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Article · March 2024

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Elite Journal of Medicine. Volume 2 issue 2(2024), Pp. 78-84
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Serum Bilirubin Levels in Patients with Acute Appendicitis in Western Uganda: A Multicenter Study

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Abstract
Globally, acute appendicitis, requiring emergency surgery, occurs in 7 to 22 cases per 10,000 persons. The study aimed to assess the correlation between acute appendicitis and serum bilirubin. This was observational prospective cohort study, conducted in Western Uganda from November 2023 to January 2024, involved 62 adult patients diagnosed with acute appendicitis. Eligibility was determined by an Alvarado score exceeding 7. Serum levels of bilirubin were measured, with hyperbilirubinemia defined as >1.1 mg/dl for total bilirubin. Intraoperative severity of appendicitis was compared with biomarker levels. Hyperbilirubinemia was evident in 35.5% (95% CI: 23.7-48.7%). Elevated serum procalcitonin and bilirubin are observed in patients with acute appendicitis. The presence of heightened bilirubin levels is significantly associated with complicated appendicitis.

Keywords*: serum bilirubin, acute appendicitis, Uganda*

Introduction
With a frequency of 7 to 22 cases per 10,000 persons, acute appencitis is one of the major acute abdominal disorders needing emergency surgery; globally, appendectomy is the most common emergency treatment Lee and colleagues, 2010). Serum bilirubin has recently been introduced in several studies as cheap and reliable biomarker in diagnosis of acute appendicitis. Based on a study by Akai *et al* in Japan, serum bilirubin is currently considered one of the better biomarkers used to predict acute appendicitis, and more specifically, in the severe form of the disease. A high level of serum bilirubin (>1.1 mg/dL) was found to be significantly associated with the occurrence of acute appendicitis.[1]

However Akai et and colleagues [1] conducted a retrospective study. Similar findings were published in India by Bakshi *et al.*[2] in 2021, when it was discovered that the total serum bilirubin test had a 91.43% sensitivity and an 88.00% specificity in predicting complex appendicitis. Cholestasis, hemolysis induced by gram negative bacteria and inflammatory process in acute appendicitis are factors which have been thought to induce hyperbilirubinemia in acute appendicitis.[3] In developing countries, there are limited studies correlating acute appendicitis with

Citation: Buhendwa CR**,** Edyedu I, Hidalgo I, Msafiri SL, Iyivuze O, Kumbowi KP, Okuku MD, Angira KS, Luc MM, Obeagu EI. Serum Bilirubin Levels in Patients with Acute Appendicitis in Western Uganda: A Multicenter Study. Elite Journal of Medicine, 2024; 2(2): 78-84

serum bilirubine in uganda, there is no litterature concerning seum procalcitonine and bilirubin in diagnosis of acute appenidicitis and related complications.

Methodology

Study design
This research, which included both FRRH and HRRH, was an observational prospective cohort study.

Study area
The research was conducted at HRRH and FRRH.

Study population.

All patient with clinical features of acute abdomen

Target population
All patients admitted with features of acute appendicitis.

Eligible patient
All patients above 18 years with features of acute appendicitis and required an operation.

Study participants
Included all the eligible patient who consented to participate in the study**.**

Inclusion Criteria
All patients above 18years with features of acute appendicitis

Exclusion Criteria
- Patients with others causes of jaundice: obstructive jaundice, chronic hemolysis.
- Patients with others bacterial infection and multiorgan faire due to trauma

Sample size calculation.
Daniel's formula (1999) was used to establish the required minimum sample size.
$n = z^2xp\ (1-p)/d^2$
Using findings by Obsa *et al.* [4] in Ethiopia.
p=0.44,
Z=1.96 (for 95% Confidence interval),
d= Margin of error set at 5%
$n = (1.96)^2\ x0.44\ (1-0.44)/\ (0.05)^2$
n = 378

Adjusting the sample size for finite population
Since there was no information on the prevalence of appendicitis in the Ugandan population at the time of the planned study, Ellen's [5] explanation of Slovin's method was used to establish the sample size. The group under research for this time would be those who were hospitalized between April

2022, and June 2023, on average, for acute appendicitis, according to hospital records. This matches to the anticipated data collecting period.

$\boldsymbol{Sample\ size\ (N) = \frac{n_s}{1+\frac{n_s-1}{n}}}$, Where N: adjusted population size; ns: estimated sample size and n: population under study

$\boldsymbol{N = \frac{378}{1+\frac{378-1}{65}} = 56}$ Participants

Therefore, minimum sample size required for objective one was 56.

Adding 10% to cater for loss of follow up, the sample size required was 62 participants.

Sampling Technique

In this study all patient with features of acute appendicitis presenting in surgical department of FRRH and HRRH during the study period satisfying the legibility criteria were recruited using the Consecutive sampling technique.

Data processing and analysis plan

The data were summarized using Epi-data software, and the Statistical Package for the Social Sciences (SPSS Inc., Chicago, USA, version 22.0 for Windows) was utilized for analysis. Age and the length of symptoms were examples of continuous variables that were presented using the mean ± standard deviation. Gender and other categorical characteristics were expressed using frequencies.

Ethical considerations

Approvals

The Institutional Research and Ethics Committee of BSU offered ethical clearance to various collaborating hospitals. These patients' routine data were gathered, anonymized, and then examined. Patients were told that their decision not to participate were not have an impact on how they are being treated.

Informed Consent

Informed, written consent was acquired, and recruiting was done voluntarily. After the participants had fully understood the details of the study in both local languages (RUNYORO and English), and in both English and Spanish, their informed permission was requested. If a participant didn't want to register, they had to do so. The participant was allowed to leave the study whenever they wanted to. We utilized the format for the BSU IREC permission form.

Results

Most of the participants in this study were younger than 25 years (85.5%) with a mean age of 20.92±3.34 years, males (54.8%) and did not have a formal employment status (74.2%). Baseline demographic characteristics are presented in Table 1 below.

Table 1:Baseline sociodemographic characteristics of the study participants

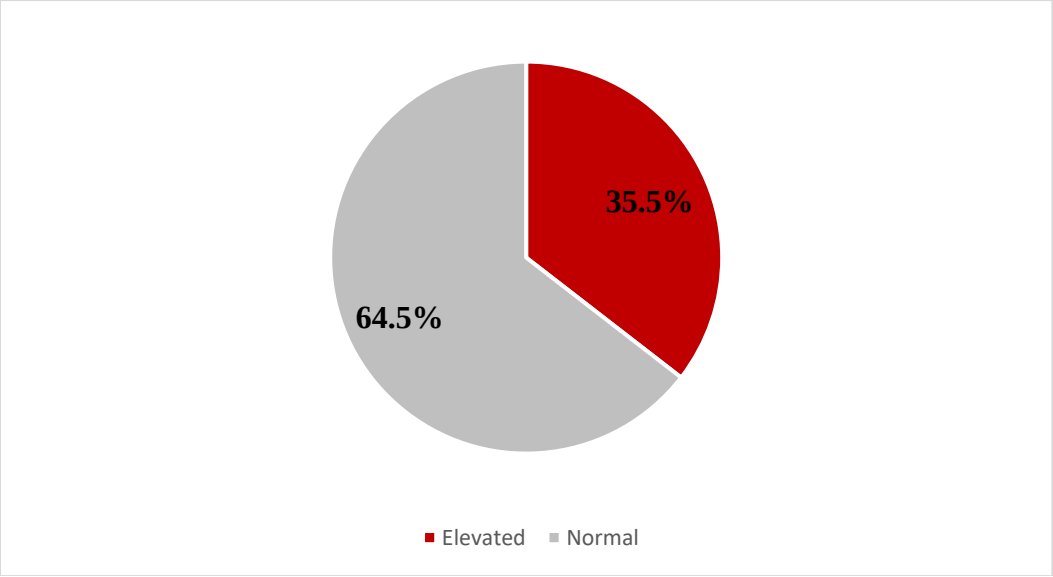
VARIABLES	CATEGORIES	FREQUENCY	PERCENTAGE
SITE	Hoima	38	61.3
	Fort Portal	24	38.7
AGE (YEARS)	<25	53	85.5
	≥25	9	14.5
SEX	Female	28	45.2
	Male	34	54.8
OCCUPATION	Non formal	46	74.2
	Formal	16	25.8

Majority of the participants presented with migratory abdominal pain (56.5%), nausea (59.7%), and anorexia (67.7%). All study participants (100%) had fever, Fever, rebound tenderness, right iliac tenderness, and leukocytosis. Results are indicated below in the table 2.

Proportion of serum hyperbilirubin among study participants

Hyperbilirubinemia was observed among 35.5% (95%CI: 23.7-48.7%). Results is presented in the figure 1 below.

Figure 1: Proportion of serum hyperbilirubin among study participants



Discussion.

The study's mean serum bilirubin was 0.97 mg/dl (0.3–1.9), and 35.5% of patients had serum bilirubin levels higher than 1.1 mg/dl. This result is comparable to that of Indian research by Ramasamy Ramu *et al*. [6], in which patients with acute appendicitis had a mean blood bilirubin of 0.9 mg/dl; yet, only 29% of patients had high serum bilirubin levels over 1 mg/dl. This discrepancy might be explained by the different research population and testing apparatus.
Similar to research done in India by Biradar *et al*[7] where the mean bilirubin levels in patients diagnosed with acute appendicitis were 0.7 ± 0.4 mg/dl, other authors observed a slightly lower mean of serum bilirubin. Furthermore, Biradar *et al* discovered that hyperbilirubinemia only affected 16.7% of the subjects. This difference might be explained by the difference in study population and region. Also, that the difference in cut of level of serum bilirubin in the study of Biradar and colleagues and our study might be the raison.[7]
Gram-negative bacteria enter the body through the appendis muscularis propria, which explains why individuals with acute appendicitis have higher serum bilirubin levels. As a result, bacteria were directly invaded or translocated through the portal system and liver, blocking the bilirubin's excretion through the bile ducts (endotoxin activity). Additionally, it has been noted that cholestasis and hemolysis can be brought on by the common isolated bacteria that cause appendicitis, *Bacterioides fragilis* and *E. coli*.[3]

Conclusion

Serum bilirubin levels are generally higher in patients suffering from acute appendicitis. Elevated bilirubin levels are highly associated with complicated appendicitis, especially in cases when there is perforation of the appendix.

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