

Research Article

A new Predictive Factor for Complicated Appendicitis: Hyponatremia

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Abstract

Objectives: Acute appendicitis is the most common abdominal surgical procedure, which is associated with a high risk of perforation. Perforation may lead to intraabdominal abscess and sepsis, resulting in complicated appendicitis. The present study investigated whether hyponatremia could be a predictive factor for complicated appendicitis.

Methods: The study included 295 patients operated due to acute appendicitis, and retrospectively evaluated operation records, pathology results, serum levels of Na, CRP, WBC count, neutrophil count, lymphocyte count and NLR (neutrophil/lymphocyte) values. Patients were divided into two groups as complicated appendicitis (Group 1) and non-complicated appendicitis (Group 2) for comparison. The normal range of sodium was accepted as 135–145 mEq/l.

Results: The mean age of the patients was 33.77 (18–82) years and there were 188 (63.72%) male and 107 (36.27%) female. The mean age was 40 years and 28 years in Group 1 and Group 2, respectively ($p < 0.01$). The ratio of females was 47% ($n = 31$) in Group 1, and 33.2% ($n = 76$) in Group 2 ($p = 0.04$). The mean CRP value was 113.72 mg/dl in Group 1 and 12.56 mg/dl in Group 2 ($p < 0.01$). The mean percentage of lymphocytes was 12.20 in Group 1 and 14.40 in Group 2 ($p = 0.049$). The mean sodium value was 133 mEq/l in Group 1 and 138 mEq/l in Group 2 ($p < 0.01$). The cut-off value for sodium was found to be 134 mEq/l (sensitivity: 78.79%; specificity: 93.01%; AUC: 0.903).

Conclusion: The levels of sodium, CRP and lymphocytes were found to be predictive of complicated appendicitis. The cut-off value for sodium was found to be 134 mEq/l, with high sensitivity and specificity.

Keywords: Acute appendicitis, complicated appendicitis, sodium, hyponatremia

Cite This Article: Ustuner MA, Deniz A. A new Predictive Factor for Complicated Appendicitis: Hyponatremia. EJMI 2020;4(3):401–404.

Abdominal pain is a significant cause of hospital admission, and accounts for almost 10% of adults presenting at the emergency department for reasons other than injuries.^[1] Acute appendicitis is the most common condition causing surgical acute abdomen among patients presenting with abdominal pain. The estimated lifetime prevalence is 7–8%.^[2,3] It is associated with significant morbidity (10%) and mortality (1–5%) despite the developments in diagnosis and treatment.^[4] The most important cause of morbidity is complicated appendicitis due to a local ab-

cess or peritonitis upon the perforation of the appendix.^[5,6] Several laboratory tests have been reported in the literature for differentiating between complicated appendicitis and acute appendicitis, such as C-reactive protein (CRP), leukocyte count, neutrophil count and sedimentation rate.^[7] The levels of interleukin IL-1b and IL-6, which are responsible for severe inflammatory response, are elevated and increase antidiuretic hormone (ADH), resulting in hyponatremia when a serious infection occurs in the body.^[8,9] The present study investigated the predictive value of hyponatremia.

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Submitted Date: May 27, 2020 **Accepted Date:** June 21, 2020 **Available Online Date:** June 22, 2020

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tremia in differentiation between complicated appendicitis and acute appendicitis.

Methods

The study included 295 patients operated due to acute appendicitis at the SBU Gulhane Training and Research Hospital between January 1, 2019 and January 1, 2020. Operation records, pathology results, serum levels of Na, CRP, WBC count, neutrophil count, lymphocyte count and NLR (neutrophil/lymphocyte ratio) values were evaluated retrospectively. Patients were divided into two groups as complicated appendicitis (Group 1) and non-complicated appendicitis (Group 2) for comparison. The complicated appendicitis group (Group 1) consisted of patients with a pathology result of phlegmonous or perforated appendicitis, and those with an intraabdominal abscess or peritonitis observed during the operation. The remaining appendicitis cases were assigned to Group 2. The study excluded patients with a pathology result of lymphoid hyperplasia.

The normal range of sodium was accepted as 135–145 mEq/l. Patients with acute or chronic renal failure, inappropriate ADH syndrome and who were receiving diuretics were excluded from the study.

Statistical Analysis

Statistical analyses were performed using the IBM SPSS for Windows Version 21.0 and MedCalc trial version for Windows. Numerical variables were summarized as median (minimum-maximum). Categorical variables were summarized as frequency (percentage). The normality of continuous variables was evaluated using a Kolmogorov-Smirnov

test. The differences between groups for continuous variables were determined using a Mann–Whitney U test. Categorical variables were compared using a Chi-square test. The odds ratio was used to measure the association between sodium levels and complicated/non-complicated appendicitis. The predictive effect of sodium was measured by calculating the area under the receiver operator characteristic (ROC) curve. The optimal cut-off value was defined as the highest sum of sensitivity and specificity. A p-value of less than 0.05 was considered significant.

Results

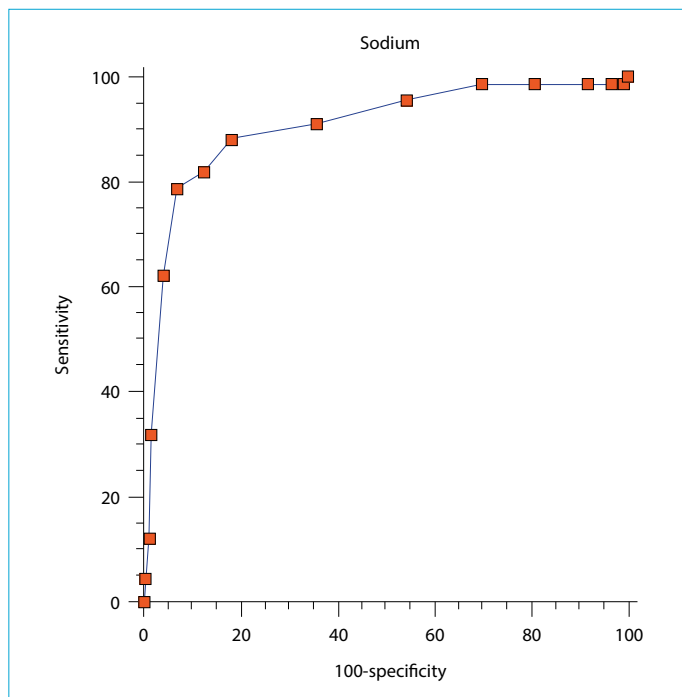
The mean age of the patients was 33.77 (18–82) years and there were 188 (63.72%) male and 107 (36.27%) female. The mean age was 40 years and 28 years in Group 1 and Group 2, respectively ($p < 0.01$). The ratio of females was 47% ($n = 31$) and 33.2% ($n = 76$) in Group 1 and Group 2, respectively ($p = 0.04$). Conventional (open) surgery was performed on 53 patients (80.3%) in Group 1 and 168 patients (73.4%) in Group 2, while laparoscopic surgery was performed on 13 (19.7%) and 61 (26.69%) patients in Group 1 and Group 2, respectively ($p = 0.325$). The mean level of CRP was 113.72 mg/dl in Group 1 and 12.56 mg/dl in Group 2 ($p < 0.01$). The mean WBC count was 14.73 $10^3/\mu\text{l}$ in Group 1 and 14 $10^3/\mu\text{l}$ in Group 2 ($p = 0.624$). The mean percentage of neutrophils was 79.75 in Group 1 and 78.40 in Group 2 ($p = 0.112$). The mean percentage of lymphocytes was 12.20 and 14.40 in Group 1 and Group 2, respectively ($p = 0.049$). The mean NLR value was 6.58 in Group 1 and 5.56 in Group 2 ($p = 0.056$). The mean sodium level was 133 mEq/l and 138 mEq/l in Group 1 and Group 2, respectively ($p < 0.01$) (Table 1).

Table 1. Comparison of Group 1 and Group 2

| Variables | Complicated (Group 1) | Non-Complicated (Group 2) | p | OR (95% CI) |
|----------------------------|-----------------------|---------------------------|--------|------------------|
| Age | 40 (18-82) | 28 (18-69) | <0.001 | |
| Gender | | | | |
| Female | 31 (47) | 76 (33.2) | 0.040 | |
| Male | 35 (53) | 153 (66.8) | | |
| Type of operation | | | | |
| Open | 53 (80.3) | 168 (73.4) | 0.325 | |
| Lap | 13 (19.7) | 61 (26.6) | | |
| CRP (mg/dl) | 113.72 (0.90-492.60) | 12.56 (0.17-136) | <0.001 | |
| WBC ($10^3/\mu\text{l}$) | 14.73 (7.60-35.30) | 14 (4.30-31.20) | 0.624 | |
| Neutrophils (%) | 79.75 (53-95.40) | 78.40 (44.60-95.70) | 0.112 | |
| Lymphocytes (%) | 12.20 (2.40-38.40) | 14.40 (2-46.70) | 0.049 | |
| NLR | 6.58 (1.38-39.75) | 5.56 (0.96-45.95) | 0.056 | |
| Sodium (mEq/l) | 133 (130-146) | 138 (106-157) | <0.001 | |
| Sodium (mEq/l) | | | | |
| ≤134 | 52 (78.8) | 16 (7) | <0.001 | 49.446 |
| >134 | 14 (21.2) | 213 (93) | | (22.696-107.727) |

Table 2. ROC analysis of sodium levels

| | |
|--------------------------------|-------------|
| Area under the ROC curve (AUC) | 0.903 |
| Standard error | 0.0239 |
| 95% confidence interval | 0.863-0.934 |
| p value | <0.0001 |
| Cut-off value | 134 |
| Sensitivity | 78.79% |
| Specificity | 93.01% |

**Figure 1.** Sensitivity and specificity of sodium value, ROC analysis.

The cut-off value for sodium was found to be 134 mEq/l (sensitivity: 78.79%; specificity: 93.01%; AUC: 0.903; 95% Confidence Interval 0.863–0.934) (Table 2, Fig. 1).

Discussion

The levels of Na and CRP and the percentage of lymphocytes among laboratory tests were found effective in pre-operatively predicting complicated appendicitis ($p < 0.05$), while the percentage of neutrophils and NLR had produced no statistically significant effect ($p > 0.05$). The cut-off level for sodium was found to be 134 mEq/l.

Complicated appendicitis is defined as intraabdominal abscess and/or fecal peritonitis caused by a perforated appendicitis.^[10,11] Tomography (CT), which is the gold standard for the diagnosis of acute appendicitis, has a sensitivity of 90% and a specificity of 94%.^[12] Leeuwenburgh et al. compared MRI and a combination of ultrasound (US) and CT for the diagnosis of perforated appendicitis. In the said study, almost half of the patients were misdiagnosed using

both methods (MRI 43% and combined US+CT 52%).^[13] The challenge of diagnosing complicated appendicitis requires new diagnostic methods.

IL1b and IL-6, severe inflammatory components, play a role in the development of hyponatremia. Circulating cytokines passing through the blood-brain barrier affect the neurons originating in the supraoptic and paraventricular nuclei through the Janus tyrosine kinases (JAK) of the Signal transducer and activator of transcription (STAT) family, and other transcription factors. Subsequently, a cytokine-mediated non-osmotic ADH secretion increases the renal tubular reabsorption of free water, and results in dilutional hyponatremia.^[9,11,14,15]

Hyponatremia has been demonstrated to be an effective predictive factor for perforated/ gangrenous appendicitis, ischemic intestinal obstruction and colon perforation, necrotizing soft tissue infections and gangrenous cholecystitis.^[16-20] Hyponatremia, which is among the most common electrolyte imbalance, is known to increase morbidity and mortality within the first 30 days of surgical procedures.^[21]

A study by Pham et al. established that hyponatremia ($\text{Na} \leq 135$ mEq/L) was an independent predictive factor for the diagnosis of complicated appendicitis in children, and increased the risk of complicated appendicitis by three times.^[22] Besli et al., in turn, reported a sodium level of ≤ 138 mEq/l in children to be a risk factor for complicated appendicitis. (82.5% specificity and 31.1% specificity).^[7] Käser et al. reported a sodium level of < 136 mmol/l in hyponatremia that was found to be predictive factor for colon perforation.^[23]

Limitations: The limitations of the present study were its single-center and retrospective design.

Conclusion

In conclusion, hyponatremia was determined as a predictive factor for complicated appendicitis. The cut-off value for sodium was found to be 134 mEq/l.

Disclosures

Ethics Committee Approval: Ethics committee approval was obtained from the SBU Gulhane Training and Research Hospital (Date: May 19, 2020 Decision No: 2020-216).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – M.A.U.; Design – A.D., M.A.U.; Supervision – M.A.U.; Materials – A.D., M.A.U.; Data collection &/or processing – M.A.U.; Analysis and/or interpretation – M.A.U.; Literature search – M.A.U., A.D.; Writing – M.A.U., A.D.; Critical review – M.A.U.

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