



# HIV Infection: Its Impact on Patients with Appendicitis in Botswana

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## Abstract

**Background** To compare the presentation, management, and outcome of HIV-positive patients with appendicitis to those of HIV-negative patients with appendicitis. **Summary Background Data:** The literature is limited regarding the impact of HIV infection on patients with appendicitis.

**Methods** A retrospective review of patients with appendicitis and known HIV status admitted to Princess Marina Hospital, Gaborone, Botswana, aged 13 years and greater was performed from January 2013 to December 2015. Data on patient demographics, presentation, laboratory findings, management, and outcomes were analyzed.

**Results** A total of 295 patients with appendicitis and known HIV status were identified, of which 119 (40.3%) were HIV positive. The median [IQR] ages for HIV-positive and HIV-negative patients were 34 [29–42] and 26 [20–33] years, respectively. The male-to-female ratio for the same two groups was 0.8:1 and 1.4:1, respectively. Presenting symptoms, signs, and white blood cell count were similar in both groups. HIV-positive patients had significantly higher overall (4.2 vs. 0.0%,  $p = 0.010$ ) and postoperative (4.4 vs. 0.0%,  $p = 0.024$ ) mortality rates. There was no significant difference in the total complication rate between HIV-positive and HIV-negative patients (13.2 vs. 7.9%,  $p = 0.192$ ). Compared to HIV-positive patients with a CD4 count  $\geq 200$ , patients with a CD4 count  $< 200$  have a significantly higher postoperative mortality rate (17.6 vs. 1.4%,  $p = 0.023$ ) and a trend toward a higher total postoperative complication rate (31.3 vs. 10.8%,  $p = 0.054$ ).

**Conclusion** Within our setting, HIV infection, particularly with a CD4  $< 200$ , was correlated with significantly higher mortality in patients with acute appendicitis.

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s00268-019-05040-9>) contains supplementary material, which is available to authorized users.

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## Introduction

Appendicitis in HIV-positive patients (HPP) was first reported in 1986 [1, 2]. Some studies have reported a higher incidence of appendicitis [2–5] and increased number of complications, in this HIV-positive group [2–4, 6], while others have suggested an incidence and outcomes similar to those of HIV-negative patients (HNP) [2, 3, 7]. These published findings are in the context of the well-documented result that highly active antiretroviral therapy (HAART) significantly improves the life expectancy of patients infected with HIV [6, 8].

Many studies have demonstrated that the clinical presentation of appendicitis in HPP and HNP has not been found to differ significantly [2, 3, 7, 9, 10]. Most HPP with appendicitis experience most of the classic symptoms and signs associated with appendicitis [4, 11, 12]. According to certain studies, leukocytosis may be less prevalent in HPP with appendicitis (66.7%) [4] as compared to HNP with appendicitis (80%) [3, 11].

The current wisdom is that surgical decision making for patients with appendicitis should not be influenced by their HIV status alone [2, 10–13]. This is supported by studies that have reported similar intraoperative and pathologic findings in HPP and HNP [3, 5]. Our review of the literature did not yield any study in which CD4 count was used as a decision-making tool.

Botswana's HIV prevalence of 21.9% in 2013 is third highest in the world after Lesotho and Swaziland [14]. This study is the first to examine the impact of HIV on patients with appendicitis in Botswana.

## Materials and methods

This study was conducted at Princess Marina hospital, the largest tertiary and teaching hospital in Botswana. We performed a retrospective medical record review of patients aged 13 years and older with a clinical diagnosis of appendicitis and known HIV status from January 2013 to December 2015. Length of hospital stay was the number of days in the wards from admission to discharge, with same-day discharge considered zero. Complex appendicitis was defined as gangrenous or perforated appendicitis based on pathologic findings.

Data analysis was performed using IBM SPSS Statistics 25. Association between categorical variables was tested using Chi-squared, Mann–Whitney U test, and Fisher's exact test.  $P$  value  $< 0.05$  was chosen to indicate statistical significance.

Permission to conduct this study was granted by the Institutional Review Board at Princess Marina Hospital and the Ministry of Health and Wellness of Botswana. No patient identifiers were collected in order to ensure anonymity.

## Results

A total of 295 patients with appendicitis and known HIV status were admitted to Princess Marina Hospital from January 2013 to December 2015, of which 119(40.3%) were HIV positive (Fig. 1). The median ages [IQR] (range) in years for HPP and HNP were 34 [29–42] (13–61) and 26 [20–33] (13–90), respectively (Fig. 2).

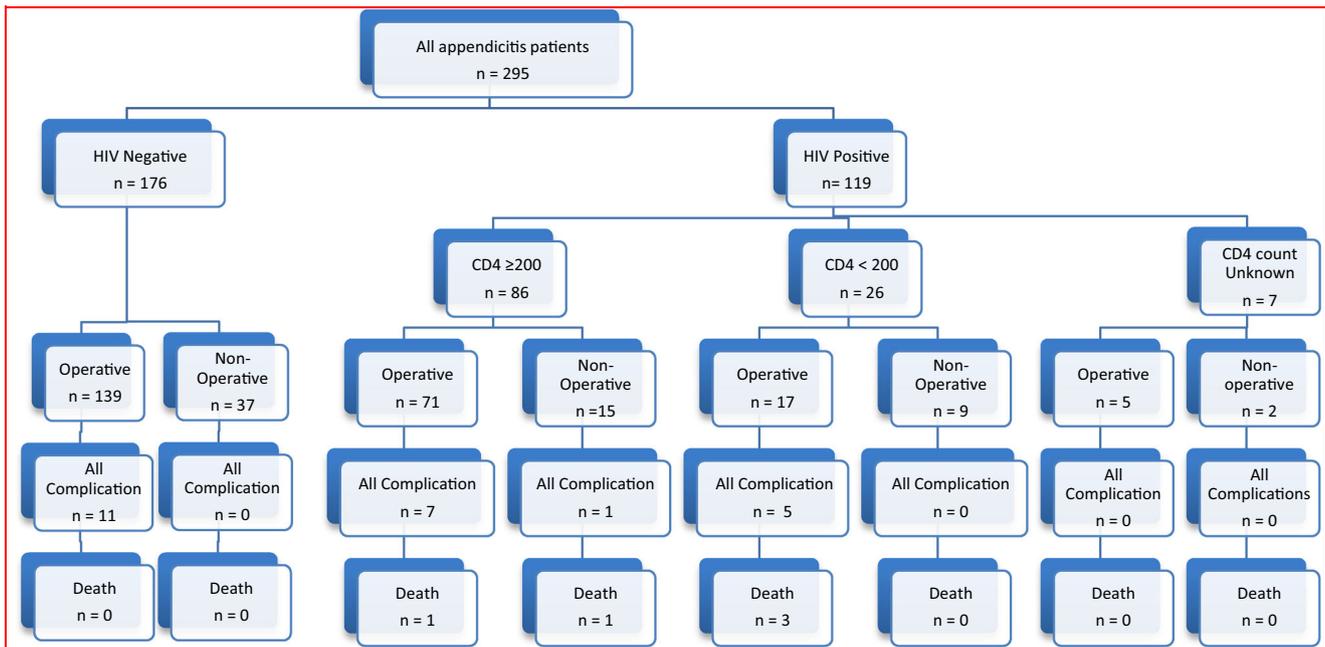
There was a higher proportion of females among HPP (57.1%, 68/119) as compared to HNP (42.0%, 74/176) ( $p = 0.011$ ). The male-to-female ratio for HPP and HNP was 0.8:1 and 1.4:1, respectively, with an overall ratio of 1.1:1.

The median [IQR] (range) pre-hospital duration of symptoms for HPP and HNP was similar at 2 [1–4] (0–21) and 1 [1–3] (0–21) days, respectively ( $p = 0.108$ ). Presenting symptoms were similar between the two groups, with anorexia slightly more prevalent among HPP than among HNP ( $p = 0.030$ ). Physical signs and white blood cell count were not significantly different between HPP and HNP. Many HPP had a pulse rate of  $>100/\text{min}$  ( $p = 0.023$ ) (Table 1).

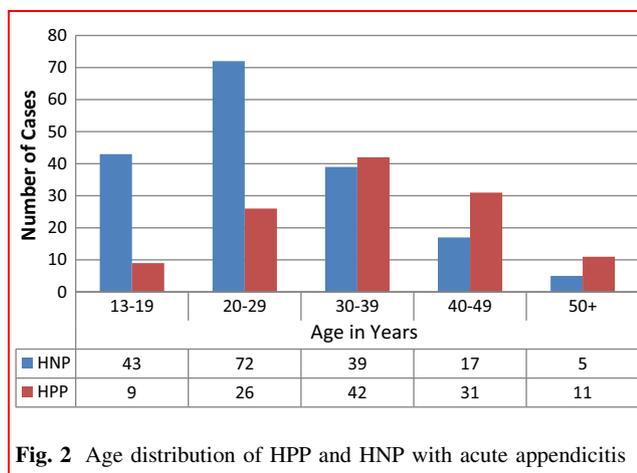
The proportion of patients who underwent operative management was similar among HPP (76.5%, 91/119) and HNP (79.0%, 139/176), with an overall operative rate of 78.0% (230/295). All appendectomies were performed with an open approach except for one uneventful laparoscopic appendectomy for a HIV-negative patient. Among the 91 HPP who underwent appendectomy, eight patients had failed initial in-hospital non-operative management (i.e., medical management with antibiotics) and one patient required readmission for recurrent appendicitis two months after discharge. Among the 139 HNP who underwent appendectomy, eight patients had failed initial non-operative management and two patients required readmission for recurrent appendicitis at 1 and 12 months after discharge. The overall failure rates of non-operative management at 1 year for HPP and HNP were 24.3% (9/37) and 21.3% (10/47), respectively ( $p = 0.518$ ). Of the 9 HPP who failed non-operative management, one patient underwent appendectomy and then died (CD4 count = 132), while 8 patients underwent appendectomy without complication (CD4 count = 174 for one,  $\geq 200$  for six, and unknown for one). The one-year recurrence rate for acute appendicitis after successful in-hospital non-operative management was 3.4% (1/29) for HPP and 5.1% (2/39) for HNP ( $p = 1.000$ ).

The negative appendectomy rates for HPP and HNP were similar based on available pathology reports, at 10.0% and 9.2%, respectively. Both groups also had similar proportions of complex appendicitis based on pathology reports (Table 2).

Importantly, HIV-positive patients with acute appendicitis had a higher overall mortality rate, whether managed operatively or non-operatively, than HIV-negative patients (4.2 vs. 0.0%,  $p = 0.010$ ). When the cohort of patients managed with an operation was analyzed, the postoperative mortality rate was still higher for HIV-positive patients (4.4 vs. 0.0%,  $p = 0.024$ ). The total postoperative complication rate was not significantly higher for HIV-positive patients (13.2 vs. 7.9%,  $p = 0.192$ ) (Table 3).



**Fig. 1** Summary flowchart



**Fig. 2** Age distribution of HPP and HNP with acute appendicitis

Among HNP, complications consisted of nine surgical site infections, two mechanical bowel obstructions, and no death; among HPP, there were five surgical site infections, one acute renal injury, two mechanical bowel obstructions, and five deaths. The overall complication rate was not significantly different between HNP and HPP (8.0 vs. 15.1%,  $p = 0.150$ ) (Table 4). In non-operated cases, one patient died of acute renal injury attributed to sepsis; interestingly, this patient was HIV positive with a CD4 count of 607 and initial WBC count of 38.4 after presenting with only 2 days of abdominal pain. Pertinent details of the five deaths are summarized in Table 5.

Excluding the seven HPP who had missing data, the median [IQR] CD4 count for HPP was 424 [224–600].

Using a cutoff of  $<200$  to define immunosuppressed patients, there were no clinically significant differences in their presentation, white blood cell count, mode of management, length of hospital stay, and pathology (data not shown). The mortality rate among operatively managed HIV-positive patients with a CD4 count  $<200$  was significantly higher compared to the operatively managed patients with a CD4 count  $\geq 200$  (17.6 vs. 1.4%,  $p = 0.022$ ). These immunosuppressed patients (CD4 count  $< 200$ ) also had higher overall and infectious post-operative complication rates than those with a CD4 count  $\geq 200$  (29.4 vs. 10.0% and 23.5 vs. 7.1%, respectively); however, these differences did not reach statistical significance ( $p = 0.052$  and  $0.069$ , respectively) (Table 6).

## Discussion

This is the first study in Botswana looking at the impact of HIV status on the presentation, management, and outcome of patients with a common acute surgical condition: appendicitis. The high prevalence of HIV in Botswana, coupled to the frequency with which local surgeons are asked to manage patients with appendicitis, makes the topic particularly relevant. Our findings are similar to those of more recent studies, with HIV status having minimal impact on the presentation but contributing to a significantly higher mortality in patients with appendicitis [2, 3].

Our study cohort had a higher proportion of HIV-positive patients (40.3%) than the 13.1% described in the only

**Table 1** Presenting symptoms, signs, and WBC count in relation to HIV status

Symptoms	HIV negative	HIV positive	<i>p</i> value
<i>Anorexia</i>			
Yes	151 (85.8%)	105 (88.2%)	<b>0.030</b>
No	24 (13.6%)	9 (7.6%)	
Unknown	1 (0.6%)	5 (4.2%)	
<i>Pain shift to RIF</i>			
Yes	96 (88.6%)	66 (81.5%)	0.067
No	77 (9.7%)	45 (11.8%)	
Unknown	3 (1.7%)	8 (6.7%)	
<i>Nausea/vomiting</i>			
Yes	137 (77.8%)	89 (74.8%)	0.095
No	38 (21.6%)	25 (21.0%)	
Unknown	1 (0.6%)	5 (4.2%)	
<i>Signs</i>			
<i>Temperature</i>			
<37.3 °C	100 (65.4%)	72 (69.2%)	0.517
≥37.3 °C	53 (34.6%)	32 (30.8%)	
<i>Pulse rate</i>			
≤100/min	116 (65.9%)	61 (52.6%)	<b>0.023</b>
>100/min	60 (34.1%)	55 (47.4%)	
<i>Tenderness</i>			
Yes	167 (95.4%)	114 (98.3%)	0.192
No	8 (4.6%)	2 (1.7%)	
<i>Percussion tenderness</i>			
Yes	128 (75.3%)	81 (70.4%)	0.363
No	42 (24.7%)	34 (29.6%)	
<i>While Blood Cell</i>			
<i>WBC count</i>			
<10,000/mm <sup>3</sup>	157 (89.7%)	109 (94.8%)	0.296
≥10,000/mm <sup>3</sup>	18 (10.3%)	6 (5.2%)	

Bold values indicate statistical significance

Missing data summarized in Supplemental Table 1

RIF Right iliac fossa

**Table 2** Pathology report in relation to HIV status

	HIV negative <i>n</i> = 119	HIV positive <i>n</i> = 80	<i>p</i> value
<i>Pathology report<sup>a</sup></i>			
Normal appendix	11 (9.2%)	8 (10.0%)	0.054
Inflamed appendix	60 (50.4%)	29 (36.3%)	
Complex appendix	48 (40.3%)	40 (50.0%)	
Others <sup>b</sup>	0 (0.0%)	3 (3.7%)	

<sup>a</sup>Pathology report was missing in 20 HNP and in 11 HPP

<sup>b</sup>A case of low-grade adenocarcinoma and two cases of chronic appendicitis

paper, and we were able to find looking specifically at this parameter in patients with HIV and appendicitis [3]. This was likely due to the higher prevalence of HIV infection in our population (21.9%) as compared to the reported rates of 6.7–10% elsewhere [3, 14]. In many studies including our own, the HPP with appendicitis were older than appendicitis patients in the general population [2–4, 11, 15]. Unlike some of the other studies [3], we found a female predominance among patients with appendicitis in the HIV-positive group, with M/F ratio of 0.8:1. This may be due to the higher female HIV prevalence in our general population aged 15–49 years. According to a recent study, 20.8% of females and 15.6% of males in Botswana were HIV positive [14].

With respect to clinical presentation, the minor differences we identified in anorexia and tachycardia between HPP and HNP, albeit statistically significant, were not clinically relevant. Although other studies have reported lower rates of leukocytosis in HPP [3, 15, 16], we found no difference. This could be due to the free access to highly active anti retroviral therapy (HAART) available for all citizens of Botswana. Because of this readily available therapy, one would expect an associated elevation in the CD4 counts of such patients, which may be reflected by the relatively high CD4 count in our study population. Our HPP with appendicitis had a higher mean CD4 count at 424 than the 209.3 reported in Tanzania [3].

As mentioned above, the management of HPP and HNP with appendicitis did not differ, suggesting that HIV status alone was not an important factor in surgeon decision making. While some studies report higher rates of complex appendicitis among HPP [3, 11, 12], we found no significant difference when available pathology reports were reviewed in both HPP and HNP.

The current literature regarding postoperative complications is limited to surgical site infection and mortality rates [3, 12, 13, 17]. While some studies demonstrated higher surgical site infection rates among HPP with low CD4 count [3], ours found no difference. In our study, immunosuppressed patients (CD4 count < 200) did have higher overall and infectious postoperative complication rates than those with CD4 count ≥ 200; however, these differences did not reach statistical significance.

The most important findings to emerge from our study were the increased overall and postoperative mortality rates in HIV-positive patients with appendicitis. The higher mortality rate among HIV-positive patients is likely correlated with greater immunosuppression as illustrated by our finding of higher postoperative mortality rates among patients with a CD4 count < 200. In light of these findings, HIV-positive patients with appendicitis and CD4 counts < 200 may stand to benefit most from a timely diagnosis and treatment plan, including prompt fluid resuscitation,

broad-spectrum antibiotics, and appendectomy. This should probably be in conjunction with a multidisciplinary approach assessing and treating immunodeficiency as well as any concurrent opportunistic infections.

**Table 3** Postoperative complications and mortality in relation to HIV status

Finding	HIV negative	HIV positive	<i>p</i> value
<i>Mortality</i>			
All patients	0 (0.0%)	5 (4.2%)	<b>0.010</b>
Postoperative patients	0 (0.0%)	4 (4.4%)	<b>0.024</b>
<i>Any complication</i>			
Yes	11 (7.9%)	12 (13.2%)	0.192
No	128 (92.1%)	79 (86.8%)	

Bold values indicate statistical significance

**Table 4** Type and rate of complications in relation to HIV status

Complications	HIV negative	HIV positive
Mechanical bowel obstruction	2 (1.5%)	2 (2.3%)
Acute renal injury	0 (0.0%)	1 (1.2%)
Surgical site infection	9 (6.5%)	5 (5.8%)
Death	0 (0.0%)	5 (5.8%)
Total	11 (8.0%)	13 (15.1%)

**Table 5** Patient characteristics, management, CD4 count, and cause of death among mortalities

Year	Age in years	Sex	HIV status	Appendectomy	CD4 count	Cause of death
2013	33	F	Positive	Yes	177	Sepsis
2013	34	F	Positive	Yes	467	Undocumented
2013	38	F	Positive	Yes	149	Sepsis
2013	54	M	Positive	Yes	132	Sepsis
2015	37	F	Positive	No	607	Sepsis

**Table 6** Postoperative complications and mortality in relation to CD4 count

Finding	CD4 < 200	CD4 ≥ 200	<i>p</i> value
<i>Mortality</i>			
All patients	3/26 (11.5%)	2/86 (2.3%)	0.081
Postoperative patients	3/17 (17.6%)	1/70 (1.4%)	<b>0.022</b>
Any complication, postoperative	5/17 (29.4%)	7/70 (10.0%)	0.052
Infectious complication, postoperative	4/17 (23.5%)	5/70 (7.1%)	0.069

Bold value indicates statistical significance

## Limitations

As in any retrospective study in a resource-limited environment, data were sometimes lacking, and follow-up of patients was a challenge. Data on patient comorbidities were not available. Although we had the CD4 count for the majority of HPP, we did not have data on whether they were on HAART. The diagnosis of appendicitis in our hospital is mainly clinical, and the few sonograms performed to rule out other pathology were not included in the analysis. We do not use Alvarado score in the diagnosis of appendicitis in our hospital as the hemogram lacks report on left shift of WBC count. Our low negative appendectomy rate (9.5%) based on pathology report, in comparison with other studies, 15–20.6% [16, 18–20], may serve as indirect evidence of accuracy of the clinical diagnosis in this cohort.

The general availability of adequate HAART coverage may distinguish our context and limit the applicability of our findings to contexts where there is no similar access to therapy.

## Conclusion

High prevalence of HIV infection did not seem to significantly alter patient presentation or affect surgeon management of patients with acute appendicitis. Patients with acute appendicitis who were HIV positive had higher overall and postoperative mortality rates compared to

patients who were HIV negative. While the higher mortality rates among HIV-positive patients with appendicitis are likely positively correlated with their degree of immunosuppression, further studies are required to determine the optimal management of these patients, focusing on the effects of immunosuppression and surgical decision making to improve patient outcomes.

**Authors contributions** This study was conceived by AGB. The study design was made by AGB, MH, and GA. Data were collected by AGB and analyzed by AGB and MH. Data interpretation was done by all authors. The first draft of the manuscript was made by AGB and critically revised by all authors. All authors have approved this version of the manuscript to be submitted and published by World Journal of Surgery.

#### Compliance with ethical standards

**IRB Approval** Permission to conduct this study was granted by the Institutional Review Board at Princess Marina Hospital and the Ministry of Health and Wellness of Botswana. No patients were contacted, or their identifiers were collected in order to ensure anonymity.

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