

# Clinical Correlation between Hyponatremia and Complicated Appendicitis, A Prospective Cohort Study

*Fareeba<sup>1</sup>, Arooj Zahra<sup>2</sup>, Nazrah Shabbir<sup>3</sup>, Zahid Rasheed<sup>4</sup>, Sheikh Ahmed Idrees<sup>5</sup>, Waheed Bashir<sup>6</sup>, M. Waqas Raza<sup>7</sup>*

## Abstract

**Introduction:** Acute appendicitis is a frequent surgical emergency; therefore, prompt diagnosis and management are essential. Certain clinical predictors are used to diagnose it. However, no such predictor is available to assess the complicated appendicitis in the absence of radiological investigations like CT scan. Serum sodium levels have gained a lot of attention in recent times to assess the severity of the disease and is believed to be a clinical parameter in the diagnosis of complicated appendicitis preoperatively.

**Methods:** This study involves correlation of hyponatremia with complicated appendicitis. We included 236 patients in this study, meeting the inclusion and exclusion criteria. For each patient, preoperative serum sodium levels were measured and correlated post operatively.

**Results:** Our study reported a strong correlation between hyponatremia and its pre-operative accuracy in diagnosis of complicated appendicitis.

**Conclusion:** Hyponatremia can be considered as a reliable marker of complicated appendicitis due to its cost effectivity and easy availability in emergency departments.

**Keywords:** Complicated appendicitis, Clinical markers, Hyponatremia, Low-income country, Cost effective marker

<sup>1,2,3,6</sup>post graduate trainee general surgery department RTH, <sup>4</sup>Senior Registrar general surgery HFH, <sup>5</sup>Post graduate trainee internal medicine ITH, <sup>7</sup>professor of surgery RTH, Rawalpindi

## 1. Introduction

Acute appendicitis (AA) is the most common acute emergency in surgical ER.<sup>1</sup> Appendicitis is the inflammation of the vermiform appendix.<sup>2</sup> It is most seen in middle aged population.<sup>3</sup> It typically presents acutely within 24 hours of the onset of symptoms of fever, loss of appetite, pain right iliac fossa or umbilicus but can also present late.<sup>4</sup> Acute appendicitis can be either complicated (CA) or uncomplicated (UCA).<sup>5</sup> Complicated appendicitis can be either gangrenous, perforated, abscess or a phlegmon.<sup>6</sup> Uncomplicated appendicitis can be managed conservatively with IV antibiotics.<sup>7</sup> Whereas, complicated appendicitis needs aggressive management due to its related complications such as paralytic ileus, surgical site infections and prolong hospital stay.<sup>5</sup>

Current concurrences are unable to predict CA from UCA. A CT scan is widely used to diagnose AA,<sup>4</sup> but carries a lot of drawbacks like cost effectivity, non-readily availability, radiation exposure, contrast associated injury, time consuming and delayed results. Various clinical and laboratory parameters are used for this purpose.<sup>8</sup> The clinical parameters like tachycardia (>100/min), fever (>37.5c), elevated CRP (50mg/l), leukocytosis (>10nl/l) neutrophilia (>85%)<sup>9</sup> symptoms for more than 24 hours and abdominal pain for more than 48 hours are likely to be associated with complicated appendicitis. However, these

parameters are inadequate to differentiate between CA and UCA. Serum sodium levels preoperatively is shown to be a reliable laboratory parameter in aiding the diagnosis of CA. Moreover, it is readily available and cost effective and does not take a lot of time.<sup>10</sup> This hyponatremia is attributed to certain inflammatory changes in the body. Various inflammatory cytokines release such as IL-6 which stimulates the release of vasopressin, leading to increased water retention and decreased sodium levels.<sup>10,11</sup> The rationale of this study is to assess the diagnostic accuracy of hyponatremia in correlation with complicated AA.

## 2. Materials & Methods

A prospective cohort study was conducted by collecting data from 236 patients who were presented in the surgical emergency of Rawalpindi Teaching Hospital and were operated for acute appendicitis between May 2023 to February 2024. All patients between the age of 15-45 years presented in the surgical emergency were included in the study. Whereas pregnant females, patients of renal failure and children below 15 years were excluded from the study. All patients underwent open appendectomy and intra-operative findings were correlated with preoperative serum sodium levels.

We divided patients into two groups, complicated (CA) and uncomplicated (UCA) groups and their sodium

levels were obtained at the time of admission in the emergency department. Normal sodium levels in uncomplicated group are from 135-145 mEq/L whereas, in complicated group sodium levels were expected to be 128-135 mEq/L.

Statistical analysis was performed using SPSS version 26.0. Data was collected in single format Microsoft Excel sheet. The significance of serum sodium levels was assessed by using paired T test. Numerical data was depicted as mean  $\pm$  SD. P-value was set at  $<0.05$  which is considered significant using ROC curve.

### 3. Results

A total of 236 patients underwent open appendectomy between May 2023 to February 2023, mean age was 27.6 years and 121 among them were female and 115 male patients. Out of these, 145 patients had serum sodium level of 128-135mEq/L and the per operative findings showed that 129 patients had complicated appendicitis while 61 had acutely inflamed appendix which was uncomplicated [Table-1 and 2].

**Table-1 showing total number of patients, their time of presentation, preoperative serum sodium levels and per-operative findings.**

	age	gender		Perit onitis	Neutrop hil		Present ation			Intraoperative				
	Mean	Male	Female	Mean	80- 90	60- 80	<2 4 hou rs	>24 hou rs	acutely inflam ed	abscess	phlegmon	gangrenous	perforated	
NA+	128135 meq/L	28.26	67	78	.25	102	43	51	94	16	58	28	29	14
	135145 meq/L	26.70	48	43	.38	64	27	27	64	61	1	16	2	11

**Table 2: One sample T-Test was applied which showed significant results between complicated and uncomplicated groups.**

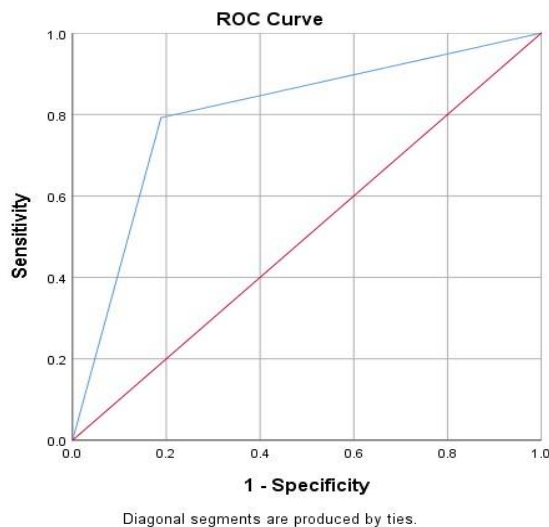
	N	Mean	Std. Deviation	Std. Error Mean
UCA	236	.3602	.48107	.03131
CA	236	.6610	.47437	.03088

### 4. Discussion

Acute Appendicitis is one of the most common surgical emergencies<sup>12,1</sup> where early diagnosis and earlier intervention are required to prevent the complications of CA. The diagnosis of acute appendicitis is still a diagnostic dilemma due to its atypical symptoms and the unreliability of different scoring systems and the cost effectiveness of radiological investigations makes it difficult to distinguish CA from UCA. Gomes et al. introduced classification for the grading of appendicitis based on its intraoperative findings. Grades 1&2: Hyperemia and fibrinous exudative is considered as uncomplicated, Grade3 A: Segmental necrosis, Grade3: Necrosis of the base of the appendix, Grade4 A: localized abscess, Grade4 B: Regional peritonitis, and Grade5: Diffuse peritonitis. Grade 3,4&5 are considered complicated appendicitis.<sup>12</sup>

A systemic review reported recently states that, serum sodium level can be used as a marker in patients with acute appendicitis to further confirm its correlation.<sup>13</sup> Hyponatremia is the most common electrolyte abnormality in admitted patients and it is considered to be a poor prognostic factor in patients with longer hospital stay.<sup>14</sup> Studies have been done in the past that shows the incidence of hyponatremia in post operative patient as IL-6 and Vasopressin levels increases after surgery.<sup>15,16</sup> In surgical patients it can be used to predict morbidity and mortality.<sup>17,18</sup> This correlation can be explained by neuroendocrine pathway, that implicates the release of IL-6, leading to the release of vasopressin (Anti diuretic Hormone) which ultimately leads to hyponatremia.<sup>19</sup> Several non-osmotic stimuli for the release of vasopressin have been identified, including hypovolemia, pain, nausea, and certain drugs.<sup>20</sup> As serum electrolytes are a part of routine investigation in patients presenting in emergencies in our hospital, therefore due to its easy availability and cost effectiveness it is suggested to assess the role of serum sodium in predicting CA. Several studies, included in our literature review,<sup>7,10,11,21</sup> have been done previously that suggest its correlation with CA. Hyponatremia

being a predictive marker of severity, can affect the management of patients.<sup>10,22</sup>



**Figure 1: ROC representing the curve obtained to predict accuracy of pre-operative hyponatremia in complicated appendicitis. AUC = 0.739, 95% CI:95%, p-value <0.05.**

## 5. Conclusion

The study was intended to assess the correlation between Hyponatremia and complicated appendicitis. Our study showed significant results therefore it should be used in the emergency department as it is cost effective and easily available.

## References

1. Douglas Smink M, MPH David I Soybel, MD. Management of acute appendicitis in adults. uptodate. 2023.
2. Deppen. MWJRALJG. Appendicitis. NIH NLM Logo. 2023.
3. Oguntola AS, Adeoti ML, Oyemolade TA. Appendicitis: Trends in incidence, age, sex, and seasonal variations in South-Western Nigeria. *Ann Afr Med*. 2010;9(4):213-7.
4. Krzyzak M, Mulrooney SM. Acute Appendicitis Review: Background, Epidemiology, Diagnosis, and Treatment. *Cureus*. 2020;12(6):e8562.
5. Symeonidis NG, Pavlidis ET, Psarras KK, Stavratsi K, Nikolaidou C, Marneri A, et al. Preoperative Hyponatremia Indicates Complicated Acute Appendicitis. *Surg Res Pract*. 2022;2022:1836754.
6. Romano A, Parikh P, Byers P, Namias N. Simple acute appendicitis versus non-perforated gangrenous appendicitis: is there a difference in the rate of post-operative infectious complications? *Surg Infect (Larchmt)*. 2014;15(5):517-20.
7. Lauren M. Poston B, a, Tripp Leavitt, MD, b Samantha Pope, BA, c Hannah Hill, MS, d Luis E. Tollinche, MD, FASA, a, c David C. Kaelber, MD, PhD, MPH, e, f and Jonathan A. Alter, MD, a, c. Preappendectomy hyponatremia is associated with increased rates of complicated appendicitis. NIH NLM Logo. 2023.
8. Pogorelić Z, Mihanović J, Ninčević S, Lukšić B, Elezović Baloević S, Polašek O. Validity of Appendicitis Inflammatory Response Score in Distinguishing Perforated from Non-Perforated Appendicitis in Children. *Children (Basel)*. 2021;8(4).
9. Käser 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.
10. Messias B, Cubas I, Oliveira C, Hashimoto F, Mocchetti E, Ichinose T, et al. Usefulness of serum sodium levels as a novel marker for predicting acute appendicitis severity: a retrospective cohort study. *BMC Surgery*. 2023;23(1):312.
11. Symeonidis NG, Pavlidis ET, Psarras KK, Stavratsi K, Nikolaidou C, Marneri A, et al. Preoperative Hyponatremia Indicates Complicated Acute Appendicitis. *Surgery Research and Practice*. 2022;2022:1836754.
12. Gomes CA, Sartelli M, Di Saverio S, Ansaloni L, Catena F, Coccolini F, et al. Acute appendicitis: proposal of a new comprehensive grading system based on clinical, imaging and laparoscopic findings. *World Journal of Emergency Surgery*. 2015;10(1):60.
13. Giannis D, Matenoglou E, Moris D. Hyponatremia as a marker of complicated appendicitis: A systematic review. *Surgeon*. 2020;18(5):295-304.
14. Thompson C, Hoorn EJ. Hyponatraemia: an overview of frequency, clinical presentation and complications. *Best Pract Res Clin Endocrinol Metab*. 2012;26 Suppl 1:S1-6.
15. Chung H-M, Kluge R, Schrier RW, Anderson RJ. Postoperative Hyponatremia: A Prospective Study. *Archives of Internal Medicine*. 1986;146(2):333-6.
16. Kudoh A, Takase H, Katagai H, Takazawa T. Postoperative interleukin-6 and cortisol concentrations in elderly patients with postoperative confusion. *Neuroimmunomodulation*. 2005;12(1):60-6.
17. Leung AA, McAlister FA, Rogers SO, Jr., Pazo V, Wright A, Bates DW. Preoperative hyponatremia and perioperative complications. *Arch Intern Med*. 2012;172(19):1474-81.
18. Teo CB, Gan MY, Tay RYK, Loh WJ, Loh NW. Association of Preoperative Hyponatremia With Surgical Outcomes: A Systematic Review and Metaanalysis of 32 Observational Studies. *J Clin Endocrinol Metab*. 2023;108(5):1254-71.
19. 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.
20. Ellison DH, Berl T. Clinical practice. The syndrome of inappropriate antidiuresis. *N Engl J Med*. 2007;356(20):2064-72.
21. Sheen J, Bowen J, Whitmore H, Bowling K. Hyponatremia as a Marker of Complicated Appendicitis: A Retrospective Analysis. *Cureus [Internet]*. 2022 2022/07//; 14(7):[e26672 p.]. Available from: <http://europepmc.org/abstract/MED/35949749>
22. Ozdemir DB, Karayigit A, Dizen H, Unal B. Role of hyponatremia in differentiating complicated appendicitis from uncomplicated appendicitis: a comparative study. *Eur Rev Med Pharmacol Sci*. 2022;26(21):8057-63.