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Cohort Study

Predictors and management outcomes of perforated appendicitis in sub-Saharan African countries: A retrospective cohort study

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ABSTRACT

Background: Previous studies have found an association between various predictors and perforated appendicitis. However, there is limited evidence of studies determining the severity of acute appendicitis (AA) in resource-limited settings. Thus, this study aimed to identify predictors and outcomes of perforated appendicitis (PA) in sub-Saharan countries.

Methods: This is a retrospective cohort study of 298 adult patients who underwent surgical intervention for acute appendicitis. Demographic characteristics, clinical parameters, intraoperative findings, length of hospital stay, and postoperative complications were collected. We computed multivariate logistic regression to identify predictors of PA. P-value <0.05 was considered statistically significant.

Results: Of 298 patients, PA was 142(47.65%). The identified risk factors for PA are referred patients (AOR = 3.932; 95% CI (2.201–7.027), fever >38 °C (AOR = 4.569; 95% CI (2.249–9.282), and duration of symptoms >2 days (AOR = 2.704; 95% CI (1.400–5.222). Perforation was associated with an increased rate of postoperative complications (45.07vs. 6.41%; P < 0.001) and a longer length of hospital stay (3 vs. 5 days; P < 0.001).

Conclusions: The incidences of PA in our study are consistent with other reports in developing countries. Referred patients, longer duration of symptoms >2 days, and presence of fever >38 °C were the best predictors of PA. The overall total postoperative complications and the length of hospital stays were higher in PA. Based on our findings, we recommend that the identified predictors should be considered during the preoperative diagnosis and subsequent management.

1. Introduction

Acute appendicitis (AA) remains a common cause of surgical emergencies, with an estimated lifetime risk of 9% in the USA, 8% in Europe, and 2% in Africa [1]. Although the exact incidence of perforated appendicitis (PA) in low and middle-income countries (LMIC) is not well known due to limited data, it has been estimated to be high compared to western countries, with substantially increased morbidity and mortality [2–12]. Length of hospital stay is also prolonged, which poses additional health care expenses [13,14]. This translates into a significant health care burden in resource-limited settings; therefore, much effort has been needed to improve diagnosis and outcome.

Failure of early diagnosis and delayed management are considerably high in the potentially poor surgical access area, because of multiple reasons: low socioeconomic status, urban-rural discrepancy, prehospital delays, long referral chain, limited infrastructure, human resources, and poor diagnostic capacity [15–19].

The diagnostic accuracy could be improved by using different scoring systems that involve clinical profiles, serologic markers, and radiological findings [20–23]. Nevertheless, with limited resources in imaging and investigation modalities, diagnosing appendicular perforation is more challenging. Consequently, the potential of simple laboratory tests and clinical parameters in the prediction of perforated appendicitis has attracted the interest of clinicians working in LMICs [13,23–25].

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Abbreviations

AA	acute appendicitis
PA	perforated appendicitis
NPA	Non-perforated appendicitis
LMIC	low and middle-income countries

According to the guidelines developed by the World Society of Emergency Surgery (WSES), adopting a tailored individualized diagnostic approach is recommended for stratifying the risk and disease probability and planning an appropriate stepwise diagnostic pathway in patients with suspected AA, depending on the demographic and clinical parameters [26]. Generation of predictive tools and utilizing them to differentiate non-perforated from perforated AA allows the clinicians to choose between conservative and surgical management [27]. Early surgical intervention has long been advocated to mitigate the risk of perforation and subsequent complications [28]. However, recent studies have shown that conservative management might be an alternative in selected cases [29]. In line with these insights, appendicectomy as standard management for all cases of AA is now under scrutiny.

Despite the observed difference between many studies, numerous serologic markers and clinical parameters have been proven helpful in predicting perforated appendix [20–25].

Therefore, the current study investigated clinical predictors associated with perforated appendicitis and evaluated the postoperative complications and duration of hospital stay in adult patients in resource-limited settings.

2. Methods

2.1. Study design and participants

After securing approval from the institutional review board, we retrospectively retrieved the medical records of all patients who underwent an operation for AA in the University's specialized and teaching hospital from September 2019 and January 2021. This study was performed under the Declaration of Helsinki Ethical Principles for Medical research involving human subjects' protocol. Informed written consent was waived due to the retrospective nature of the study design. This study was reported in line with STROCSS criteria [30] and registered at www.researchregistry with a registry number: researchregistry7934. The information of all patients was anonymized, and confidentiality was assured throughout the research.

During the study period, all adult patients aged between 18 and 60 years of age who underwent an operation for AA were retrieved initially; cases confirmed to be AA by intraoperative findings were included in the study. We excluded patients with incomplete medical records. We also exclude patients with negative appendectomy; normal appendix removed surgically in patients suspected of having AA.

2.2. Data collection techniques

Data extraction was performed independently by two trained data collectors from all medical records using standardized pretested questionnaires. Data retrieved from the medical records included demographic characteristics, clinical presentations, laboratory results (CBC), duration of hospital stay, postoperative complications, and whether the appendix was found perforated or not. Our study categorized patients into PA (n = 142) and NPA (n = 156) groups based on the intraoperative findings.

Perforated and non-perforated appendicitis was defined based on reports of previous studies. PA is diagnosed on the bases of intraoperative findings: a visible hole or perforation in the appendix, purulent free fluid, and intra-abdominal abscess collection. NPA is diagnosed on the bases of intraoperative findings: acutely inflamed appendix without any signs of perforation, purulent free fluid, and intra-abdominal abscess collection.

The primary outcome measure was to identify the predictors associated with the PA. The secondary outcome variables were postoperative complications and length of hospital stay.

Leukocytosis was considered when the total white blood cell count exceeds 12,000/μL. Fever was defined by the objective measures of axillary temperature >38 °C. A percentage of neutrophils >74% was considered high. Patients transferred from rural and surrounding health centers for better management were considered referred patients. Duration of illness is defined as the time from the patient first feeling ill until the time of admission to the emergency surgical unit. Length of hospital stay was defined as a day between hospital admission and discharge to home. Postoperative complications were defined as the development of wound infection, ileus, dehiscence, and pneumonia until 4 weeks after discharge from the hospital.

2.3. Statistical analysis

We entered, coded, and analyzed the data using SPPS 26.0 software for Windows (SPSS Inc., Chicago, IL, USA). Demographic characteristics, clinical parameters, intraoperative findings, length of hospital stay, and postoperative complications of each group were analyzed. We presented the categorical data as frequency and percentage, and the continuous variables were expressed as median and interquartile ranges. We used the Mann-Whitney *U* test for continuous variables between study groups. We used a Pearson Chi-square test to compare categorical variables between study groups. We checked the Multicollinearity by VIF, tolerance, and confidence index. We utilized univariate analysis to identify the effects of potential predictors on PA. To further analyze the relationship between predictors and outcome variables, predictors with P-value < 0.05, were included in multivariate binary logistic regression.

Results are shown as adjusted OR with 95% CI. A two-tailed p-value < 0.05 was considered statistically significant. We used Hosmer and Lemeshow test to assess the goodness of fit, and the model was the best fit with a P-Value of 0.72.

3. Result

Of the 298 patients included in the current study, the incidence of PA was 47.65%. While the age, sex, ASA class, and co-existing distributions between the two groups were comparable, the number of referred patients from poor surgical access areas in the PA group was significantly high compared with the NPA group [PA vs. NPA: 60.25% vs 39.75%; p-value < 0.001] (Table 1).

Concerning clinical presentation, there was no difference in migratory pain and nausea with or without vomiting. However, a high frequency of anorexia and a longer duration of symptoms was observed in PA compared with NPA groups. On physical examination, temperature >38 and rebound tenderness was significantly high in PA compared with NPA, while direct tenderness was similar between the two groups.

With regards to laboratory values, the PA group had significantly elevated values in WBC count (13.74 vs 14.77 * 103), lymphocyte percentage (11.05 vs 9.6), and neutrophil percentage (80.9 vs84.31) compared with the NPA group (Table 2).

Multiple logistic regression analysis showed that the significant predictors associated with PA were patients referred from the poor surgical access area, duration of symptoms >2 days, and temperature >38. However, anorexia, WBC count, lymphocyte, and neutrophil percentage did not increase the odds of PA despite being significantly different between the two groups (Table 3).

Of the total patients, the incidence of postoperative complications was 76(25.5%). The overall rate of complications was 38.02% and 15.49% in the PA and NPA groups, respectively (P < 0.001). The median

Table 1
Demographic characteristics of the study participants between two groups.

Variables		NPA group (n = 156)	PA group (n = 142)	Total (n = 298)	P value
Age		26(18–60)	24(18–65)	25(18–65)	0.062
Sex	Male	108(%)	84(%)	192(%)	0.07
	Female	48(%)	58(%)	106(%)	
ASA class	ASA I	142 (47.6%)	128(43%)	270(90.6%0	0.807
	ASA II	10(3.4%)	10(3.4%)	20(6.8%)	
	ASA III	4(1.3%)	4(1.3%)	8(2.6%)	
Co-existing	Yes	14(4.7%)	14(4.7%)	28(9.4%)	0.068
	No	142 (47.6%)	128(43%)	270(90.6%)	
Referred	Yes	94(60.25%)	44(31%)	138(46.3%)	**<0.001**
	No	62(39.75%)	98(69%)	160(53.7%)	

ASA class; American Society of Anesthesiologist Classification.

Table 2
Comparison of clinical parameters between two groups.

Variables		NPA group (n = 156)	PA group (n = 142)	Total (n = 298)	P-value
Clinical presentation					
Duration of illness (Days)		1(0.04–10)	3(0.13–15)	2(0.04–15)	**<0.001**
Migratory pain	No	60(%)	50(%)	110(%)	0.561
	Yes	96(%)	92(%)	188(%)	
Anorexia	No	42(%)	16(%)	58(%)	**0.001**
	Yes	114(%)	126(%)	240(%)	
Nausea/ vomiting	No	30(10.07%)	16(5.37%)	46(15.44%)	0.057
	Yes	126 (42.28%)	126(42.28%)	252 (84.56%)	
Physical examination					
Temperature >38 °C	No	136(%)	88(%)	224(%)	**<0.001**
	Yes	20(%)	54(%)	74(%)	
Direct tenderness	No	10(%)	4(%)	14(%)	0.143
	Yes	146(%)	138(%)	284(%)	
Rebound tenderness	No	80(%)	52(%)	132(%)	0.057
	Yes	76(%)	90(%)	166(%)	
Laboratory values					
WBC ((1000/ μL)		13.74(5.5–68.7)	14.77 (3.55–23.6)	13.9 (3.55–68.7)	**0.003**
Lymphocyte (%)		10.05(1.6–43.2)	9.6 (1.34–35.3)	10 (1.34–43.2)	0.08
Neutrophil (%)		80.9(39.7–95)	84.31 (38.5–92.3)	83.4 (38.5–95)	**0.001**

WBC; white blood cell count.

Table 3
Multivariable logistic regression analysis of predictors associated with PA.

Variables	Adjusted OR (95% CI)	P-value
Referred patients	3.932(2.201–7.027)	**<.0001**
Anorexia	1.898(.896–4.021)	.094
Fever (T > 38 °C)	4.569(2.249–9.282)	**<.0001**
Duration of symptom >2 days	2.704(1.400–5.222)	**.003**
WBC count >12 *10^3	1.255(.596–2.645)	.550
Neutrophils >74%	1.430(.693–2.950)	.333

Table 4
Postoperative complications and length of hospital stay between two groups.

Variables	PA	NPA	P-value
Length of hospital stay	3(1–13)	5(1–28)	**<0.001**
Postoperative complication	54 (38.02)	22 (15.49)	**<0.001**
Wound site infection	44	16	**<0.001**
Postoperative ileus	7	4	0.279
Pneumonia	3	2	0.426

length for the hospital stay was statistically significantly reduced in the NPA (3 vs 5 days; P < 0.001) compared with the PA group (Table 4)

4. Discussion

Perforated appendicitis (PA) and subsequent abscess formation are common in adult patients, particularly in resource-limited settings. Therefore, there is a need to establish a reliable resource-oriented prediction tool to improve the diagnostic accuracy of appendicular perforation.

These prediction tools might reliably guide preoperative diagnosis and subsequent management options. The incidence of PA in adult patients varies between 15.8% and 20% in developed countries [2,3] which increase to 20%–60% in LMICs [4–10]. However, some studies reported a lower range of PA, but we realized that such studies depend on histopathological findings rather than the clinical picture, which is confusing [11,12].

Our study has demonstrated that the overall incidence of a perforated appendix (PA) was 47.65%. This result lies within the reported range by other LMICs. This discrepancy could be explained by the fact that in the sub-Saharan countries, there are limited diagnostic capacity, trained expertise, and a lack of a standard referral system to provide optimal emergency surgical care, which might increase the risk of perforation [15–19].

Moreover, the provision of emergency surgical care has not gotten the desired attention/the attention given was not enough compared to other infectious diseases; in effect, this causes unequal health care access within the countries [16]. In the same way, the national health survey done by S. N. Zafar et al. [19], reported that the disparity of surgical access in developing countries remains a substantial concern, especially in rural areas. Understanding the epidemiologic patterns of PA in LMICs is necessary for planning and reevaluating healthcare resource utilization.

The findings of this study indicate that the duration of symptoms> 2 days, referred patients, and the presence of fever (>38 °C) were the independent predictors of PA.

We categorized the duration of symptoms into < and >2 days to investigate their association with PA. However, there was an inconsistent category of symptom duration between works of literature [4,8,13–15]. Certainly, the delays in diagnosis and surgical intervention have a linear relationship with perforation. C.K. Narsule et al. [31] reported that the odd appendiceal perforation rises linearly with time. A positive association between the rate of appendicular perforation and the duration of symptoms of AA in adults is well established [4–8,18].

In our study, the median duration of symptoms before hospital admission in PA was three days.

Several studies confirmed that the longer duration of symptoms before seeking medical attention was directly associated with appendicular perforation in children and the elderly [14,21,32–34].

Consistently our data also showed that the longer duration of symptoms before hospital admission (>2 days) had 2.7 increased odds of

perforation.

PA rates were much higher in patients referred from no surgical access areas. Despite the need for further research, patients with rural origins were identified as an independent predictor of poor outcomes [6,10,17,35]. Referred patients who demand surgical emergencies, including AA, frequently delay medical care, particularly in sub-Saharan countries [6–8,10], and such delay inevitably leads to perforation.

In LMICs, delayed presentation for surgical care is common and multifactorial. The difficulty in accessing the emergency surgical services or delay in transfer to a regional hospital could be the possible justification [7,35,36]. A prospective study on the inter-facility transfer of surgical emergencies in a developing country by Khan et al. [37] found that the physiologic derangement was statistically significantly increased in the transferred patients compared to non-transferred patients.

Consequently, when the patients arrive at the tertiary center, the untreated AA may cause perforation and subsequent abscess formation with peritonitis [35]. Congruently, our study also depicted that referred patients from nearby or rural health centers were significantly associated with a high risk of perforation. Another reason for delayed referral in LMICs was a shortage of infrastructure, well-established patient pathways, trained expertise, and lack of comprehensive protocols, which remains a challenging issue for the surgical referral system [38]. The discrepancy in perforation rate between referred and a non-referred patient suggests disparities in access to timely surgical care. Therefore, expanding emergency surgical services for rural health centers should be prioritized in forthcoming national health policies.

Another factor associated with appendicular perforation was the presence of fever. However, fever is not a specific sign of a perforated appendix, as other infectious diseases can present with fever. In cases where patients are suspected of having PA and have a fever, these patients might need prompt surgical intervention to prevent associated postoperative complications and prolonged hospital stay. Several studies have shown the significance of fever in predicting the likelihood of having PA [13,14,33,39,40].

On the other side, our study demonstrated that elevated neutrophils and WBC count did not increase the likelihood of PA despite their values being significantly different between PA and NPA groups. These results were in line with many other studies [4,18,20,24,41]. In disagreement with our finding, several studies found that the elevated neutrophils and WBC count are statistically significantly increased in the PA group compared to the NPA group [3,13,20,40,42].

There are several possible justifications for the observed difference in the findings of the current and prior studies. First, the study subjects of previous studies were children and geriatrics patients. Secondly, several studies utilized different neutrophil and WBC count cut-off values.

Furthermore, variations of statistical analysis, selection bias, and standard of clinical setup in a diverse health context may have influenced the results.

The overall rate of complication was statistically significantly lower in the NPA group compared to the PA group (38.02% vs 15.49%; $p < 0.001$). In agreement with our results, several studies reported a significantly high postoperative complications rate in the PA group [32,43].

In the same way, the median length of hospital stays was shorter in the NPA group (3 vs 5 days; $P < 0.001$), as revealed in our study. Consistent with our findings, previous studies also showed a prolonged hospital stays in PA compared with the NPA group [32,43].

The main limitation of our study is it's an experience of a single institution and the retrospective nature of the study design. We excluded hospital delay duration, the time between hospital admission, and the operation time due to inconsistent documentation. The documented duration of symptoms on medical records was in day's form, which posed difficulty in comparing with previously published studies. Moreover, histopathological examination is not available in our study center. The presence of perforation was confirmed solely by intraoperative findings, which might underestimate the perforation rate. In the same way, this study was conducted in a resource-poor setting, where the CT scan and other advanced radiological investigations are inaccessible in the clinical setup. The lack of radiological investigation and histopathological examinations might affect the accuracy of preoperative diagnosis and intraoperative findings.

5. Conclusion

The incidence of appendicular perforation is relatively similar to other developing countries. Referred patients from other health centers, duration of symptoms (>2 days), and the presence of fever were the best predictors of a perforated appendix. Future studies that adequately involve different variables in multi-center institutions for developing prediction tools are necessary. Based on the findings of our study, we recommend adopting resource-oriented prediction tools to reduce the rate of PA and associated postoperative complications.

Ethical approval

Ethical approval was obtained from ethical review board of Wolkite University.

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Registration of research studies

1. Name of the registry: ClinicalTrials.gov
2. Unique Identifying number or registration ID: UIN: research registry 7934
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): www.researchregistry.com

Guarantor

Dereje Zewdu.

Consent

Informed written consent was waived due to the retrospective nature of the study. The information of all patients was anonymized for the current study and confidentiality was assured throughout the research.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104194.

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