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ORIGINAL ARTICLE

Appendicitis in the HIV Era: a South African perspective

Ritesh Gigabhoy[1] · **Shalen Cheddie**[2,3] · **Bhugwan Singh**[1]

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Abstract The relationship between HIV infection and the clinical spectrum of appendicitis has not been fully elucidated in the South African context. The aim of this study is to compare the surgical management, histopathology, and outcomes between HIV-positive and HIV-negative patients undergoing surgery for appendicitis. A retrospective chart analysis was performed of 50 patients who underwent surgery for appendicitis at King Edward VIII Hospital, Durban, South Africa between January 2012 and December 2012. Patients were stratified by HIV serostatus into HIV-positive and HIV-negative groups. Fifty patients underwent surgery for appendicitis during the study period. Of the 50 patients, 14 were HIV-positive (28 %) and 36 were HIV-negative (72 %). Perforated appendicitis was more frequent in the HIV-positive group (50 vs. 25 %, $p > 0.05$). There was a significantly higher laparotomy rate in HIV-positive patients (71 vs. 33 %, $p < 0.05$). Granulomatous inflammation of the appendix was only noted in HIV-positive patients ($n = 3$). There was no significant difference in the complication rate between the two groups ($p > 0.05$) and no difference in the mean length of hospital stay (7.8 ± 4.89 vs. 5.8 ± 3.94 days, $p > 0.05$). In this retrospective study, perforated appendicitis was seen to be more common in HIV-positive patients resulting in a higher laparotomy rate in this group. Granulomatous inflammation was only found in HIV-positive patients. There was no difference seen in the complication rate, length of hospital stay, and mortality between HIV-positive and HIV-negative patients.

Keywords TB · HIV · Appendicitis · Appendicectomy · HAART

Introduction

South Africa, with a total of 6.4 million HIV-positive individuals, has the highest number of HIV-infected people in the world [1]. Whereas in the developed world the reported incidence of appendicitis is 15 %, in Africa the incidence of appendicitis is reported to be about 1 % [2]. Recent evidence suggests that the incidence of appendicitis in the developing world is increasing, possibly due to changing dietary patterns and urbanization [3–5]. Despite the increasing number of HIV-infected patients, there is a paucity of literature investigating the relationship between appendicitis and HIV in the South African context. Studies from North America have yielded conflicting results with respect to clinical presentation and post-operative outcomes between HIV-positive and HIV-negative patients presenting with appendicitis [6, 7].

The aims of this study are to determine the epidemiology of appendicitis in HIV-infected patients as well as to compare the clinical presentation, surgical management, histopathology, and outcomes between HIV-positive and HIV-negative patients undergoing surgery for appendicitis.

✉ Shalen Cheddie
scheddie@gmail.com

[1] Nelson R Mandela School of Medicine, College of Health Science, Department of General Surgery, King Edward VIII Hospital, University of KwaZulu-Natal, Durban, South Africa

[2] Nelson R Mandela School of Medicine, College of Health Science, Department of General Surgery, Madadeni Hospital, University of KwaZulu-Natal, Durban, South Africa

[3] PO Box 25044, Gateway, Durban 4321, South Africa

Methods

Ethical approval to conduct this study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC no. 061/15). A retrospective chart analysis of 50 adult patients (≥16 years) who underwent surgery for appendicitis at a single surgical unit at King Edward VIII Hospital, an academic regional referral hospital in urban KwaZulu-Natal, from January 2012 to December 2012, was done. Variables included in the data analysis were age, gender, HIV status and antiretroviral therapy, clinical presentation, and clinical examination findings (right iliac fossa mass, generalized peritonitis, and localized right iliac fossa tenderness). The white cell count and CD4 counts (the latter only in HIV-positive patients) were measured on admission.

All patients underwent voluntary counseling and testing for HIV. The peritoneal fluid at laparotomy was sent for microbiological sampling including Ziehl-Nielsen staining for acid-fast bacilli. All appendix specimens underwent histopathological evaluation. The type of surgery (either Lanz appendectomy vs. laparotomy) and intra-operative findings (such as an appendiceal mass, perforated appendix, and acute appendicitis) were compared in both groups. Outcome measures included the length of hospital stay and complication rate in both groups. The complications documented included wound sepsis, enterocutaneous fistula, laparostomy closure, and septic shock. Student's *t* test was used for continuous variables and a Fisher's exact test was used for categorical variables. A p value of <0.05 was considered statistically significant. GraphPad software (GraphPad software, LaJolla, USA) was used for the statistical analysis.

Results

Fifty patients underwent surgery for appendicitis during the study period. The mean age was 27 years (range 16–53 years). Males ($n = 33$) accounted for 66 % of admissions. Of the 50 patients, 14 were HIV-positive (28 %) and 36 were HIV-negative (72 %). In the HIV-positive group, the mean CD4 count was 284 cell/mL (range 34–680 cells/mL). Fifty percent of HIV-positive patients ($n = 7$) were on highly active antiretroviral therapy (HAART).

There was no statistically significant difference in the mean duration of symptoms between the HIV-positive and HIV-negative groups (4 vs. 2 days, $p = 0.055$). There was a statistically significant increase in localized right iliac fossa tenderness on clinical examination in HIV-negative patients ($n = 24$) than in HIV-positive patients ($n = 4$, $p < 0.05$). Eight patients (57 %) presented with generalized peritonitis in the HIV-positive group compared to 12 (33 %) in the HIV-negative group ($p > 0.05$). A right iliac fossa mass was palpable in 2 of the 14 HIV-positive patients. There were no palpable right iliac fossa masses in the HIV-negative group ($p < 0.05$).

The mean white cell count was 10.4×10^9/L in the HIV-positive group and 11.75×10^9/L in the HIV-negative group ($p > 0.05$). An abdominal ultrasound was undertaken in 6 cases (12 %) for diagnostic uncertainty. The ultrasound findings noted included an appendix mass in our cases, free fluid in one case, and an acutely inflamed appendix in one case. In one patient, a computed tomography scan confirmed an inflammatory appendicular mass.

A Lanz appendicectomy was performed in 4 (28 %) HIV-positive patients versus 24 (66 %) HIV-negative patients. Ten (71 %) HIV-positive and 12 (33 %) HIV-negative patients underwent a laparotomy resulting in a significantly higher laparotomy rate in the HIV-positive group ($p < 0.05$) (Table 1).

The microbiological findings from intra-operative peritoneal fluid sampling from the two patient groups are outlined in Table 2.

Table 3 outlines the histopathology of appendix specimens in the two patient groups. In the HIV-positive group, granulomatous inflammation was identified in 3 out of 14 (21 %) cases. There were no cases of granulomatous inflammation in the HIV-negative group ($p < 0.05$). There was no significant difference in the intra-operative findings, namely perforated appendicitis, acute appendicitis, and appendix mass, between the two groups (Table 4).

In the HIV-positive group, the 3 (21 %) complications noted included wound sepsis, severe peritonitis that required a laparostomy closure, and septic shock. In the HIV-negative group, there were also 3 (8 %) complications that included wound sepsis, low output enterocutaneous fistula (which closed spontaneously after a week), and laparostomy closure.

There was no significant difference in complications between the two groups ($p > 0.05$). The mean length of hospital stay was 7.8 ± 4.89 days in the HIV-positive group versus 5.8 ± 3.94 days in the HIV-negative group ($p > 0.05$). There were no mortalities in either patient group at 30-day follow up.

Discussion

Despite the high prevalence of HIV in our surgical practice, only 28 % of patients undergoing surgery for appendicitis were noted to be HIV-positive; 50 % of these patients were on HAART. Crum-Cianflone et al. have shown that while

Table 1 Comparison between Lanz appendicectomy and laparotomy in HIV-positive and HIV-negative patients

Surgery	HIV-positive ($n = 14$)	HIV-negative ($n = 36$)
Lanz	4 (28 %)	24 (66 %)
Laparotomy	10 (71 %)	12 (33 %)

p value <0.05

Table 2 Microbiology of peritoneal fluid sampling in HIV-positive and HIV-negative patient groups

Microbiology results	HIV-positive (n = 14)	HIV-negative (n = 36)
Acinetobacter baumanii	1 (7 %)	0
Escherichia coli	1 (7 %)	5 (14 %)
Group A Streptococcus	1 (7 %)	2 (5 %)
Acid fast bacilli	1 (7 %)	0
Pseudomonas aeruginosa	1 (7 %)	0
No growth	11 (78 %)	30 (83 %)

HIV-positive patients have a four times increased risk of developing appendicitis, those patients on HAART had a lower risk of developing appendicitis [8]. In our study, the mean CD4 cell count in HIV-positive patients undergoing surgery for appendicitis was 284 cells/mL (34–680 cells/mL), suggesting significant immune-suppression. However, the CD4 count has not been shown to be a risk factor for the development of appendicitis in HIV positive patients; furthermore, a low viral load has been shown to reduce the risk of developing appendicitis in HIV-positive patients on HAART [8].

Localized right iliac fossa tenderness in HIV-negative patients occurred more frequently than in HIV-positive patients ($p < 0.05$), implying a more robust localized inflammatory response in the immune-competent patient. More than half of HIV-positive patients (57 %) presented with generalized peritonitis. The mean duration of symptoms between the HIV-positive group and HIV-negative group were similar (4 vs. 2 days, $p < 0.05$) which infers that a delay in presentation was not the cause for the more advanced clinical findings. Giiti et al. have shown that the incidence of perforated appendicitis in HIV-positive patients was 30.8 % while Flum et al. have shown an appendix perforation rate of 24 % [6, 7]. It is postulated by Giiti that the high perforation rate may be due to the underlying suppression of cell-mediated immunity and inability to contain the inflammatory process. In our study, the mean white cell count did not differ between the two groups to suggest a suppressed immune response in HIV-positive patients. The majority of HIV-positive patients (64 %) had complicated appendicitis.

Table 3 Histopathology of appendix specimens from HIV-positive and HIV-negative groups

Histopathology	HIV-positive (n = 14)	HIV-negative (n = 36)	p value
Negative	0	1	–
Acute appendicitis	8	30	0.070
Reactive lymphoid hyperplasia	3	5	0.660
Granulomatous inflammation	3	0	0.018

Table 4 Intra-operative findings in HIV-positive and HIV-negative groups

Intra-operative findings	HIV-positive (n = 14)	HIV-negative (n = 36)	p value
Appendix mass	2 (14 %)	4 (11 %)	1.0
Perforated appendix	7 (50 %)	9 (25 %)	0.1
Acute appendicitis	5 (35 %)	23 (64 %)	0.1

In our study, the laparotomy rate was significantly higher in HIV-positive patients than in HIV-negative patients (71 vs. 33 %). This can be attributed to the higher percentage of generalized peritonitis (57 vs. 33 %) at initial presentation mandating an exploratory laparotomy rather than a Lanz appendectomy. Kong et al. have reported a laparotomy rate of 62.5 % and a Lanz appendectomy rate of 35.5 % in a mixed patient cohort from an urban regional hospital in South Africa [4]. There was no significant difference in the intra-operative findings of perforated appendicitis and right iliac fossa mass between the two groups.

HIV immune-suppression predisposes to opportunistic infections that may mimic acute appendicitis leading to unnecessary surgery. These opportunistic infections include Mycobacterium species (including *Mycobacterium tuberculosis*, *Mycobacterium kansasii*, and *Mycobacterium avium* complex), cryptosporidiosis, and a variety of other unusual pathogens such as *Strongyloides stercoralis*, spirochetosis, *Salmonella typhi*, group A streptococcus, and *Streptococcus pneumonia* [6]. In our study, histopathology of appendix specimens showed acute appendicitis to be the most common histological finding in both patient groups ($p > 0.05$). Granulomatous inflammation of the appendix was identified only in the HIV-positive patients (n = 3 (21 %)). Flum et al. have shown mycobacterial infection in only 3.6 % of cases in HIV-positive patients [6]. The high rate of granulomatous inflammation may be attributed to the high incidence of TB in South Africa (second highest annual incidence worldwide) [1]. Chamisa had shown in a mixed patient cohort that only 8.6 % of patients demonstrated parasites and atypical histology [9].

We observed no difference in complication rates between the two groups. The incidence of surgical site infection was 7 % in both groups. Giiti et al. have shown a surgical site infection rate of 11.5 % in HIV-positive patients [7]. It has been shown that wound complication rates are generally higher in HIV-infected patients following emergent abdominal surgery [10]. The length of hospital stay was similar in both groups. Giiti et al. have shown an increased length of hospital stay in HIV-positive patients, explained by a higher rate of complicated appendicitis in their patient cohort [7]. We observed no mortalities at 30 days follow up. Chamisa has shown a mortality rate of 1.2 % while Madiba et al. have shown a mortality rate of 2 % in a mixed patient cohort [10, 11]. Mortality rates were higher in cases of perforated appendicitis [9].

The limitations to this study include the small sample size that may have failed to demonstrate significant differences between the HIV-positive and HIV-negative groups. An accurate measure of immunosuppression in the HIV-positive group could not be made due to the lack of viral load data.

Conclusion

Localized right iliac fossa tenderness occurs more commonly in HIV-negative patients. Perforated appendicitis is more common in HIV-positive patients resulting in a statistically significant increase in the laparotomy rate. Acute appendicitis is still the most common histopathological finding; however, atypical histology, namely granulomatous inflammation, only occurred in HIV-positive patients. There was no significant difference in the complication rate, length of hospital stay, and mortality between HIV-positive and HIV-negative patients who underwent surgery for appendicitis in this study.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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