International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 11 November 2024

Page No: 2073-2080

DOI: https://doi.org/10.47191/ijmscrs/v4-i11-33, Impact Factor: 7.949

Study on the Clinical Performance of Serum Hyponatremia in the Determination of Complicated Acute Appendicitis in the Adult Population at the General Hospital Zone No. 3, OOAD Aguascalientes

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ABSTRACT

Background: Appendicitis is the most common abdominal infection and is the main surgical emergency worldwide, affecting approximately 1 in 11 people during their lifetime. Nowadays, distinguishing between uncomplicated and complicated appendicitis is increasingly important due to the increasing evidence supporting the possibility of treating uncomplicated appendicitis with antibiotics instead of resorting directly to surgery. This differentiation requires combining clinical findings with laboratory and imaging studies. In our hospital setting, where the use of C-reactive protein, procalcitonin or imaging studies represent an increase in the costs of health services or are not routinely available, the use of prediction systems that include inexpensive and accessible serum markers could improve early identification and therefore prompt management in this group of patients.

Objective: To identify the clinical performance of hyponatremia in patients undergoing open appendectomy with transoperative findings of complicated acute appendicitis in the adult population at the General Hospital of Zone No. 3, Aguascalientes, México.

Material and methods: Retrospective, cross-sectional and instrumental study, at the General Hospital of Zone No. 3, part of the Mexican Social Security Institute (IMSS), Aguascalientes delegation. By reviewing the records of adult patients undergoing appendectomy with intraoperative findings of complicated acute appendicitis, in the period from February 1, 2023 to February 1, 2024, obtaining preoperative serum sodium values, seeking to identify the diagnostic accuracy of hyponatremia in the determination of complicated acute appendicitis.

Results: There was a significant diagnostic performance with hyponatremia at its cut-off point of 133 mEq/L in the determination of complicated acute appendicitis. A sensitivity of 100%, specificity of 81.4%, NPV of 100%, PPV of 45.2%, LR+ of 2.16, LR- of 0.652 and a Youden index of 0.814 were determined.

Conclusion: Hyponatremia can be useful in the diagnostic approach to acute appendicitis in hospitals with limited resources, guiding the surgical resolution of the condition, as well as the rapid establishment of a postoperative intravenous antibiotic regimen, reducing hospital expenses after limiting the morbidity generated by severe forms of this disease.

ARTICLE DETAILS

Published On:
25 November 2024

Available on:
https://ijmscr.org/

INTRODUCTION

Appendicitis is the main surgical emergency worldwide [1]. According to the official portal of the Mexican Social Security Institute (IMSS), 38,546 beneficiaries nationwide underwent an appendectomy in 2017 [2].

According to the updated guidelines derived from the first consensus conference of the World Society of Emergency Surgery [3] on the diagnosis and treatment of acute appendicitis, the differentiation between complicated and uncomplicated acute appendicitis can be better defined based on intraoperative findings of appendicular perforation, intra-abdominal abscess or purulent peritonitis, rather than on histopathological findings, determining effective post-surgical management through the rapid addition and

maintenance of a broad-spectrum antibiotic regimen according to the degree of disease, improving overall results and decreasing hospital costs derived from morbidity [4] [5]. Laparoscopic appendectomy is the treatment of choice in cases of complicated acute appendicitis, since nonsurgical treatment, which includes the use of short courses of broad-spectrum antibiotics and percutaneous drainage, provides a significant risk of recurrence, with reported rates of between 12% and 24%, as well as a high incidence of appendix tumors in patients over 40 years of age, ranging from 3% to 17% of cases [6] [7] [8].

Decreased serum sodium levels have been investigated as a possible predictive marker of intra-abdominal complications [9] [10]. Inflammatory states, with or without an infectious focus, have been reported in which the presence of hyponatremia was evident, due to non-osmotic vasopressin secretion. The underlying pathophysiology suggests that proinflammatory cytokines, such as interleukin 6, increase the release of antidiuretic hormone. This increase causes hyponatremia through the mechanism known as "immuno-neuroendocrine interface" [11].

In this context, we proposed a protocol to identify the clinical performance of hyponatremia in patients undergoing open appendectomy with transoperative findings of complicated acute appendicitis in the adult population.

MATERIALS AND METHODS

Study Design.

A retrospective, cross-sectional, instrumental study was performed in the General Surgery Department at General Hospital Zone 3 of the Mexican Institute of Social Security (IMSS), with a sample size of 55 patients.

Study Population.

Patients aged 18 to 65 years, of both genders, insured by the Mexican Social Security Institute, and assigned to General Hospital of Zone 3, Aguascalientes Delegation. These patients underwent appendectomy for a diagnosis of acute appendicitis from February 1, 2023, to February 1, 2024.

Observation Unit.

Medical records of patients aged 18 to 65 years who underwent appendectomy at General Hospital of Zone No. 3, OOAD Aguascalientes, during the period from February 1, 2023, to February 1, 2024.

Selection Criteria

Inclusion Criteria.

- Patients with a diagnosis of complicated acute appendicitis.
- Serum sodium levels obtained within 24 hours prior to surgery.
- Aged 18-65 years.
- Patients insured by the IMSS and assigned to General Hospital of Zone 3, in Aguascalientes, México.

Exclusion Criteria.

- Patients with a known diagnosis of congestive heart failure.
- Patients with a known diagnosis of chronic kidney disease.
- Patients with a known diagnosis of hepatic cirrhosis classified as Child-Pugh C or D.
- Patients with a known diagnosis of syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Sample Size.

Using the Epidat epidemiological data analysis software, the sample size was calculated for diagnostic tests in paired groups with 90% power. The calculation was based on sensitivity and specificity values reported by Pérez-Soto et al. [12] (S: 54.9%, E: 70.83%) in Mexican population. We use intraoperative findings as the gold standard for complicated acute appendicitis diagnosis through hyponatremia. A total sample of 55 patients was obtained.

Data Control and Quality Assurance Methods.

Data were collected using a structured data collection instrument and stored in a Microsoft Excel 365 spreadsheet. Cross-verification was performed by the authors to ensure the correct inclusion of the data.

Statistical Analysis.

Data from clinical and electronic medical records of patients in the General Surgery department at General Hospital of Zone 3 were consolidated into an Microsoft 365 Excel database and processed using SPSS v.25 for Windows. After calculating prevalence, clinical test performance was analyzed using ROC curves. Metrics such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios were calculated using cross-tabulation of ROC curve values. Finally, the Youden index was estimated, and a Fagan nomogram was constructed to determine post-test probability.

Ethical considerations.

This study was conducted under strict ethical principles, prioritizing the safety, privacy, and respect of participants. All data collection procedures complied with the General Health Law on Health Research and the principles of the Declaration of Helsinki. The protocol was reviewed and approved by the Ethics Committee of HGZ No. 3, Aguascalientes, ensuring compliance with current ethical and legal regulations.

According to Article 17 of the Regulations of the General Health Law on Health Research, this study is classified as **risk-free research**, as it employs retrospective and documentary techniques without direct intervention on the physiological, psychological, or social variables of the participants.

This study adheres to the requirements outlined in Title V of the Federal Health Law, specifically Articles 96, 97, 98, 99, 100, 101, and 102.

RESULTS

The study population consisted of patients from the Mexican Institute of Social Security assigned to General Zone Hospital No. 3, OOAD in Aguascalientes, who underwent appendectomy due to complicated acute appendicitis from February 1, 2023, to February 1, 2024. Preoperative serum sodium levels were obtained to assess the diagnostic accuracy of hyponatremia in identifying complicated acute appendicitis. Patients older than 65 and younger than 18 were excluded, yielding a sample of 55 patients.

Among the 55 patients analyzed (n=55), the most prevalent age range was 26–40 years, particularly 26–33 years, followed by 34–40 years. Males were predominant in most age groups except for those aged 49–55 and 56–63, where the gender distribution was more balanced.

The mean age was 37.29 years (±12.205), the median was 35 years, and the mode was 22. The youngest patient was 18 years old, and the oldest was 64. Male patients accounted for 65.5% (n=36) of the sample, while females comprised 34.5% (n=19).

Regarding comorbidities, 80% (n=44) of patients had no comorbid conditions. Among those with comorbidities (n=11), 27.3% (n=3) had both type 2 diabetes mellitus and hypertension, another 27.3% (n=3) had only type 2 diabetes, 18.92% (n=2) had some form of neoplasia, 9.1% (n=1) had chronic nonspecific ulcerative colitis, 9.1% (n=1) had type 1 diabetes mellitus, and 9.1% (n=1) had only hypertension.

Males showed a higher prevalence of cancer diagnosis prior to surgery, at 3.6% (n=2) of the total (n=55), while type 2 diabetes and hypertension were more prevalent among females, affecting 5.5% (n=3). No significant relationships or correlations between variables were identified (chi-square=11.564, p=0.073; Spearman correlation=0.195, p=0.154).

Table 1. Relationship and correlation between gender and comorbidities

	Chi square	Spearman correlation
Value	11.545	0.195
Significance	0.073	0.154
Chi square, Spearman correlation. SPSS ver.25		

Preoperative sodium levels measured within 24 hours of appendectomy averaged 136.69 mEq/L (±4.207), with a median and mode of 136 mEq/L. The lowest recorded sodium level was 125 mEq/L, and the highest was 146 mEq/L. The most common sodium level was 136 mEq/L, observed in 20% of patients (n=11).

Hyponatremia was defined as a serum sodium level below the normal range of 135–145 mEq/L. In this study, 29.1% (n=16) of patients had hyponatremia before surgery, while 70.9% (n=39) did not.

Table 2. Preoperative sodium

mEq/L	Frequency	Percentage
125	1	1.8 %
128	1	1.8 %
130	1	1.8 %
131	2	3.6 %
132	2	3.6 %
133	7	12.7 %
134	2	3.6 %
135	2	3.6 %
136	11	20.0 %
137	6	10.9 %
138	2	3.6 %
139	1	1.8 %
140	7	12.7 %
141	3	5.5 %
142	1	1.8 %
143	4	7.3 %
144	1	1.8 %
146	1	1.8 %

Total	55	100 %
Preoperative serum sodium. Fuente: SPSS ver.25		

Intraoperative findings confirmed complicated acute appendicitis in 100% (n=55) of cases. Of these, 72.7% (n=40) had complicated appendicitis with localized peritonitis, while 27.3% (n=15) had complicated appendicitis with generalized peritonitis.

Intraoperative incidents occurred in 10.9% (n=6) of cases. A single patient (1.8%) required reoperation due to an appendiceal stump leak. However, all patients (100%, n=55) were discharged successfully.

Table 3. Intraoperative incidents and postoperative adverse events.

	Frequency	Percentage
Intraoperative: In addition to complicated appendicitis, a 2 cm perforation in the ascending colon was noted, so a right hemicolectomy + end-to-end ileostomy was performed.	1	1.8 %
Intraoperative: The presence of a lysed appendiceal base secondary to appendiceal perforation was noted, so a right hemicolectomy + mixed side-to-side ileo-transverse anastomosis was performed.	1	1.8 %
Intraoperative: The presence of a lysed appendiceal base secondary to appendiceal perforation was noted, so a cechectomy + manual end-to-side ileocolic anastomosis was performed.	1	1.8 %
Intraoperative: The presence of apparent liver metastases was noted in the context of a patient with a diagnosis of rectal cancer prior to appendectomy.	1	1.8 %
Intraoperative: The presence of ileitis + typhlitis is noted, without requiring any other type of surgical management apart from appendectomy.	1	1.8 %
Intraoperative: The presence of a retroperitoneal abscess associated with complicated appendicitis is noted, so drainage and lavage of the abdominal cavity is performed.	1	1.8 %
Postoperative: The patient comes 36 hours after appendectomy for complicated appendicitis, with acute abdomen and tomographic findings of a retroperitoneal abscess. Intraoperatively, leakage of the appendicular stump is evident, performing primary invaginating closure, abscess drainage and lavage of the abdominal cavity. The patient is discharged home after 36 hours of hospital stay.	1	1.8 %
None	48	87.3 %
Total	55	100 %
Medical-surgical resolution pathway after intraoperative incidents and post-surgical adverse events.		

A ROC curve was generated using sodium levels as a test variable and complicated acute appendicitis as the state variable. These data suggest that hyponatremia has moderate concordance (per the Landis and Koch scale) in identifying complicated acute appendicitis, with statistical significance. The area under the curve (AUC) was 0.60, with a narrow confidence interval (95% CI: 0.44–0.76), and a cutoff point of 133 mEq/L was established based on this curve.

Table 4. Area under the ROC curve. Hyponatremia and complicated acute appendicitis

Area	Std. Error [a]	asymptotic significance [b]	95% confidence interval Lower limit	Upper limit
0.60	0.082	0.005	0.44	0.76
Statistical significance of the ROC curve. SPSS ver.25				

Table 5. Coordinates of the ROC curve hyponatremia and complicated acute appendicitis		
Positive if greater than or equal to	Sensitivity	1 - Specificity
147	0	0
146	0	0.01854613
144	0	0.116541632
143	0	0.12513189
142	0	0.16852312
141	0	0.21845154
140	0	0.31451515
139	0	0.35515181
138	0	0.36451515
137	0	0.44152151
136	0	0.61515481
134	0	0.71515154
133	1	0.81458121
132	1	0.91215112
131	1	0.954315151
125	1	1
Coordinates on the values of serum sodium in blood a. the smallest cut-off value is the minimum observed test value minus 1 and the largest cut-off value is the maximum observed test value plus 1, the subsequent ones are average. SPSS ver.25		

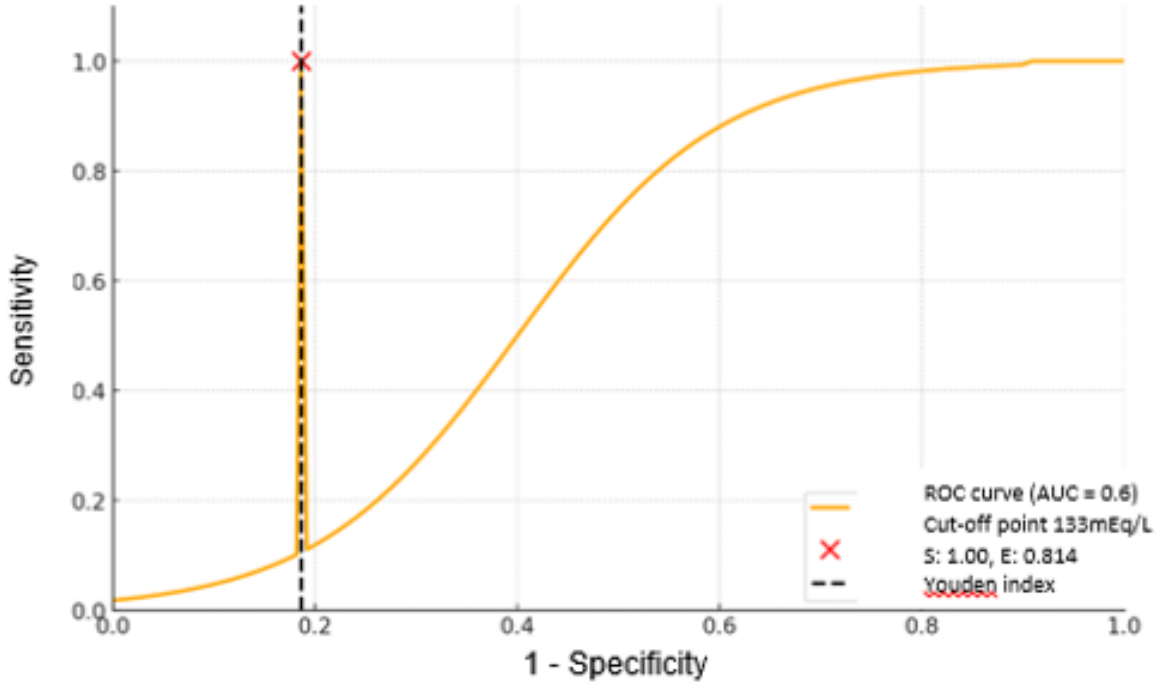
The sensitivity and specificity for detecting complicated acute appendicitis at a serum sodium level of 133 mEq/L were 100% and 81.4%, respectively. Although the positive predictive value (PPV) was low due to the prevalence of the condition in the sample, the negative predictive value (NPV) and sensitivity were high, making it a reliable indicator for ruling out complications when sodium levels exceeded 133 mEq/L.

Table 6. Diagnostic analysis for hyponatremia and complicated acute appendicitis.	
Sensitivity	1.0 (IC 95%: [1.0, 1.0])
Specificity	0.385 (IC 95%: [0.815, 0.985])
Positive predictive value (PPV)	0.452 (IC 95%: [0, 0.4])
Negative predictive value (NPV)	1.0 (IC 95%: [1.0, 1.0])
Positive likelihood ratio (LR+)	2.16
Negative likelihood ratio (LR-)	0.652
Diagnostic estimates for the sodium cut-off point in the identification of complicated acute appendicitis. SPSS ver.25	

In this analysis, the PPV was 38.5%, and the NPV was 100%, meaning that out of 100 patients with sodium levels ≤133 mEq/L, 38 would actually have complicated acute appendicitis, while the rest would be false positives. Conversely, none of the patients with sodium levels >133 mEq/L exhibited complications.

The Youden index was calculated as 0.814 using the formula (Sensitivity + Specificity – 1), reflecting the high discriminatory power of the cutoff point for distinguishing patients with complicated acute appendicitis. While sodium levels below 133 mEq/L indicated a high probability of complications, they were not definitive due to the low PPV. Hyponatremia below 133 mEq/L serves as a diagnostic aid requiring complementary methods for confirmation.

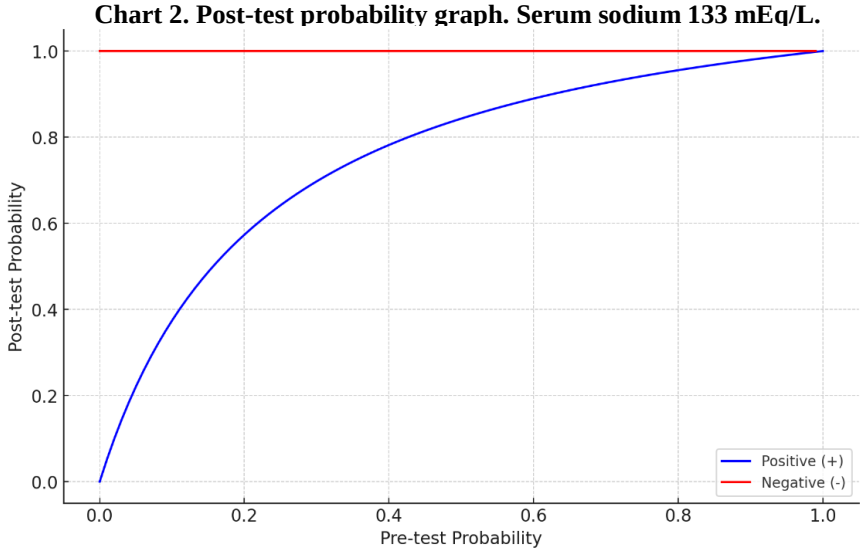
Chart 1. Youden index for cut-off point of 133 mEq/L in complicated acute appendicitis.



Youden index in patients with complicated acute appendicitis with a sensitivity of 100% and specificity of 81.4%. SPSS ver.25

Based on the likelihood of developing complicated acute appendicitis at a cutoff of 133 mEq/L, a positive test (sodium ≤133 mEq/L) increased the post-test probability, especially with a high pre-test probability. Conversely, a negative test (sodium >133 mEq/L) reduced the likelihood of complications.

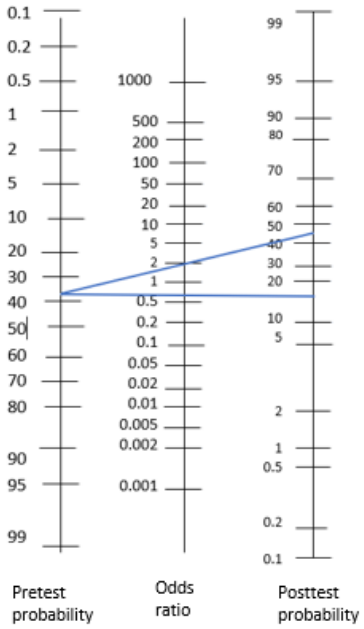
Chart 2. Post-test probability graph. Serum sodium 133 mEq/L.



Demonstration of the variation in post-test probabilities for positive and negative results as a function of the pre-test probability. Blue line indicates post-test probability and red line indicates post-test probability for a negative result. SPSS ver.25

According to Fagan's nomogram, a preoperative sodium level of 133 mEq/L or lower increased the post-test probability of complications from a pre-test value of 37% to a post-test value of 46%.

Chart 3. Fagan nomogram



DISCUSSION

In our investigation, we determined the clinical performance of hyponatremia and its relationship with the severity of complicated acute appendicitis. It demonstrated an adequate positive predictive value in estimating the risk association, highlighting its importance as a cost-effective tool prior to surgical intervention for effectively and proactively addressing complicated forms of this surgical condition.

Hyponatremia exhibited sensitivity and specificity of 100% and 81.4%, respectively, suggesting that it can be a useful indicator in the early diagnosis of severe disease forms. These values indicate that hyponatremia is effective in identifying patients with complicated appendicitis. However, it is important to note that it is not 100% sensitive, necessitating its use as a predictive aid rather than a completely reliable marker for complications.

Comparatively, Pérez-Soto et al. [12] reported a sensitivity and specificity of 54.79% and 70.83%, respectively, for hyponatremia in identifying complicated acute appendicitis. These values were lower than those presented in this study, potentially due to differences in patient selection and management at our hospital. Notably, the aforementioned author studied 274 patients over a seven-year period, using intraoperative findings or imaging evidence of perforation, appendiceal abscess, or phlegmon as the gold standard.

A ROC curve point of 133 mEq/L (AUC of 0.6) was identified as particularly relevant for complicated acute appendicitis. Our sample showed a 29.1% prevalence of hyponatremia, indicating that hyponatremia in patients with complicated appendicitis was statistically significant and suggesting that decreased serum sodium levels may be associated with an acute inflammatory state [10][11].

The positive and negative predictive values were 45.2% and 100%, respectively. This indicates that out of 100 patients with sodium levels ≤133 mEq/L, 45 would indeed have complicated acute appendicitis. A low PPV implies that while hyponatremia is a useful risk indicator, other clinical and diagnostic indicators are necessary to confirm the presence of complications. A 100% NPV suggests that all patients with sodium levels >133 mEq/L would not present complications.

The mean patient age was 37.29 years, with a higher prevalence of complications observed in young adults. However, it is essential to note that complicated appendicitis is not limited to specific age groups and can be severe at older ages. These results may be due to the sample distribution and study timeframe, emphasizing the need for therapeutic decisions based on risk assessment rather than age.

A higher prevalence of complicated appendicitis was observed in males, accounting for 65.5% of cases. This could be associated with gender-specific differences in immune response and pain thresholds [20].

LIMITATIONS, STRENGTHS, AND NEW RESEARCH PERSPECTIVES

Limitations and Strengths

The retrospective design, single-center population, and convenience sampling could be limitations of this study. However, a significant strength is adherence to the definition of complicated acute appendicitis according to internationally recognized consensus guidelines. Additionally, this study provides a comprehensive diagnostic performance evaluation of hyponatremia, including measures such as the Youden index and both positive and negative likelihood ratios, for identifying severe forms of acute appendicitis in adult populations.

New Research Perspectives

While hyponatremia proved to be a useful marker for identifying signs of complications in acute appendicitis, incorporating other acute-phase reactants such as procalcitonin, interleukin-6, C-reactive protein, D-dimer, or imaging studies could enhance diagnostic precision. Hyponatremia alone was not conclusive as a sole predictor of severity in acute appendicitis due to its low positive predictive value.

CONCLUSION

A significant diagnostic performance was observed with hyponatremia at a cutoff point of 133 mEq/L for determining complicated acute appendicitis. However, while hyponatremia demonstrated an adequate ability to rule out the presence of complicated acute appendicitis due to its 100% NPV, its PPV was low at 45.2%. This indicates that while a positive hyponatremia finding correlates with complications, it is not specific enough to confirm them. However, it is reliable for exclusion when sodium levels are normal or elevated.

This biomarker can be valuable in the diagnostic approach to acute appendicitis in resource-limited hospitals, guiding the immediate surgical resolution of the condition through open surgery, as well as the rapid initiation of postoperative broad-spectrum intravenous antibiotic therapy and its continued administration during hospitalization. This approach can reduce hospital costs by limiting morbidity associated with severe forms of this condition.

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