



RESEARCH ARTICLE

SERUM BILIRRUBIN LEVELS AS A PREDICTOR OF SEVERITY IN ACUTE APPENDICITIS

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ABSTRACT

Background: Acute appendicitis is one of the main causes of abdominal pain that requires surgical treatment, it occurs at any stage of life with a lifetime risk of 7% in general population; clinical findings are usually sufficient to make diagnosis, but definitive diagnosis is made at the moment of surgery; there isn't a reliable marker of acute appendicitis but it has been hypothesized that serum bilirubin levels increase in complicated appendicitis cases and that it can be measured before appendectomy to predict severity levels. **Objective:** To determine if the increase in serum bilirubin levels has a positive predictive value of severity in patients with acute appendicitis. **Material and methods:** Observational, prospective and analytical cross-sectional study in patients diagnosed with acute appendicitis, who attended the Emergency Department to identify the positive predictive value of bilirubin. Bilirubin levels were determined by obtaining a cut-off point greater than 1.0 mg/dl for total bilirubin, >0.8 mg/dl for indirect bilirubin and >0.2 for direct bilirubin; considering the standard Gold the diagnosis with the intraoperative macroscopic findings. Sampling was random and the sample size was probabilistic. It was analyzed with descriptive statistics in addition to diagnostic tests with 95% CI, using the statistical package SPSS. **Results:** 59 patients with acute appendicitis were selected, mean age 34.4 ± 14.3 years, 34 (58%) were female, 20 (33.9%) were overweight, 4 (6.8%) had arterial hypertension. Of the complications corresponded to abscess and perforation in 9 (31%), perforation with 8 (27.6%). The severity of the episodes of acute appendicitis occurred in 41 (69%). The effectiveness of bilirubins to detect severity, showed in the total with 82% (95% CI 64-92), the direct 73% (95% CI 58-84), indirect in 62% (95% CI 31-83). The discriminative capacity of indirect bilirubin with 0.52, the direct one with 0.44 and total with 0.35. **Conclusions:** total bilirubin has a higher positive predictive value of severity in patients with acute appendicitis and the indirect higher discriminative value.

INTRODUCTION

Acute appendicitis represents the most common indication for emergency abdominal surgery worldwide. It is a condition that occurs most frequently between the second and third decades of life, generally has a sudden onset, and the clinical picture evolves towards the deterioration of the patient, potentially leading to serious health repercussions, including death. In our hospital, it is the most common surgical emergency. In the last two years, there have been 208 confirmed cases of acute appendicitis in our unit, with the majority being resolved through open appendectomy. Due to the high incidence, we consider it important to have a biochemical indicator that can help us predict the presence of complicated acute appendicitis. Considering that its diagnosis is predominantly clinical (with support from some biochemical and imaging studies), the definitive diagnosis occurs when analyzing intraoperative findings, with no exact marker to determine the presence of complicated vs. uncomplicated acute appendicitis.

Recently, it has been proposed that hyperbilirubinemia be used to support the diagnosis of complicated acute appendicitis, as there are reports in the literature suggesting that an increase in bilirubin levels is associated with a clinically more severe stage of acute appendicitis. Therefore, the purpose of this study is to identify if the elevation of serum bilirubin levels is effective in determining the degree of severity in patients with suspected acute appendicitis.

MATERIALS AND METHODS

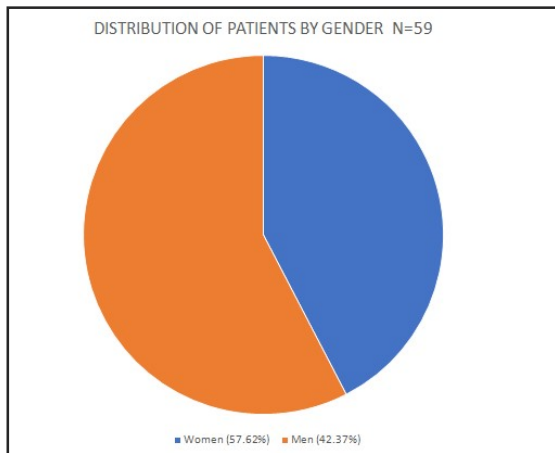
A prospective, cross-sectional, analytical observational study was conducted, with prior protocol authorization from the Research Ethics Committee of the "Hospital de Alta Especialidad de Veracruz." The study included patients of any gender over 18 years of age who were admitted to the Emergency Department of the Hospital de Alta Especialidad de Veracruz with a clinical diagnosis of acute appendicitis. Patients who refused to participate, those with a history of liver, hemolytic, and/or biliary tract pathology, patients diagnosed with acute appendicitis in whom serum bilirubin levels were not measured prior to surgical intervention, and pregnant patients were excluded from the study.

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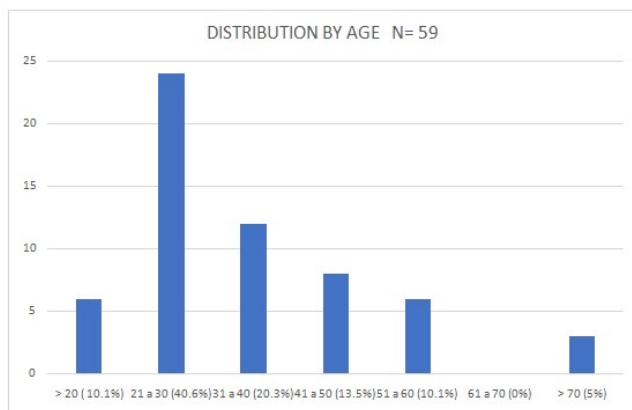
Sampling was non-randomized, and the sample size was calculated using a formula for descriptive studies without knowing the population size. Once a patient with a clinical diagnosis of probable acute appendicitis was identified, the study protocol was explained, and an informed consent form was provided, in which they agreed to participate in our study. Subsequently, a blood sample was taken, including serum bilirubin levels, in addition to routine pre-surgical tests. Serum bilirubin levels were analyzed, using the following cutoff points: 1.0 mg/dl for Total Bilirubin, >0.8 mg/dl for Indirect Bilirubin, and >0.2 for Direct Bilirubin. The data were recorded in an Excel table designed for this purpose, which included all the variables under study. Descriptive data analysis utilized measures of central tendency such as mean, median, mode, diagnostic tests with a 95% confidence interval, supported by the statistical package SPSS v26.0.

RESULTS

A total of 59 patients with acute appendicitis treated at the Emergency Department of the Hospital de Alta Especialidad de Veracruz were selected through a probabilistic sample to assess the effectiveness of serum bilirubin levels as a predictor of severity. Among these, there was a predominance of female patients with 34 cases and 25 male patients (57.62% and 42.37%, respectively) as shown in Graph 1. The mean age was 34.4 ± 14.3 years, as observed in Graph 2. Comorbidities found included type 2 diabetes mellitus, hypertension, and obesity.



Graph 1. Distribution of patients by gender



Graph 2. Distribution of patients by age

Table 1. Comorbidities of the patients

Characteristics	Average	Standard Deviation
Age in years	34.4 (min. 18, máx. 77)	14.3
Gender	Frequency	Percentage
Female	34	58
Male	25	42
Physical constitution		
Normal weight	24	40.7
Overweight	20	33.9
Obesity I	11	18.6
Obesity II	2	3.4
Obesity III	2	3.4
Comorbidity		
None	49	83.1
Hypertension	4	6.8
Type 2 Diabetes	2	3.4
Type 2 Diabetes, Obesity	2	3.4
Urinarytract Infection	1	1.7
Type 2 Diabetes, Hypertension	1	1.7

Source: Hospital de Alta Especialidad de Veracruz

According to the WHO classification of BMI, overweight was the most common comorbidity with 20 patients (33.9%), while the second most common was arterial hypertension with 4 patients (6.8%), as seen in Table 2. According to the current classification of acute appendicitis by the Mexican Association of General Surgery, complicated acute appendicitis predominated with 41 cases (69.4%), as shown in Graph 3. In these cases, intraoperative findings were, in order of frequency: appendicitis with abscess and perforation in 18.64% of cases, perforation without abscess in 16.94% of cases, and abscess without perforation in 13.55%. Total cecal appendix necrosis was found in 8.47% of cases, as shown in Table 2. Acute appendicitis was non-complicated in 18 cases. The preoperative evolution days ranged from 0 days (6.7%) to 22 days (1.6%), with 1 and 2 days being the most frequent timeframes, each with 17 cases. The average preoperative evolution time was 2.74 days, as shown in Table 3. The effectiveness of serum bilirubin levels as a positive predictive value of severity in patients with acute appendicitis showed total bilirubin with 82% (95% CI 64-92), direct bilirubin with 73% (95% CI 58-84), and indirect bilirubin with 62% (95% CI 31-83), as detailed in Table 4. The area under the ROC curve evaluates the discriminative capacity of acute appendicitis severity or its ability to differentiate subjects with and without severity in acute appendicitis. Indirect bilirubin had a value of 0.52, direct bilirubin 0.44, and total bilirubin 0.35. This indicates that with a value of 0.5, our null hypothesis is confirmed: bilirubins are not a predictor of severity in acute appendicitis, as detailed in Figure 1.

Discussion: In our study, we evaluated 59 patients who met the inclusion criteria and underwent surgical intervention at the Hospital de Alta Especialidad de Veracruz to assess the effectiveness of serum bilirubin levels as a predictive value of severity. They had an average age of 34.4 years, with a minimum age of 18 and a maximum of 77. Female patients predominated at 57.62%. This differs from what Sotelo-Anaya E. mentions, who states that acute appendicitis occurs most frequently between the ages of 15 and 35 and is more common in men than in women. The average days of preoperative evolution of acute appendicitis before surgical intervention were 2 days with 18 cases (30.5%), and 3 days with (16.9%), with a higher number of complicated cases when this number of days was exceeded. Of the 41 complicated cases (69.4%), abscess and perforation corresponded to 31%, and perforation to 27.6%. Severity was observed in 69%. Marco Gamero in

Table 2. Intraoperative findings

Intraoperative findings	Total	Percentage
Without complications	18	30.5%
Abscess	8	13.5%
Perforation	10	16.9%
Necrosis	5	8.4%
Abscess + Perforation	11	18.6%
Perforation + Necrosis	3	5%
Abscess + Necrosis	3	5%
Abscess, Perforation + Necrosis	1	1.6%

Source: Hospital de Alta Especialidad de Veracruz

Table 3. Days of preoperative evolution

N= 59

Days of Preoperative Evolution	Frequency	Percentage %
0	4	6.77
1	17	28.81
2	17	28.81
3	10	16.94
4	6	10.16
6	1	1.69
9	1	1.69
10	2	3.38
22	1	1.69

Source: Hospital de Alta Especialidad de Veracruz

The effectiveness of serum bilirubin as a positive predictive value of severity in patients with acute appendicitis showed in the total with 82% (95% CI 64-92), direct 73% (95% CI 58-84), indirect in 62% (95% CI 31- 83)

Table 4. Diagnostic effectiveness of serum bilirubin for severity in patients with acute appendicitis

Diagnostic Test	Total Bilirubin (95% CI)	Indirect Bilirubin (95%CI)	Indirect Bilirubin (95% CI)
Sensitivity	56 (41-71)	73 (58-84)	12 (5-25)
Specificity	72 (49-87)	39 (20-61)	83 (61-94)
Positive Predictive Value	82 (64-92)	73 (58-84)	62 (31-83)
Negative Predictive Value	42 (26-59)	39 (20-61)	29 (19-43)
% False positives	28 (12-51)	61 (38-80)	17 (6-39)
% False negatives	44 (30-59)	27 (26-42)	89 (74-95)

Source: Have

The area under the ROC curve represents the evaluation of the discriminative capacity of severity in acute appendicitis or its ability to differentiate subjects with severity and without severity. It shows indirect bilirubin with 0.52, direct with 0.44 and total with 0.35, as detailed below

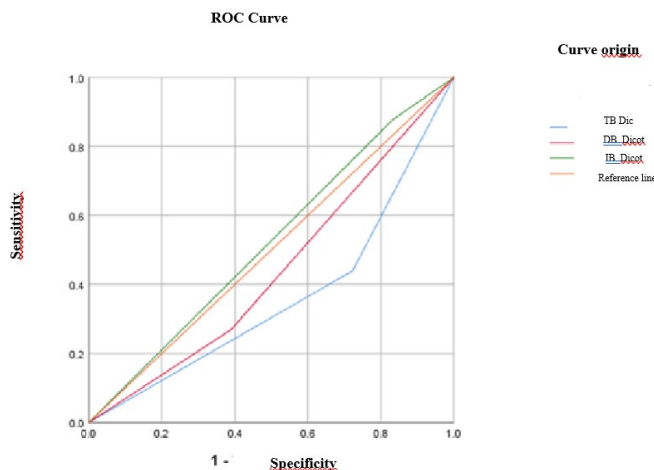


Figure 1. Area under the ROC curve of bilirubin to detect severity in acute appendicitis N=59

AREA UNDER THE CURVE					
Test result variables	Area	Error Desv	AsymptoticSignificance	95% AsymptoticConfidence Interval	
				LowerLimit	UpperLimit
TotalBilirubin (BT) dicot	.358	.077	.085	.207	.510
Direct Bilirubin (BD) dicot	.440	.083	.464	.277	.602
IndirectBilirubin (BI) dicot	.522	.083	.786	.359	.685

The test result variables: Total Bilirubin (BT), Direct Bilirubin (BD), Indirect Bilirubin (BI) have at least one tie between the real positive state group and the real negative state group. The statistics could be biased

a. Under the non- parametric assumption
 b. Null hypothesis: true area= 0.5

Source: Hospital de Alta Especialidad de Veracruz

2009 in Peru reported that 49% of cases were complicated appendicitis (we found 69.4%). The effectiveness of serum bilirubin levels in sensitivity was 56% for total bilirubin and 73% for direct bilirubin, the latter being similar to studies by Palma-Ramírez E. and colleagues. They determined the levels of total serum bilirubin (BT), indirect (BI), and direct (BD) bilirubin before surgery in patients with suspected acute appendicitis in 82 patients over 18 years old, finding that, at the best cutoff level, BT (≥ 1 mg/dl) had a sensitivity of 80% and BD (≥ 0.2 mg/dl) had a sensitivity of 70.6%. In an observational retrospective study conducted by Alanis-Rivera B. and colleagues, which evaluated 225 patients with acute appendicitis, hyperbilirubinemia was related to a 17-fold increased risk of perforated appendicitis with a sensitivity of 74.34% and a positive predictive value (PPV) of 62.8%. Another study by Vaziri M. and colleagues assessed 80 patients diagnosed with acute appendicitis, measuring preoperative bilirubin levels, and found that patients with perforated acute appendicitis had higher levels of bilirubin in blood (1.04 ± 0.5 mg/dl vs. 0.7 ± 0.1 mg/dl), with this difference being statistically significant ($p < 0.01$). A study by Emmanuel A. and colleagues evaluated 555 patients, measuring preoperative serum bilirubin levels, and found that hyperbilirubinemia had a sensitivity of 88% and a PPV of 91% for acute appendicitis; furthermore, patients with perforated (complicated) appendicitis had higher levels of serum bilirubin ($p = 0.01$) and a higher likelihood of having hyperbilirubinemia ($p < 0.001$), with a sensitivity for complicated acute appendicitis of 70%. However, as a positive predictive value of severity in patients with acute appendicitis, total bilirubin showed 82%, direct bilirubin 73%, and indirect bilirubin 62%. In contrast, the area under the ROC curve, which helps differentiate subjects with severity from those without, showed indirect bilirubin at 0.52, direct bilirubin at 0.44, and total bilirubin at 0.35.

CONCLUSION

In this study, the determination of serum bilirubin levels in the preoperative period has a sensitivity of up to 82%, but it lacks specificity as a reliable marker for the severity of acute appendicitis. Based on the findings obtained in our hospital unit, we cannot recommend its determination for this purpose. In our study, the positive predictive value (PPV) of total bilirubin was 82%, which, in comparison to the study by Emmanuel A. and colleagues and by Alanis Rivera and colleagues, showed PPVs of 91% and 62.8%, respectively. This demonstrates that the results of our study are very similar to those of previous studies.

Conflict of Interest: None

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