative morbidity and mortality. While the precise pathophysiological connection between severe inflammation and hyponatremia is still unknown, a number of studies have shown that pro-inflammatory cytokines like interleukin (IL-) 1 $\beta$  and IL-6, as well as the secretion of antidiuretic hormone (ADH), are likely involved in the process of hyponatremia development in cases of severe inflammation.[6,7]

We looked into the connection between preoperative hyponatremia and acute appendicitis complications &

s because early detection of CA cases would benefit from timely surgical management.

## Materials And Procedures

The institutional scientific review board gave its approval to the current study. Throughout a 6-year period (January 2019–December 2023), we retrospectively examined the medical records of all non-pediatric patients who underwent surgery for acute appendicitis and were older than 14 years. Patients with American Society of Anesthesiology (ASA) score  $\geq 3$ , appendiceal neoplasms, appendicitis during pregnancy, and incomplete data were not included in the study. Patient demographics including age and gender, laboratory results upon admission, preoperative imaging results, surgical notes, and histology notes were all included in the study data.

The patients were divided into two groups: those with noncomplicated appendicitis (NCA) and those with complicated appendicitis (CA). The primary criteria for enrolling patients in the CA group were the presence of an intraabdominal peri appendiceal abscess or peritonitis, as documented in the patients' operative notes, and intraoperative findings of a perforated or gangrenous appendix. In situations where the operative notes were ambiguous, histological confirmation of transmural necrosis was also sought. The patients with CA were further divided into two subgroups (perforation–no perforation) based on evidence of appendiceal perforation. Hyponatremia is defined as a serum sodium level  $\leq 135$  mEq/L and normonatremia as a serum sodium level  $> 135$  mEq/L and  $\leq 145$  mEq/L, based on our institution's laboratory normal serum sodium levels.

The study's main finding was the correlation between the presence of a perforated appendix and the diagnosis of complicated appendicitis, which was found to be caused by low serum sodium levels found at the time of admission. The identification of preoperative (demographic traits and presenting symptoms) and postoperative (complications) parameters also linked to complicated appendicitis was a secondary outcome.

Depending on the type of variables tested and sample size, was used to perform the statistical analysis. The statistical tests used were Student's t, Pearson's chi-square, and Fisher's exact. The distribution's

normality was examined using the Shapiro-Wilk test's mean. Using the receiver operating characteristic curve (ROC) analysis, the cutoff value for the prediction of CA was evaluated, and the means of the area under the curve (AUC), sensitivity, and specificity were determined. The p-value threshold for statistical significance was set at less than 0.007.

**Findings**

A total of 150 patients had appendicitis during the study period; these patients were identified and included in the analysis. Based on recorded data, it was discovered that 65 patients (47.8%) had NCA, and 78 patients (52.5%) had CA. The bulk of female patients had CA (40, 65.2%) as opposed to NCA (21, 34.5%). Conversely, a higher proportion of male patients (40, 58.6%) presented with NCA, indicating a significantly higher proportion of female patients ( $p \leq 0.003$ ) with CA. Patients in the CA group had a mean age that was significantly higher than those in the NCA group ( $p \leq 0.014$ ), indicating that older patients typically experience more severe appendicitis. The most typical preoperative presentations for patients in both groups along with the main postoperative complications that include urinary and pulmonary infections, deep surgical site infections, and superficial surgical site infections with an intraabdominal abscess.

Other than the preoperative observation of abdominal guarding, which was more common in patients in the CA group ( $p < 0.001$ ), there were no appreciable differences between the two groups in terms of postoperative complications or presentation forms. While preoperative sodium levels were normal in most patients in both groups, hyponatremia was found in patients with CA significantly more often than in patients with NCA (41.3% vs. 1.5%, respectively,  $p < 0.001$ ). Of the 68 patients with CA, 38 (55.6%) had no evidence of an appendiceal perforation, and 30 (44.2%) had a documented perforation. The AUC of the admission serum sodium level ROC curve, which identified patients with CA, was 0.785 (95% CI: 0.718–0.868) (Figure 1). A cutoff value of  $\leq 135$  mEq/L demonstrated 41.3% sensitivity, 98.2% specificity, 96.7% positive predictive value, and 60% negative predictive value when utilized in our study to identify patients with hyponatremia. When the performance-no perforation subgroups of CA patients were compared, there was a difference in preoperative sodium levels between the two groups. Following classification of all study participants into perforation-no perforation subgroups, comparison showed that preoperative sodium levels were significantly lower in patients with perforation (36.5%) than in patients without perforation (19.3%) ( $p \geq 0.048$ ).

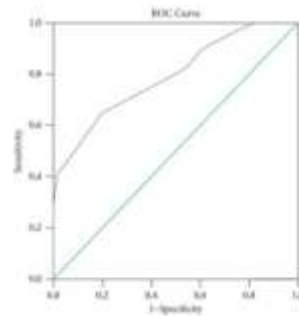


TABLE 1: Patient classification in noncomplicated appendicitis and complicated appendicitis according to sex (Pearson's  $\chi^2$  test), age (Student's *t*-test), preoperative presentation (abdominal guarding, nausea/vomiting, and fever—Pearson's  $\chi^2$  test and peritonitis—Fisher's exact test), postoperative complications (superficial SSI, deep SSI, and systematic—Fisher's exact test), and preoperative sodium levels (Fischer's exact test).

Patient demographics		NCA, n = 65	CA, n = 68	P
Sex	Male, n (%)	40 (58.8)	28 (41.2)	0.006
	Female, n (%)	21 (34.4)	40 (65.6)	
Age	Mean (SD)	33.8 (14.7)	45.8 (21.5)	0.017
	Abdominal guarding	20 (32.8)	48 (70.6)	<0.001
Preoperative presentation	Peritonitis	0 (0%)	4 (5.8%)	NS
	Nausea/vomiting	28 (45.9%)	32 (47.3%)	NS
	Fever	7 (11.5%)	10 (14.7%)	NS
Preoperative sodium levels	Normonatremia	60 (98.4%)	40 (58.8%)	0.001
	Hyponatremia	1 (1.6%)	28 (41.2%)	
	Superficial SSI	3 (4.9%)	7 (10.3%)	
Postoperative complications	Deep SSI abscess	1 (1.6%)	4 (5.8%)	NS
	Systematic	1 (1.6%)	5 (7.3%)	NS

NCA, noncomplicated appendicitis; CA, complicated appendicitis; SD, standard deviation; SSI, surgical site infection; NS, nonsignificant.

## Discussion

The current study showed that preoperative hyponatremia was more commonly detected in patients with documented perforations than in those without, as well as in patients who were found to have CA as opposed to NCA. Given that CA is typically linked to poor outcomes, finding preoperative hyponatremia during a routine, inexpensive laboratory test may suggest a higher risk of appendiceal gangrene and/or perforation. This discovery may have an impact on how patients are managed, possibly prompting earlier surgical intervention and the abandonment of observational or nonoperative approaches.

In many clinical scenarios, such as community-acquired pneumonia and spontaneous bacterial peritonitis in liver cirrhosis, hyponatremia has been linked to a poor prognosis and an extended hospital stay. [9,10]

Preoperative hyponatremia has been shown to be linked to higher perioperative morbidity and mortality in the surgical setting. It has been discovered that hyponatremia at admission is beneficial in both diagnosing necrotizing soft-tissue infections and forecasting the patients' mortality. Hyponatremia was found to be a potential predictor of small bowel obstruction, bowel perforation, and/or ischemia in cases of gangrenous cholecystitis among other admission variables. [11,12]

A growing amount of data points to a possible link between hyponatremia and perforations or ischemia of the visceral wall. According to Swart *et al*, the so-called "immuno-neuroendocrine interface," in which interleukin-6 (IL-6) plays a significant role, can explain the clinical association between severe inflammatory stimulus and hyponatremia. Many proinflammatory cytokines, such as IL-6, are released during inflammation, starting the acute phase response. Circulating IL-6 activates the lamina terminalis's subfornical organ and organum vasculosum by either diffusing or being transported across the blood-brain barrier. The ultimate result of this activation is thirst and increased vasopressin secretion by neurons in the paraventricular and supraoptic nuclei. Hyponatremia is the result of combining increased water intake with antidiuresis brought on by cytokine-mediated osmotic vasopressin secretion.

Previous reports in both adult and pediatric populations have evaluated a potential relationship between hyponatremia and the severity of appendicitis. Kim *et al* examined the relationship between different clinical and laboratory parameters and intraoperatively diagnosed perforated or gangrenous appendicitis in a retrospective study involving 1550 adults with acute appendicitis. They discovered that hyponatremia may be suggestive of complex appendicitis. In sigmoid diverticulitis or appendicitis in patients older than 50 years, Ka'iser *et al* assessed hyponatremia as a marker of colon perforation. They found that while hyponatremia can be regarded as such a marker, its low sensitivity means that its absence cannot predict the absence of colon perforation. The authors do not specify, though, if the subgroup of patients with perforated appendicitis and hyponatremia had the same relationship with hyponatremia. Wu *et al* examined the prognosis, risk factors, and clinical features of acute appendicitis in adults receiving hemodialysis. They discovered that appendiceal perforation was present in 66% of the patients with preoperative hyponatremia, but there was no discernible difference between the hyponatremia group and the non-hyponatremia group. [12,13]

In pediatric populations, the relationship between the severity of appendicitis and hyponatremia was also examined. A prospective diagnostic accuracy study by Lindestam *et al* with 80 children suffering from acute appendicitis confirmed a strong correlation between appendix perforation and plasma sodium concentration of  $\leq 136$  mmol/L. In a study involving 184 pediatric patients, Pogorelic *et al* found that a sodium concentration cutoff value of  $\leq 135$  mmol/L gave the best possible sensitivity (94.5%) and specificity (88.4%), with hyponatremia being confirmed as a promising new biochemical marker indicating complicated appendicitis. In a retrospective case control study, Besli *et al* discovered no distinction in sodium levels between kids with and without complicated appendicitis. Additionally, this study found that patients with CA had lower baseline sodium levels; a sensitivity of 82.2% and specificity of 31.5% were obtained with a cutoff level for basal Na  $\leq 138$  mEq/L [29]. Pham *et al* and Serradilla *et al* conducted comparable retrospective investigations and came to the same. [14,15]

**Conclusion:**

hyponatremia was substantially linked to CA. Giannis et al came to the conclusion that serum sodium level measurement should be taken into consideration in patients suspected of having complicated acute appendicitis after conducting a systematic review that included seven studies from both pediatric and adult populations.

The retrospective design and relatively small sample size of this study, which is primarily attributable to its single-institution design and a small number of missing data that impact the study's power, are among its limitations. An additional constraint stems from the disparities observed among different research investigations regarding the threshold value assigned to serum sodium concentrations. Our study defined hyponatremia as a serum sodium level of  $\leq 135$  mEq/L. However, other studies used  $< 135$  mEq/L,  $\leq 136$  mEq/L, or  $< 136$  mEq/L arbitrarily, which made comparing the results less trustworthy.

**Final Thoughts**

Finally, our research showed a correlation between preoperative hyponatremia and CA. An inexpensive, routine laboratory test called serum sodium levels may serve as an auxiliary marker to help surgeons diagnose perforated or gangrenous acute appendicitis earlier. Prospective studies in the future will shed more light on the relationship between hyponatremia and the severity of appendicitis, enabling the best possible clinical care.

**Information Availability:** Upon request, the corresponding author will provide the data (nominal and ordinal) used to support the study's findings.

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