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Predictors of complicated appendicitis among patients presented to public referral hospitals in Harari region, Eastern Ethiopia: a case-control study

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ABSTRACT

Background: Complicated appendicitis makes up a significant proportion of acute appendicitis. There are well established associated factors for the development of complications, but the magnitude varies between developed and developing countries. This study was aimed to look for possible incriminated factors for higher rate of complicated appendicitis among patients treated in public hospitals found in the Harari region, Eastern Ethiopia.
Method: Multi-center case-control study with 1:2 was conducted on adult complicated appendicitis patients. The sample size of 414 was determined using an Open Epi and a simple random sampling technique was used to select the samples. Kobo collect was used for data collection by trained medical doctors. Data analysis was made using a statistical package for social studies version 23. The findings were presented in tables and elaborated in texts. Binary logistic regression analysis was conducted to determine association between predictors and outcome variable with adjusted odds ratio at 95% confidence interval, p value less than 0.05.
Result: A total of 402 patients included in the study with 268(66.7%) simple appendicitis and 134(33.3%) complicated appendicitis. More patients with complicated appendicitis had a history of another health facility visit compared to the simple appendicitis groups. Duration of chief complaint, history of constipation, having history of visit to health facilities without surgical intervention for their current problem and fever has shown moderate to strong associations on binary logistic regression analysis.
Conclusion: Delayed presentation, patients who had a history of a visit to primary health care facilities and private clinics where surgical intervention not available were also found to have an increased risk of developing complicated appendicitis.

Introduction

Complicated acute appendicitis is defined as perforated appendicitis, peri-appendicular abscess or peritonitis or defined as acute inflammation of the peritoneum secondary to infection of the appendix (appendicial mass) [1,2] while Simple appendicitis is an inflamed appendix, in the absence of gangrene, perforation, or abscess around the appendix [3].

Complicated appendicitis accounts for approximately 30% of children treated in USA, and they are associated with increased hospital cost, length of stay and adverse outcomes [4]. Study by Perez and Allen from USA showed slightly lower cases of complicated appendicitis, 25% according to among appendicitis operated in one year [5]. Concerning the presentation of patients with anticipated complications, patients in the complicated appendicitis group had longer overall time (OT), time elapsed from onset of pain to time of surgical intervention, and pre-hospital time (PT) [6]. The complication rate for the surgical treatment of complicated appendicitis remains around 10% and includes severe morbidity, such as wound dehiscence, abscess formation, and bowel obstruction [7].

A paucity of population-based studies on the incidence of appendicitis from developing countries highlights a significant gap in the literature [8,9], but from observations during hospital practice, a more significant proportion of patients with appendicitis present with different courses and degrees of complications. The factors associated with these complications were not well known. As a result, this study was aimed to assess the independent factors associated with complicated appendicitis in our setting, compare the findings with developed countries, and finally forward possible recommendations to tackle the current problem.

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Methods and materials

Study settings and period

The study was conducted at Hiwot Fana Specialized University Hospital (HFSUH) and Jugol General Hospital (JGH), found in Harari region, eastern Ethiopia from February 01 to 28, 2021. HFSUH is the major, 210 bedded teaching hospital serving as major referral center for about five million populations in eastern Ethiopia and the JGH has 95 beds that serves a population in Harar town and surrounding Oromia region. Both hospitals provide specialized and general health care services among which general surgery is one during the study time.

Study design and population

Case-control study with a ratio of 1:2 was conducted based on the medical record of patients admitted for acute appendicitis from January 01, 2018, to December 31, 2020, from both hospitals. All patients diagnosed with acute appendicitis admitted to both public hospitals were taken as a source population. All adult patients (older than 18 years of age) with a complete medical records and who had variables of interest were included in the study. However, we excluded incidental appendectomy cases and patients transferred from other health facilities for which the surgery was already performed, because complete information was not available from the medical record chart to categorize as simple or complicated appendicitis. STRCOSS guideline used to organize the manuscript [10].

Sample size determination and sampling procedure

The sample size was determined using double population proportion exposure difference formula by considering the major determinant variables. An Open Epi version 7.2.0.1 statistical software package was used with n=sample size; r=ratio of control to cases, 1:2; p = average proportion exposed/measure of variability; Z_B=desired power (typically 0.84 for 80%); Z_a=desired level of statistical significance (typically 1.96); P1=12.6 and P2=34: the effect size/ P1 (proportion of exposed among cases) and P2 (proportion of exposed among comparisons) rate of postoperative complication for cases and comparisons respectively [11]. So, by considering the largest sample number, the calculated sample size becomes 414, including a 10% top-up case for incomplete sample data. Accordingly, the final sample size for the cases was 138 and for the control 276.

A simple random sampling technique was used to select the patient's medical record using the medical record number (MRN) after identifying and sorting out for both cases and controls. We used ultrasonography results done by senior radiologists in addition to clinical judgment for the diagnosis of appendiceal mass, which is a variety of complicated appendicitis managed conservatively with antibiotics only. For nearly all outcomes, intraoperative findings confirmed by the operating surgeon were used to allocate as complicated and simple appendicitis. The entire simple appendicitis and complicated appendicitis patients except patients with a diagnosis of appendiceal mass which was categorized as complicated appendicitis were managed surgically. Patients with a diagnosis of appendicial mass were treated with IV antibiotics only and discharged home after 7 days. The sample taken from both hospitals were proportionally divided according to the caseload. Accordingly, the consecutive three years (January 01, 2018, to December 31, 2020) recorded data from Hiwot Fana Specialized University hospital were 930 patients (211 were complicated acute appendicitis and 719 simple acute appendicitis) and from Jugol referral hospital 422 patients (131 complicated acute appendicitis and 291 simple acute appendicitis)

Data collection

We used an online data collection tool (Kobo collect) after preparing a standardized structured checklist using relevant literature and general surgery textbook [12–16]. The patient's socio-demographic characteristics (age, sex and address), clinical presentation pattern (chief complaint, nausea, vomiting, diarrhea, constipation, failure to pass feces and flatus, characteristics of pain, history of visit to health facility before admission and treatment), history of comorbidity(diabetes mellitus, hypertension and cardiopulmonary disease), pre-treatment vital signs (systolic blood pressure, pulse rate, respiratory rate, and temperature), laboratory results (white blood cell count, neutrophil percentage, lymphocyte, platelet count, and hemoglobin level) were filled by reviewing the patient's medical record. The data were collected by three trained surgical residents and supervised by investigators.

Operational definitions

- *Incomplete antibiotics treatment* single or double dose of antibiotics given for less than seven days initially for unfirmed cause of acute abdomen which later diagnosed as acute appendicitis.
- *Correct body temperature* correction made to axillary body temperature where 0.5 °C was added to correct to core body temperature.
- *Fever:* A core body temperature of more than 37.7 °C[17].
- *Constipation* refers to bowel movements that are infrequent or hard to pass according to Rome IV criteria [18,19].
- *Conservative management:* Non-operative management given for acute appendicitis. e.g. Appendiceal mass
- Fecolith: hard concretion of stool blocking the lumen of appendicitis or freely seen in the peritoneum.

Data quality control

The consistency of the tool with the information on the patient card was checked, and we have modified the tool accordingly before the commencement of actual data collection. Data collectors were trained before the actual data collection on the contents of the tools, techniques of data collection, and ethical considerations. The collected data were double-checked for any incompleteness and inconsistencies before being uploaded online to the central server.

Statistical analysis

The uploaded data on the central server was downloaded in worksheet/excel format and exported to statistical package for social science (SPSS) version 23 for further data cleaning and analysis. Frequency and cross-tabulation were conducted to check for any missing and incorrect values. Missing values were deleted, and the final corrected sample size becomes 402. Cross-tabulation with chi-square was used to present data descriptively. Binary logistic regression was used to see the association between the outcome variable and independent variables. Variables that yield a p-value of <0.05 in the bivariate logistic regression analysis were considered as a candidate for multivariable logistic regression analysis (using Enter Method) to control all possible confounders and to detect valid predictors of cases. The fitness of the model was tested by Hosmer-Lemeshow goodness of fit. The direction and strength of statistical association were measured by Crude Odd Ratio (COR) and Adjusted Odd Ratio (AOR) at a 95% confidence interval. Finally, statistical significance was declared at a p-value < 0.05.

Results

Socio-demographic characteristics of patients

A total of 414 patients' medical records were reviewed and 12 charts were excluded due to incomplete information for most of the predictors/ outcome variables. As a result, 402 patients, 134(33.3%) cases and 268 (66.7%) controls were included in the study. Overall age stratification showed 278(69.2%) were in the age group of 11–30 years 196(70.1%)

control versus 82(29.9%) cases. Two hundred forty-six (61.2%) were from urban, and the remaining 38.8% were from a rural areas. Seventy-three (29.7%) of a patient from urban had complicated appendicitis while 61(39.1%) of the rural presented with complicated appendicitis (Table 1).

Clinical characteristics

Per-umbilical pain was reported in 211(78.8%) of simple appendicitis patients and 97(72.4 %) among complicated appendicitis cases. Considering the duration of the illness before presenting to the hospital, 104(38.8 %) of simple appendicitis patients presented after 36 h while 103(76.8 %) of complicated appendicitis were stayed for more than 36 h before they visited the hospitals. The commonly reported symptoms among simple appendicitis before admission were vomiting 193 (72 %) and nausea 248(92.5 %). Eighty-six (64.2 %) of complicated appendicitis had history of visiting different health facilities for their current problem before presenting to our hospitals compared to 62(23.1 %) of simple appendicitis groups who have had a history of visit to health facilities without surgical intervention (Table 2).

Vital signs and laboratory results

The vital sign measurement depicts fever among 36(26.9 %) of complicated appendicitis versus 39(14.6 %) simple appendicitis and a pulse rate of more than 100 among 59(44.0 %) of complicated appendicitis versus 61(22.8 %) of simple appendicitis with P-values less than 0.05 (Table 3).

Factors associated with complicated appendicitis

Bi-variable logistic regression analysis revealed that duration of illness before the presentation (duration of chief complaint), personal history of constipation for more than one week before the onset of the current problem, history of visiting a health facility for the current complaint, and adjusted body temperature of greater than 37.7 °C, pulse rate of greater than 100, Neutrophil percentage of greater than 70% and normal platelet count were found to have an association with complicated appendicitis (Table 4).

Further analysis using multivariate logistic regression for adjustment was done and showed the duration of chief complaint, 36 to 72 h was found to have adjusted odds ratio (AOR) 3.2, 95% CI (1.81–5.92), and history of constipation AOR 8.38, 95%CI (2.58–27.19). Pulse rate and neutrophil percentage, which were significant under crude analysis, become insignificant on adjusted analysis with AOR 1.36, 95% CI (0.75–2.44) and 1.57(0.86–2.86) respectively (Table 4).

Discussion

It was known for many years that several factors contribute to the complication of simple appendicitis, even though the exact cause of appendicitis is poorly understood [20], Sasaki et al. showed advanced age, longer onset-to-visit interval, anorexia, tachycardia, fever, elevated C-reactive protein (CRP) level, renal dysfunction, and hyponatremia were significantly prevalent in the complicated appendicitis group than in the simple appendicitis group [21]. In the same way, our study showed that the duration of illness that lasted 36 to 72 h before presentation to a hospital had 3.2 increased odds of complicated appendicitis. Those who come after 72 h had 8.5 increased odds of developing complicated appendicitis. These finding was supported by various literature that the longer time interval between intervention and onset of pain,the more likelihood of ending up with complicated appendicitis [[13],[22],[23]].

History of constipation was found to have a significant association with complicated appendicitis. According to Buddingh et al., teenager patients who had a history of constipation had an increased risk of developing appendicitis when compared with similar age groups presented with nonspecific abdominal pain [24]. Epidemiological studies suggest that constipation may be an essential factor in the pathogenesis

Table 1
Socio-demographic characteristics of patients presented with acute appendicitis at public hospitals in Harari region, 2021.

Variables	Category	Simple appendicitis (%)	Complicated appendicitis N (%)
Age	<10	11(64.7)	6(35.3)
	11–30	196(70.1)	82(29.9)
	31–50	57(62.0)	35(38.0)
	50+	4(26.7)	11(73.3)
Sex	Female	75(64.1)	42(35.9)
	Male	193(67.7)	92(32.3)
Residence	Urban	173(70.3)	73(69.7)
	Rural	95(60.9)	61(39.1)

Table 2
Clinical presentation of patients presented with acute appendicitis at public hospitals in Harari region, 2021.

Variables	category	Simple appendicitis N = 268 (%)	Complicated appendicitis, N = 134 (%)
Chief complaint	Per-umbilical pain	211(78.8)	97(72.4)
	RLQ* pain	45(16.8)	23(17.2)
	Ill-defined pain	12(4.5)	14(10.4)
Characteristics of the pain	Colicky/ cramp/ intermittent	251(93.7)	113(84.3)
	Diffuse	3(1.1)	14(10.4)
	Continuous	14(5.2)	7(5.2)
Shifting pain	No	37(13.8)	28(21)
	Yes	224(91)	96(71.6)
Duration of pain in hours before presentation	<36 h	164(61.2)	31(23.1)
	36–72 h	82(30.6)	61(45.5)
	>72 h	22(8.2)	42(31.3)
Vomiting	No	75(28)	27(20.1)
	Yes	193(72)	107(79.9)
Nausea	No	20(7.5)	9(6.7)
	Yes	248(92.5)	125(92.3)
Failure to pass feces and flatus	No	254(94.8)	110(82.1)
	Yes	14(5.2)	24(17.9)
Constipation	No	263(98.1)	117(87.3)
	Yes	5(1.9)	17(12.7)
Diarrhea	No	259(96.6)	127(94.8)
	Yes	9(3.4)	7(5.2)
Urinary tract infection symptoms	No	255(95.1)	129(96.3)
	Yes	13(4.9)	5(3.7)
Positive psoas sign	No	133(49.6)	23(17.2)
	Yes	135(50.4)	111(82.8)
Positive obturator's sign	No	173(64.5)	40(29.8)
	Yes	95(35.5)	94(70.2)
Visit to any health facility (n = 402)	No	206(76.8)	48(35.8)
	Yes	62(23.2)	86(64.2)
Types of health facilities visited	Health center	20(32.2)	24(27.9)
	Primary hospital	19(30.7)	35(40.7)
	Private clinic	23(37.1)	27(31.4)
Types of treatment given	antibiotics	7(36.8)	13(23.2)
	Antibiotics and analgesics	9(47.4)	37(66.1)
	Injection analgesics	3(15.8)	6(10.7)

*RLP right lower quadrant pain.

Table 3
The Association of vital sign and laboratory result of patients presented with appendicitis at public hospitals in Harari region, 2021 (χ^2).

Variables	Category	Simple appendicitis , n(%)	complicated appendicitis , n(%)	P-value
Temperature (degree Celsius)	≤ 37.7	229(70.0)	98(30.0)	<0.0001
	>37.7	39(52.0)	36(48.0)	
Systolic blood pressure (mmHg)	<90	6(66.7)	3(33.3)	0.625
	>90	262(66.7)	131(33.3)	
Pulse rate /minute	<100	207(73.4)	75(26.6)	<0.0001
	>100	61(50.8)	59(49.2)	
Respiratory rate	12–25	244(69.5)	107(30.5)	0.001
	>25	24(47.1)	27(52.9)	
WBC count (cells/μL)	<11,000	139(70.6)	58(29.4)	0.114
	11,000–15,000	73(67)	36(33)	
	>15,000	56(58.3)	40(41.7)	
Neutrophil%	<70	90(72)	35(28)	0.128
	>70	178(64.3)	99(35.7)	
Lymphocyte %	<18	168(63.6)	96(36.4)	0.204
	18–45	95(72.5)	36(27.5)	
	>45	5(71.4)	2(28.6)	
Platelet count (cells/μL)	<150,000	36(55.4)	29(44.6)	<0.0001
	1,500,000–450,000	226(71.7)	89(28.3)	
	>450,000	6(27.3)	16(72.7)	

Note: mmHg: millimeter mercury, μL: microliter.

of appendicitis. According to studies from Africa and North America, populations on high fiber diets have a lower incidence of appendicitis than Westernized diets. Despite some experimental studies, tangible evidence of a causative relationship is lacking [12], but fecalith was not significantly associated with complicated appendicitis in this particular study which could be due to a small proportion of patients with fecalith.

Our study has also identified patients who had a history of visits to primary health care centers and private clinics where surgical intervention was not given to have increased odds of developing complicated appendicitis as compared to the comparison groups. Treating patients with analgesics and incomplete doses of antibiotics which yields symptomatic relief so that patients stay longer before they get surgical intervention. It was not reported in the literature about antibiotics and analgesic misuse towards the development of complicated appendicitis, but 20%–50% of antibiotic usage in acute care models is unnecessary or inadvertent, which risks longer hospital stays and drug resistance [25]. It was noticed in this study that incomplete treatment with both intravenous and/or oral antibiotics at the health facilities from which patients referred was 27/94(28.7%). From these patients, 19(70.4%) had complicated appendicitis. On the contrary, 20/57 (35.1%) simple appendicitis patients who were not given any medication This practice of antibiotic misuse for empirical treatment of abdominal pain at private clinics and primary care health facilities need further study and should be intervened by ministry of health as the long term consequence might lead to antimicrobial drug resistance.

Corrected axillary body temperature of more than 37.7 °C had a significant association with complicated appendicitis. In line to this, study by Choi JY et al. showed fever and diarrhea were risk factors of a delayed diagnosis of appendicitis. Fever and diarrhea are common symptoms that can also indicate gastroenteritis or other infectious diseases [26]. According to Jerusalem guideline, 2020 update on acute appendicitis, fever of greater than 38 Celsius mentioned as a predictor of complicated appendicitis [27].

Strengths and limitations

This study is of its first type to our understanding that studied predictors of complicated appendicitis in this specific study area. It has identified different factors associated to complicated appendicitis. On the contrary, as it was retrospective study, all the information needed was impossible to acquire and bias is inevitable.

Conclusion and recommendations

The current study identified multiple factors as having increased odds for complicated appendicitis similar to other studies conducted in low-income countries. Delayed presentations, history of visiting primary health care centers and private clinics without surgical facility and experts, were found to have increased odds of complicated appendicitis. Patients with a history of constipation were also had an increased the odds of developing complicated appendicitis. These two later factors need further study with robust data for validation.

Ethical consideration

Ethical approval was obtained from Haramaya University, College of Health and Medical Sciences, Institutional Health Research Ethics Review Committee (IHRERC) with a reference number (IHRERC/005/2021). The aim and objective of the study were explained and informed, voluntary, and written signed consent was taken from the hospital managers and medical record officers. Patients' personal identifiers

Table 4
Factors associated with complicated appendicitis in patients treated at public hospitals of Harari, Eastern Ethiopia, 2021.

Variable	Exposure categories	complicated appendicitis	simple appendicitis	OR 95%CI Crude	OR 95% CI Adjusted	P-value
Duration of chief complaint	<36 h	164(84.1%)	31(15.9%)	Reference		<0.001
	36–72 h	82(57.3%)	61(43.7%)	3.93(2.37–6.54)	3.27(1.81–5.92)	
	>72 h	22(34.4%)	42(65.6%)	10.1(5.31–19.21)	8.52(3.88–18.70)	
History of constipation	No	263(69.2%)	117(30.8%)	Reference		<0.001
	Yes	5(22.7%)	17(77.3%)	7.64(2.75–21.21)	8.38(2.58–27.19)	
Health facility visit for the current problem	No	208(81.1%)	48(18.9%	Reference		<0.001
	Yes	62(41.9%)	86(58.1%)	5.95(3.78–9.37)	6.02(3.52–10.30)	
Temperature (Celsius)	≤ 37.7	229(70.0%)	98(30.0%)	Reference		0.028
	>37.7	39(52.0%)	36(48.0%)	2.16(1.29–3.60)	2.10(1.09–4.05)	
Pulse rate	≤100	207(73.4%)	75(26.6%)			0.310
	>100	61(50.8%)	59(49.2%)	2.67(1.71–4.17)	1.36(0.75 −2.44)	
Neutrophil%	≤70	90(72%)	35(28%)			0.141
	>70	178(64.3%)	99(35.7%)	1.43(0.902–2.27)	1.57(0.86 −2.86)	
Platelet count	<150,000	36(55.4%)	29(44.6%)	Reference		
	15,000–450,000	226(71.7%)	89(28.3%)	.489(0.28–0.85)	.36(0.18 −0.72)	0.004
	>450,000	6(27.3%)	16(72.7%)	3.310(1.15–9.54)	1.76(0.47–6.58)	0.400

were excluded; information was kept confidential and used for the study purpose only. There was no direct benefit provided for the patients.

Author's contribution

BB and FM have conceived the study concept, wrote the methodology, developed the tools, collected and analyzed the data, and written the manuscript. GF Wrote methodology, participated in data Capturing, formal analysis and writing up of the original draft. AA participated in the design of the study, prepared data collection tool (kobo collect), and critical edition of the manuscript. All authors read and approved the final version of the manuscript.

Declaration of Competing Interest

None declared.

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