Original Article

OPEN ACCESS

Preoperative Hyponatremia Indicates Complicated Acute Appendicitis

Kanza Batool[1], Asifa Dian[2], Anis Ahmed[3], Muhammad Omer Nasir[4], Farhan Ahmed[5]

[1,5]Postgraduate Trainee, [2]Assistant Professor, [3]Professor, [4]Medical Officer

Dept, of General Surgery, Benazir Bhutto Hospital Rawalpindi

Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, [1,4]Drafting the work or revising it critically for important intellectual content, [3]Final approval of the study to be publish.

Funding Source: None
Conflict of Interest: None

Received: July 21, 2024
Accepted: Oct 02, 2024

Address of Correspondent
Dr. Kanza Batool
Postgraduate Trainee
Dept, of General Surgery, Benazir Bhutto Hospital Rawalpindi
Islamabad
kanzabatool26@gmail.com

ABSTRACT

Objective: This study looks at the connection between preoperative hyponatremia and the intensity of severe appendicitis in Punjab.

Methodology: This retrospective observational study was conducted at dept. of general surgery BBH hospital Rawalpindi from August 2022 to December 2023. Data was retrieved from hospital medical records of all non-pediatric recipients who underwent surgery for severe appendicitis with age more than 14 years. A blood sodium concentration of less than 135 mEq/L was defined as hyponatremia. Based on surgical results and/or histology reports, cases were divided into two categories: complex and non-complicated appendicitis.

Results: This research discovered and enrolled 68 participants in total. Elderly and female patients were reported to have complex appendicitis with greater frequency. Significantly higher rates of hyponatremia were seen in patients with severe appendicitis ($p < 0.001$) and individuals with perforations compared to those without (p 0.048).

Conclusion: The current investigation established a link between complex appendicitis and pre-operative hyponatremia. An inexpensive, standard laboratory test called serum sodium content may serve as an auxiliary marker to help surgeons diagnose gangrenous or perforated severe appendicitis earlier.

Keywords: Acute appendicitis, Hyponatremia, Preoperative Care, Peritonitis.

Cite this article as: Batool K, Dian A, Ahmed A, Nasir MO, Ahmed F. Preoperative Hyponatremia Indicates Complicated Acute Appendicitis. Ann Pak Inst Med Sci. 2024; 21(1):317-321. doi. 10.48036/apims.v21i1.826.

Introduction

The primary reason for severe abdominal discomfort and the most frequent indication for urgent abdominal surgery worldwide is severe appendicitis.[1] According to estimates, 7-8% of the population as a whole in the West will need an emergency surgical append at a certain time in their lives.[2] Both death rates and morbidity have not greatly improved despite recent advancements in imaging and therapy.[3] Most of the time, individuals have straightforward, non-complicated appendicitis (NCA). Patients with complex appendicitis (CA) had significantly poorer surgical outcomes, including higher rates of morbidity, longer recovery times, and higher hospital expenses.[4]

A ruptured or gangrenous appendix serves as a defining characteristic for the CA category of individuals with acute appendicitis.[5] Twenty to thirty per cent of instances can result in a perforation; however, rates in older adults and children are greater.[6,7] Perforation frequencies are significantly greater, particularly with children under the age of five.[8] They range from 100% in infants under the age of one year to 47.3% in youngsters under the age of five. In California, earlier surgery is linked to less postoperative problems, but later surgery entails higher hospital stays and expenses.[9] Individuals with appendiceal perforations who arrive with widespread peritonitis must have surgery as soon as possible, but determining whether the remaining patients also require an appendectomy might be challenging. Early diagnosis of CA sufferers may influence choices on when to perform surgery and if non-operative therapies are appropriate. Several scoring systems, including the Appendicitis Inflammatory Response Score (AIR), the Paediatric Appendicitis Score (PAS), and Alvarado, have been developed to evaluate individuals with serious appendicitis. It has been demonstrated that none of such scoring methods has a predicting value that is sufficient for identifying CA in the adult population, underscoring

the need for enhanced specificity indicators that are user-friendly in immediate clinical settings.[10]

Several studies link a range of laboratory (C-reactive protein, leukocytosis, neutrophil number neutrophil/lymphocyte proportion, erythrocyte sedimentation proportion, and bilirubin) and medical (a high temperature, tachycardia, and indication duration) criteria to CA to enhance detection of the condition.[11,12]

Serum sodium levels below 135mEq/L, or hyponatremia, are linked to higher rates of perioperative death and fatal injuries.[13] While the precise pathophysiological connection that exists between hyponatremia and chronic inflammation is still unknown, several investigations have shown that pro-inflammatory cytokines, like interleukin (IL-) 1β and IL-6, in addition to the release of antidiuretic hormone (ADH), are likely involved in the emergence of hyponatremia in circumstances involving grave inflammation.[14,15] We looked at the connection between preoperative hyponatremia and severe appendicitis aggravation since early diagnosis of CA cases could reap advantages from timely surgical care.

Methodology

This retrospective observational study was conducted in the Department of General Surgery, BBH Hospital, Rawalpindi, from August 2022 to December 2023. Ethical approval was obtained from the Institutional Review Board (IRB) under reference number RMU-RRF-SUR-007-24. Data was retrieved from hospital medical records of all non-pediatric recipients who underwent surgery for severe appendicitis with age more than 14 years. Patients with American Society of Anesthesiology (ASA) score ≥3, appendiceal neoplasms, appendicitis amid pregnancy, and missing data were not included in the research. Preoperative radiology results, operation notes, histological notes, laboratory results upon enrollment, and patient information including age and sex were all included in the study data. Two groups of patients were identified: one for difficult appendicitis (CA) and another for non-complicated appendicitis (NCA). Individuals in the CA category were primarily selected through their operational records, which documented intraoperative results for a split or gangrenous appendix as well as the existence of intra-abdominal peri-appendiceal abscess or peritonitis. In situations where the operating notes were ambiguous, histological confirmation of transmural necrosis was also pursued. The individuals with CA were then divided into two categories based on proof of appendiceal perforation (perforation–no perforation). Hyponatremia is defined as a serum sodium level ≤135mEq/L and normonatremia as a serum sodium range >135mEq/L and ≤145mEq/L, depending on our institution's laboratory's regular serum sodium values.

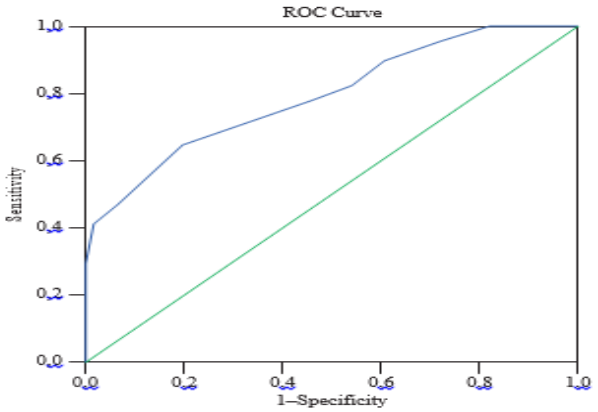
The study's main findings reveal that there was a correlation between the existence of a perforated appendix and the complex condition appendicitis that was discovered upon hospitalization, as well as decreased serum sodium concentrations. The identification of preoperative (demographic traits and presenting indicators) and postoperative (adverse effects) indicators also connected to severe appendicitis had been an additional result.

By the kind of variables examined and sample size, IBM SPSS 25.0 (SPSS Inc., Chicago, IL, USA) was used to complete the statistical evaluation. The statistical procedures employed include Student's t, Pearson's chi-square, and Fisher's exact. Through the use of the Shapiro-Wilk test means, the distribution's uniformity was verified. Using the receiver operating characteristic curve (ROC) evaluation, the threshold level for the forecasting of CA was evaluated, and the means of the area under the curve (AUC), sensibility, and precision were determined. A probability ratio (p) of below 0.05 was designated as the threshold for statistical significance.

Results

A total of 68 participants were found and incorporated into the current investigation from individuals who had appendectomies throughout the study timeframe. The recorded data indicated that 32 patients (47.05%) had NCA and 36 patients (52.95%) had CA. Among female patients, CA (24, 35.3%) was detected in the majority as opposed to NCA (15, 22.06%). Conversely, findings indicate that significantly more female patients reported with CA (p 0.006), whereas more men (29, 42.7%) reported with NCA. The CA group's average patient age was significantly greater than the NCA category's (p 0.017), indicating that older individuals often have more serious appendicitis. Table I lists the primary postoperative problems including shallow infections in the surgical area, extensive operative site infections (including intra-abdominal infection), and systemic abnormalities (pulmonary and urine infections), along with the most prevalent preoperative appearances of individuals in both categories. Other than the preoperative observation of abdominal guarding, which

was more common in patients in the CA group ($p < 0.001$), there were no significant variations between the two categories in terms of postoperative issues or presenting types. While preoperative sodium content was normal in most patients in both categories, hyponatremia was much more common in people with CA than in individuals with NCA (41.20% vs. 1.60%, accordingly, $p < 0.001$) (Table I). The receiver operator (ROC) curve of serum sodium degrees upon enrollment determining those who had CA demonstrated an AUC of 0.793 (95% CI: 0.718–0.868) (Figure 1). The minimum threshold of ≤135mEq/L, which in the present investigation was employed to separate individuals with hyponatremia, showed responsiveness of 41.40%, specificity of 98.30%, positive anticipatory value of 96.60%, and negative forecasting value of 60%. Comparison of the performance–no perforation subgroups of patients with CA revealed that there was no significant difference (p-value 0.375) in the preoperative sodium amounts between the two categories. The comparison showed that significantly more individuals who had perforation (36.7%) versus individuals without perforation (19.2%) had lower preoperative sodium concentrations ($p > 0.048$) when all research participants were divided into the perforation–no perforation categories.



Patients with non-complicated and complex appendicitis are categorized based on their sex (using Pearson's x2 test), age (using Student's t-test), preoperative presentation (using Fisher's exact test for peritonitis, abdominal guarding, nausea/vomiting, and fever), complications following the operation (using Fisher's exact test for superficial SSI, deep SSI, and systematic), and preoperative sodium concentrations.

Discussion

The current investigation showed that preoperative hyponatremia was detected more often in patients with recorded perforations other than those without perforations, as well as in individuals who were discovered to have CA as opposed to NCA. Given that CA is typically linked with a poor prognosis, identification of preoperative hyponatremia by standard, inexpensive laboratory testing may suggest a higher risk of appendiceal gangrene and/or perforation. This discovery may have an impact on how patients are managed, possibly resulting in early surgical treatment and the cessation of surveillance or nonoperative approaches. In several clinical scenarios, such as community-based pneumonia and sporadic bacterial peritonitis in liver cirrhosis, hyponatremia is linked to a poor outcome and extended hospitalization.[16–18] Pre-operative hyponatremia is linked to higher peri-operative morbidity as well as death in the surgical environment.[13] It has been discovered that hyponatremia upon admission is useful in both diagnosing necrotizing soft-tissue infections and estimating the patients' fatality.[19, 20] Hyponatremia was found to be a potential indicator of gangrenous cholecystitis, intestinal ischemia, and/or perforation in small intestine obstruction amidst a variety of admission factors.[21, 22]

A growing amount of data points to a possible link between hyponatremia and perforation or ischemia of the

Table I: Comparison of Demographic Characteristics, Preoperative Clinical Features, Sodium Levels, and Postoperative Complications Between Patients with Non-Complicated and Complicated Appendicitis.

Patient Demographics		**NCA (32) 47.05%**	**CA (36) 52.95%**	**P value**
Gender	Male, *n* (%)	29 (42.05%)	00 0%	0.006
	Female, *n* (%)	24 (35.3%)	15 (22.06%)	
Age	Mean (SD)	33.8 (14.7%)	45.8 (21.5%)	0/017
Preoperative Presentation	Abdominal guarding	10(31.3)	26(72..2)	<0.001
	Peritonitis	0(0%)	2(5.6%)	NS
	Nausea/vomiting	15(46.9%)	7(19.2%)	NS
	Fever	7(11.5%)	1(2.7%)	NS
Preoperative sodium levels	Normonatremia	31(98.4%)	21(58.33%)	
	Hyponatremia	1(1.6%)	15(41.7%)	0.001
Postoperative complications	Superficial SSI	3(4.9%)	7(10.3%)	NS
	Deep SSI abscess	1(1.6%)	4(5.8%)	NS
	Systematic	1(1.6%)	5(7.3%)	NS

visceral wall. According to Swart et al[15], the so-called "immuno-neuroendocrine interaction," in which interleukin-6 (IL-6) plays a significant role, might underlie the clinical link between strong inflammatory stimuli and hyponatremia. The accelerated phase response is triggered by the secretion of various pro-inflammatory cytokines, such as IL-6, during inflammation.[23] Circulating IL-6 activates the lamina terminalis's subfornical organ and organum vasculosum by either diffusing or being transferred over the blood-brain interface.[24] Elevated vasopressin production by neurons in the paraventricular and supraoptic nuclei and thirst are the ultimate results of this stimulation. Hyponatremia is eventually brought on by an interaction of higher water consumption and antidiuresis brought on by cytokine-mediated nonosmotic vasopressin outflow.[15]

Previous studies in elderly and paediatric groups have shed light on attempts to assess a potential relationship between the extent of appendicitis and hyponatremia. Kim et al[25] examined the relationship between different medical and laboratory criteria and intraoperatively diagnosed perforated or gangrene appendicitis in a retrospective study including 1550 older people with severe appendicitis. They discovered that hyponatremia may be indicative of serious appendicitis.

In their evaluation of hyponatremia as an indicator of colon perforation in people over 50 with sigmoid diverticulitis or appendicitis, Ka¨ser et al[11] concluded that while hyponatremia is capable of being used as such a marker, its low specificity means that its absence is unable to predict a lack of colon perforation. The researchers do not specify, nevertheless, if the particular group of individuals with perforated appendicitis and hyponatremia had the same correlation with hyponatremia.[11] Wu et al[26] examined the prognosis, risk variables, and clinical features of severe appendicitis in grown-up hemodialysis victims. They discovered that appendiceal perforation existed in 66% of individuals with preoperative hyponatremia, but there was no significant difference between this category and the nonhyponatremia category.

In pediatric populations, the relationship between the seriousness of appendicitis and hyponatremia was also examined. A recurrent diagnostic precision research by Lindestam et al.[27] that included eighty youngsters with severe appendicitis demonstrated a substantial correlation between appendiceal perforation and plasma sodium content of ≤136 mmol/L. Pogorelic et al.[28] found that a sodium level cutoff value of ≤135 mmol/L provided the best attainable sensitivity (94.7%) and specificity (88.5%) in an investigation involving 184 paediatric patients. The research also confirmed hyponatremia as an ensuring new biochemical indicator suggesting complex appendicitis. In a retrospective case-controlled study, Besli et al.[28] discovered no distinction in sodium concentrations between kids with and lacking severe appendicitis. Additionally, this investigation found that individuals with CA had reduced basal sodium concentrations; a sensitivity of 82.5% and precision of 31.1% were obtained using a cutoff threshold for basal Na ≤138 mEq/L.[29] Pham et al[12] and Serradilla et al[30] conducted comparable retrospective investigations and came to the same conclusion: hyponatremia was significantly linked to CA. Giannis et al.[31] concluded that blood sodium concentrations should be considered a perspective in patients reported of having complex acute appendicitis after conducting a comprehensive analysis that included seven research from both pediatric and mature populations.

The retrospective methodology, somewhat modest sample size (mostly because of the single-institution approach), and a limited number of missing data that reduce the study's statistical significance are some of the investigation's limitations. The differences in different research' adoption of a cutoff value for blood sodium values is another source of constraint. While other investigations utilized<135 mEq/L, ≤136 mEq/L, or <136 mEq/L, our research classified hyponatremia as a serum sodium ratio of ≤135 mEq/L. This makes comparing findings less accurate.

Conclusion

Finally, our research showed a correlation between preoperative hyponatremia and CA. A common, inexpensive laboratory test called serum sodium concentrations may serve as an auxiliary marker to help surgeons diagnose perforated acute appendicitis or gangrene early. Prospective investigations in the years to come will shed more light on the relationship between hyponatremia and the extent of appendicitis, enabling the best possible therapeutic care.

References

1. Debnath J, Kumar R, Mathur A, et al. On the role of ultrasonography and CT scan in the diagnosis of acute appendicitis. *Indian J Surg*. 2015;77:221-6. doi:10.1007/s12262-012-0772-5

2. Nshuti R, Kruger D, Luvhengo TE. Clinical presentation of acute appendicitis in adults at the Chris Hani Baragwanath Academic Hospital. *Int J Emerg Med*. 2014;7(1):12. doi:10.1186/1865-1380-7-12
3. Prystowsky JB, Pugh CM, Nagle AP. Current problems in surgery: appendicitis. *Curr Probl Surg*. 2005;42(10):688-92. doi:10.1067/j.cpsurg.2005.07.003
4. Lee JFY, Leow CK, Lau WY. Appendicitis in the elderly. *Aust N Z J Surg*. 2000;70(8):593-6. doi:10.1046/j.1440-1622.2000.01905.x
5. 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*. 2014;15(5):517-20. doi:10.1089/sur.2013.106
6. Ponsky TA, Huang ZJ, Kittle K, et al. Hospital- and patient-level characteristics and the risk of appendiceal rupture and negative appendectomy in children. *JAMA*. 2004;292:1977-82. doi:10.1001/jama.292.16.1977
7. Franz MG, Norman J, Fabri PJ. Increased morbidity of appendicitis with advancing age. *Am Surg*. 1995;61:40-4.
8. 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. doi:10.1089/sur.2019.175
9. Symer MM, Abelson JS, Sedrakyan A, Yeo HL. Early operative management of complicated appendicitis is associated with improved surgical outcomes in adults. *Am J Surg*. 2018;216(3):431-7. doi:10.1016/j.amjsurg.2018.04.010
10. Pogorelic Z, Mihanovic J, Nincevic S, Luksic B, Baloevic SE, Polasek O. Validity of appendicitis inflammatory response score in distinguishing perforated from non-perforated appendicitis in children. *Children*. 2021;8(4):309. doi:10.3390/children8040309
11. 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. doi:10.1155/2013/462891
12. Pham XBD, Sullins VF, Kim DY, et al. Factors predictive of complicated appendicitis in children. *J Surg Res*. 2016;206(1):62-6. doi:10.1016/j.jss.2016.07.023
13. 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. doi:10.1001/archinternmed.2012.3992
14. Park SJ, Shin JI. Inflammation and hyponatremia: an underrecognized condition? *Korean J Pediatr*. 2013;56(12):519-22. doi:10.3345/kjp.2013.56.12.519
15. 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. doi:10.1159/000322238
16. Thompson C, Hoorn EJ. Hyponatraemia: an overview of frequency, clinical presentation and complications. *Best Pract Res Clin Endocrinol Metab*. 2012;26:S1-6. doi:10.1016/S1521-690X(12)00019-X
17. Nair V, Niederman MS, Masani N, Fishbane S. Hyponatremia in community-acquired pneumonia. *Am J Nephrol*. 2007;27(2):184-90. doi:10.1159/000100866
18. Sigal SH. Hyponatremia in cirrhosis. *J Hosp Med*. 2012;7(Suppl 4):S14-7. doi:10.1002/jhm.1915
19. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (laboratory risk indicator for necrotizing fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med*. 2004;32(7):1535-41. doi:10.1097/01.CCM.0000129486.35458.7D
20. Yaghoubian A, de Virgilio C, Dauphine C, Lewis RJ, Lin M. Use of admission serum lactate and sodium levels to predict mortality in necrotizing soft-tissue infections. *Arch Surg*. 2007;142(9):840-6. doi:10.1001/archsurg.142.9.840
21. Falor AE, Zobel M, Kaji A, Neville A, de Virgilio C. Admission variables predictive of gangrenous cholecystitis. *Am Surg*. 2012;78(10):1075-8. doi:10.1177/000313481207801014
22. O'Leary MP, Neville AL, Keeley JA, Kim DY, de Virgilio C, Plurad DS. Predictors of ischemic bowel in patients with small bowel obstruction. *Am Surg*. 2016;82(10):992-4. doi:10.1177/000313481608201030
23. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med*. 1999;340(6):448-54. doi:10.1056/NEJM199902113400607
24. Banks WA, Kastin AJ, Gutierrez EG. Penetration of interleukin-6 across the murine blood-brain barrier. *Neurosci Lett*. 1994;179(1-2):53-6. doi:10.1016/0304-3940(94)90933-4
25. Kim DY, Nassiri N, de Virgilio C, et al. Association between hyponatremia and complicated appendicitis. *JAMA Surg*. 2015;150(9):911-2. doi:10.1001/jamasurg.2015.1258
26. Wu HC, Yan MT, Lu KC, et al. Clinical manifestations of acute appendicitis in hemodialysis patients. *Surg Today*. 2013;43(9):977-83. doi:10.1007/s00595-012-0349-8
27. Lindestam U, Almström M, Jacks J, 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. doi:10.1055/s-0039-1687870
28. 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. doi:10.1016/j.jpedsurg.2020.09.066
29. 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(1):35-40. doi:10.14744/hnhj.2019.16013
30. Serradilla J, Bueno A, De la Torre C, et al. Predictive factors of gangrenous post-appendectomy intra-abdominal abscess: a case-control study. *Cir Pediatr*. 2018;31(1):25-8.
31. Giannis D, Matenoglou E, Moris D. Hyponatremia as a marker of complicated appendicitis: a systematic review. *Surgeon*. 2020;18(5):295-304. doi:10.1016/j.surge.2020.01.002