

Management of Acute Appendicitis in HIV/AIDS Patients: A 19-year Review from the National In-Patient Sample

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ABSTRACT

BACKGROUND: Acute Appendicitis (AA), one of the most common surgical emergencies, is usually managed operatively. There is a paucity of data addressing how HIV/AIDS affects management of acute uncomplicated appendicitis.

METHODS: A retrospective review of HIV/AIDS positive (HPos) versus negative (HNeg) patients with acute, uncomplicated appendicitis over a 19-year period. The primary outcome was undergoing appendectomy.

RESULTS: Among 912,779 AA patients, 4,291 patients were HPos. HIV rates increased from 3.8/1,000 in 2000 to 6.3 per 1,000 appendicitis cases in 2019 ($p < 0.001$). HPos patients were older, less likely to have private insurance, and more likely to have psychiatric illnesses, hypertension, and a history of prior malignancy. HPos AA patients underwent operative intervention less often than HNeg AA patients (90.7% versus 97.7%; $p < 0.001$). Overall, comparing HPos to HNeg patients, there was no difference in post-operative infections or mortality.

CONCLUSION: HIV-positive status should not deter surgeons from offering definitive care for acute uncomplicated appendicitis.

KEYWORDS: Appendicitis, HIV, AIDS

BACKGROUND

Appendicitis remains one of the most common surgical emergencies worldwide. It is reported that the lifetime risk of developing acute appendicitis is approximately 7%.^{1,2} The management of acute uncomplicated appendicitis usually involves operative intervention with an appendectomy. However, there are several reasons why operative intervention may not be undertaken, including the presence of certain medical comorbidities that may preclude or prompt hesitancy to provide operative intervention. The publicly available National Inpatient Sample (NIS) dataset includes the largest number of hospitalized patients in the US over a long period and is coded with respect to significant demographics, medical comorbidities, and hospital type.³ This allows for a longitudinal, regional, and hospital type-based

review of an evolving process. With the frequency of appendicitis across the general population, there are high rates of associated medical comorbidities⁴⁻⁷ among patients presenting with acute appendicitis, including human immunodeficiency virus (HIV).⁸

HIV is a virus that predominantly affects T-cells, a type of lymphocyte involved in the adaptive immune system. HIV is known to complicate many aspects of the management of other acute and chronic medical conditions.^{9,10} It is believed that over 40 million individuals are living with HIV worldwide.¹¹ Improvements in early detection and treatments have extended the life expectancy of patients with HIV.¹² As a result, more HIV patients are likely to present with acute surgical emergencies. With these improvements in HIV therapeutics, the impact of HIV upon medical and surgical conditions has evolved over the past two decades. Historically, the presence of HIV was considered a contraindication to operative management of many elective surgical conditions. This was especially true for individuals who had progression of their disease to acquired immunodeficiency syndrome (AIDS). However, more recently, the physiologic presentation of a surgical emergency often is prioritized over other chronic medical problems⁹ when deciding on operative intervention.

Currently, there is no data addressing the effect of HIV upon the presentation and management of acute uncomplicated appendicitis. Data is also lacking with regards to how this has changed as HIV has become a more manageable illness over the last few decades. This work will undertake a review of the evolution of how HIV affects the surgical management of acute uncomplicated appendicitis. We hypothesize that HIV is now less often considered a contraindication to operative intervention for acute uncomplicated appendicitis compared to prior eras.

MATERIALS AND METHODS

This is a retrospective review of the National In-Patient Sample (NIS). The NIS is a large publicly available dataset of inpatients across the US. We reviewed patients, aged 18 years and older, with acute uncomplicated appendicitis over a 19-year period. To review the impact of HIV/AIDS status upon the management of patients with appendicitis, patients were grouped into HIV/AIDS positive (HPos) and

HIV/AIDS negative (HNeg) at the time of admission for appendicitis. The dataset was reviewed for demographics, insurance status, medical comorbidities and hospital outcomes. Variables used to measure racial and social disparities included race, insurance status, income quartile (based on zip code of residency), and hospital teaching/location status. For race, patients were grouped into White, Black, Hispanic, Asian and other. Insurance status was classified as Private, Medicare/Medicaid, or none (uninsured). Medicare and Medicaid were grouped together to assess the effect of government-based healthcare insurance versus commercial or private insurance. The hospital teaching and location status was classified as rural (non-teaching), urban non-teaching, and urban teaching.

The dataset was reviewed for comorbidity profile, looking for either the most clinically significant or most common comorbidities that were present at the time of admission to the hospital with appendicitis. This data did not include any medical comorbidity that was diagnosed by the in-hospital treating team after the patient had been admitted to the hospital. Patients were classified as being obese if they had a Body Mass Index (BMI) of greater than or equal to 30 at the time of presentation to the hospital.

To assess the impact of HIV/AIDS upon the management of patients with appendicitis, the dataset was queried for surgical intervention as to whether they underwent appendectomy, and if so, whether a laparoscopically versus open approach was undertaken. The conversion rate from a laparoscopic to an open procedure was also assessed. Further, among those who did undergo operative intervention, the time to operation was also noted. Specifically, we assessed rates of patients who underwent operative intervention within 24 hours of presentation. The hospital outcomes, including length of stay, discharge disposition location, and mortality were assessed.

All statistical analyses were performed using SIGMAPLOT 12.5. Chi-squared analysis was used for categorical data and Mann-Whitney U was used for continuous data. Results are reported as mean and standard error of the mean for continuous data. Statistical analysis included ANOVA across multiple groups, and significance was set as $p < 0.05$.

RESULTS

Overall, there were 912,779 patients admitted for acute uncomplicated appendicitis (AA) over 19 years, among whom 4,291 patients (0.47%) were HIV positive or had a diagnosis of AIDS (HPos). Over the 19 years, the rates of AA patients being reported as HPos were noted to steadily increase from a rate of 3.8/1,000 appendicitis in the year 2000 up to a rate of 6.3/1,000 appendicitis cases in 2019 ($p < 0.001$) (Figure 1). HPos patients were older (40 ± 0.5 vs 35.9 ± 0.04 years; $p < 0.001$) and less likely to be female (18.3% versus 45.9%; $p < 0.001$). With respect to race, HPos patients

Figure 1. The changing rates of HIV/AIDS positivity among patients admitted for acute uncomplicated appendicitis over the 19 years.

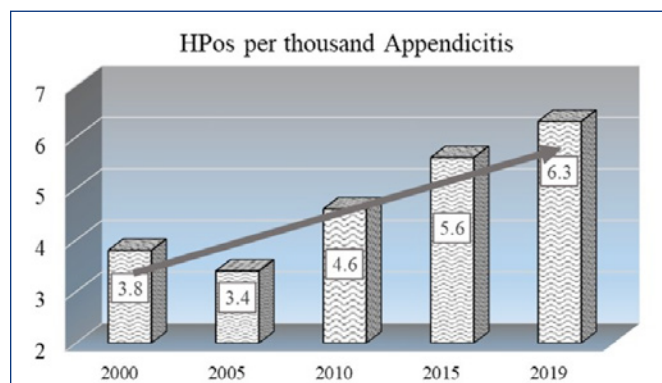


Table 1. Demographic differences between HIV-positive and negative patients presenting with acute appendicitis.

	HPos N = 4,291	HNeg N = 908,488	p-value
Age	40.0 (+/-0.5)	35.9 (+/-0.04)	<0.001
Female	18.3%	45.9%	<0.001
Race			
Black	27.9%	6.3%	<0.001
White	39.0%	52.9%	<0.001
Hispanic	15.2%	17.4%	0.2
Other	6.6%	6.7%	0.9
Insurance Status			
Private	42.2%	63.2%	<0.001
Medicare/Medicaid	40.4%	16.2%	<0.0001
Self/Uninsured	12.5%	14.3%	0.28

were significantly more likely Black (27.9% versus 6.3%; $p < 0.001$), and less likely to be White (39.0% versus 52.9%; $p < 0.001$). There was no difference in rates of patients being Hispanic (15.2% versus 17.4%; $p = 0.22$). HPos patients less often had private insurance (42.2% versus 63.2%; $p < 0.001$), and markedly more likely to have Medicare/Medicaid insurance (40.4% versus 16.2%; $p < 0.001$). There was no difference between groups with respect to those being uninsured (12.5% HPos versus 14.3%; $p = 0.28$) (Table 1). With respect to medical comorbidities, HPos patients were less likely to be obese (3.9% versus 6.5%; $p < 0.047$), but were more likely to have psychiatric illnesses (22.2% versus 10.7%; $p < 0.001$), hypertension (18.8% versus 11.0%; $p < 0.001$), a history of prior malignancy (4.5% versus 1.5%; $p < 0.001$), or be a smoker (19.7% versus 12.3%; $p < 0.001$). There was no difference in rates of diabetes (6.1% versus 4.5%; $p = 0.1$) or COPD (0.7% versus 0.3%; $p = 0.09$) (Table 2).

Overall, HPos patients were significantly less likely to undergo operative intervention for their appendicitis (90.7%

Table 2. Differing rates of medical comorbidities between HPos and HNeg acute appendicitis patients.

	HPos N=4,291	HNeg N=908,488	p-value
Anxiety	4.1%	2.7%	0.07
Hypertension	18.8%	11.0%	<0.001
COPD	0.7%	0.3%	0.095
Smoker	19.7%	12.3%	<0.001
Cirrhosis	1.6%	0.5%	0.0012
Diabetes	6.1%	4.5%	0.1
History of Cancer	4.5%	1.5%	<0.001
PyschDisease	18.1%	8%	<0.001
Obesity	3.9%	6.5%	0.048

versus 97.7%; $p<0.001$). Given the differences in demographics and patient characteristics, a multivariable regression analysis was undertaken. Accounting for age, sex, race, comorbidities, and insurance status, HPos patients were still significantly less likely to undergo operative intervention for acute uncomplicated appendicitis (OR=0.27 (95%CI=0.18–0.41)). Among HPos patients who did undergo operative intervention, there was no difference in rates of cases being undertaken via a laparoscopic approach (98.8% versus 98.7%; $p=0.85$) versus an open approach. HPos patients were significantly both less likely to undergo operative intervention within 24 hours (72.8% versus 84.5%; $p<0.001$) and were noted to have had overall longer time to operative intervention.

We next reviewed types of hospitals (rural versus urban non-teaching hospitals versus urban teaching hospitals). It was noted that HPos patients, compared to HNeg patients, were more likely to have presented to an urban teaching hospital compared to either urban non-teaching or rural hospital (67.8% versus 41.9%; $p<0.001$). Among urban teaching hospitals, HPos patients were older (40.2 \pm 0.6 versus 35.7 \pm 0.04 years; $p<0.001$), less likely female (18.4% vs 46.1%; $p<0.001$) and less likely to have private insurance (38.8% versus 59.6%; $p<0.001$). With respect to intervention in urban teaching hospitals, HPos patients were significantly less likely to undergo operative intervention (89.5% versus 96.8%; $p<0.001$) (Table 3). Among rural hospitals, comparing HPos and HNeg patients, there was no difference in age (36.8 years versus 35.9 years; $p=0.85$) or female sex (31.8% versus 44.6%; $p=0.27$) or types of insurance. Further, within rural hospitals, there was no difference in rates of operative intervention between HPos and HNeg patients (95.5% versus 97.3%; $p=0.6$) (Table 3).

Across all hospitals, HPos patients had on average a 1-day longer length of stay (2.5 \pm 0.1 versus 1.5 \pm 0.01; $p<0.001$). This was also evident when reviewing patients who were

Table 3. Rates of operative intervention for appendicitis between HPos and HNeg patients across differing hospital types.

	HPos	HNeg	p-value
All hospital types			
Appendectomy	90.7%	97.7%	<0.001
Operation within 24 hours	72.8%	84.5%	<0.001
Laparoscopic	98.8%	98.7%	0.85
Urban Teaching			
Age	40.2 (\pm 0.6)	35.7 (\pm 0.04)	<0.001
Appendectomy	89.5%	96.8%	<0.001
Rural Non-Teaching			
Age (years)	36.8 (\pm 0.7)	35.9 (\pm 0.05)	0.85
Appendectomy	95.5%	97.3%	0.6

Table 4. Outcome differences including LOS, SSI, and mortality between HPos and Hneg patients.

	HPos	HNeg	p-value
Operatively managed			
LOS (days)	2.5 (\pm 0.1)	1.5 (\pm 0.1)	<0.001
SSI	9.6%	5.7%	0.009
Mortality	0.6%	0.35%	0.35
Non-Operatively managed			
LOS (days)	3.8 (\pm 0.2)	2.7 (\pm 0.01)	<0.001
Mortality	2.5%	2.3%	0.2

Table 5. Multivariable regression analysis to predict outcomes for HPos patients with acute appendicitis, including undergoing appendectomy and mortality.

	Odds Ratio (95% CI)
Appendectomy	0.27 (0.18–0.41)
Mortality among operative management	0.95 (0.92–1.05)
Mortality among non-operative management	0.89 (0.78–1.43)

managed non-operatively, with HPos patients having a longer length of stay (3.8 \pm 0.2 versus 2.7 \pm 0.01 days; $p<0.001$). With respect to surgical site infections, combining deep and superficial surgical site infections, HPos patients compared to HNeg patients had significantly higher rates of SSI (9.6% versus 5.7%; $p=0.009$). Overall, among all patients managed operatively, there was no difference in mortality between HPos versus HNeg patients (0.6% versus 0.35%; $p=0.35$) (Table 4). On multivariable regression analysis, there was no increased risk for mortality for HPos patients whether managed operatively (OR=0.95 (95%CI=0.92–1.05) or among those who were managed non-operatively (OR=0.89 (95%CI=0.78–1.43) (Table 5).

DISCUSSION

Acute appendicitis is one of the most common surgical emergencies worldwide.^{2,13,14} Operative intervention has been considered the standard of care for acute, uncomplicated appendicitis for over 75 years.¹⁵ The incidence of acute appendicitis has been reported to be approximately 0.1% in the general population, compared to 0.5–3.5% among HIV-positive / AIDS patients.^{16,17} We undertook a review of the National In-Patient Sample (NIS) for patients who presented with acute uncomplicated appendicitis and stratified patients into those who were noted to be HIV positive or who had the diagnosis of Acquired Immunodeficiency Syndrome (AIDS) (HPos) upon presentation. Overall, it was noted that HPos patients were older, more likely to be male, and more frequently presented to an urban teaching hospital. Our finding of HPos appendicitis patients being older than the general appendicitis population is in keeping with prior reports of appendicitis in HIV-positive patients.¹⁷ Overall, those presenting to urban teaching hospitals were less likely to be managed operatively, whereas there was no difference in operative versus non-operative rates in rural hospitals. Large reviews, including our data, over an extended period of time, are needed to add to the understanding of the impact of HIV that may contribute to a body of literature that currently lacks significant consensus guidelines⁹ for the management of appendicitis.

A publication of 5 patients with *Pneumocystis carinii* pneumonia in 1981 initiated public awareness in the US of the HIV/AIDS epidemic.¹⁸ Advances in education and antiretroviral therapy have led to significant decreases in HIV/AIDS-related mortality,¹⁹ and have led to the acceptance of HIV status as a chronic medical comorbidity.^{20,21} It is estimated that 10–40% of patients who are HIV positive will present with a complaint of abdominal pain requiring a surgical evaluation and work-up.²² Despite the relative increase in HIV-specific causes of abdominal pain, including lymphomas or cytomegalovirus (CMV) gastroenteritis,^{23,24} the predominant causes of abdominal pain in the HIV patient reflect surgical illnesses common to non-HIV patients, including appendicitis, diverticulitis, or cholecystitis presenting with similar frequency as the general population.^{25,26} The work-up, therefore, of an HIV-positive patient with a possible surgical condition or surgical emergency should follow standard work-up akin to a patient without HIV or AIDS. Additional investigations such as MRI or C-reactive protein, do not add additional benefit but may lead to delays in definitive care²⁷ and higher rates of complications. Further, providers should not be swayed away from a diagnosis of appendicitis merely due to a normal presenting white blood cell count in the setting of a classic history and physical examination.

The original reports of very high peri-operative mortality among surgical patients with HIV led many to argue that non-operative management of surgical conditions should

be employed as much as possible. However, this dictum has been challenged over the past decade. Davidson et al demonstrated that a delay in the diagnosis or definitive treatment of a surgical patient with HIV/AIDS will result in increased morbidity and mortality.²⁸ It is believed that the original reports of very high morbidity and mortality rates in HIV patients requiring abdominal surgical procedures^{24,29} have significantly decreased due to early use of effective antiretroviral agents.³⁰ Significant interest has risen recently regarding the use of antibiotic therapy and non-operative management as a first-line treatment for acute uncomplicated appendicitis instead of appendectomy.^{31,32} It has been argued that non-operative management of acute appendicitis avoids the risk of post-surgical complications associated with appendectomy³³ while preserving the immune function of the appendix,³⁴ which could be key to a patient in a potentially immunocompromised state such as HIV. Conversely, the reported failure rate for non-operative management of appendicitis – as high as 30% within the first year after the initial presentation and almost 40% after 5 years – with the associated increased appendicitis-related care cost,^{35,36} would lean heavily towards surgical intervention of appendectomy as the definitive and early treatment of uncomplicated acute appendicitis. Further, McCutcheon et al demonstrated a 15-fold higher all-cause inpatient mortality with non-operative management (1.5% vs 0.1%).³⁷ Interestingly, the authors demonstrated that this difference in mortality was mostly due to the presence of underlying chronic conditions or malignancy, a finding noted among the HPos population within our study. Great caution needs to be given before undertaking non-operative management in lieu of offering definitive source control to a patient with a dysfunctional immune system.

Within our dataset, we noted that HPos patients had longer lengths of stay, and among those who were managed operatively, fewer patients underwent operation within 24 hours of presentation. Although the reason for the increased length of stay cannot be ascertained from this retrospective dataset, several possible explanations must be considered. It is possible that this was due to delay in making a definitive surgical plan while awaiting input from non-surgical specialists for management of the associated medical comorbidities, including infectious disease consultation. Further, surgeons may have a degree of uncertainty regarding the possible differential diagnosis in an HPos patient with right lower quadrant pain or, more specifically, in an HPos patient with an inflamed appendix. Acute appendicitis in HIV/AIDS patients is most commonly due to fecalith obstruction; however, HIV-related causes are also possible. Whitney et al reported that as many as 30% of HIV patients with appendicitis had HIV- or AIDS-related causes, including typhlitis, lymphoid hyperplasia and obstruction, or related to Kaposi's sarcoma.³⁸ However, many of these early studies were small and involved mainly patients with later-stage disease.

With advances in antiretroviral agents, this rate is believed to have fallen considerably.¹⁷

It was noted that HIV-positive patients carried a higher burden of medical comorbidities, including hypertension, obesity, a prior history of malignancy, and a history of psychiatric illnesses, including anxiety, requiring medical attention.¹² Mitra et al also noted an increased rate of comorbidities and neuropsychiatric conditions in older HIV patients compared to an age-matched cohort.³⁹ The increased rate of neuropsychiatric conditions is unlikely to be directly due to HIV-disease status, but rather may reflect the stressful and emotional impact of living with HIV has on life experiences.⁴⁰ These findings of increased comorbidities may also reflect increased screening for medical comorbidities once an HIV-positive patient is identified within the health system.⁴¹ Patients who are HIV positive often undergo frequent screenings and medical examinations.

We demonstrated an almost two-fold increase in the presence of HIV among patients with acute, uncomplicated appendicitis over a two-decade period. We do not believe that this reflects a spreading of HIV. Rather, this likely represents higher rates of testing by primary care providers and earlier detection of HIV.⁴² Rates of screening for HIV among populations still remain low,⁴³ and published guidelines for screening and diagnostic testing have shown only a relative effectiveness in increasing screening for HIV⁴⁴ among the general population. Our data is in concurrence with the statement by Saltzman et al, noting that HIV status should not be used to determine the suitability of the patients with urgent and emergent surgical needs.⁴⁵ Understanding this is critical because when surgical intervention was undertaken within HPOs patients, there was no difference in outcomes compared to patients without HIV.

There are several limitations to this project given the retrospective nature of this work. We were unable to account for any clinical presentation differences between patient groups; however, by opting to review only acute uncomplicated appendicitis we sought to produce a relatively homogeneous pathology in our dataset. This work did not address peri-operative care of patients with HIV/AIDS, including the rates of highly active antiretroviral therapy. Further, this work does not address immune system profiles, including presenting white blood cell count, lymphocyte number, or lymphocyte sub-populations that may have affected choice of operative versus non-operative intervention. However, the lack of these markers echoes the sentiments of Yan et al who assert that there should be no delay in offering emergent or urgent surgical care for HIV patients⁹ merely to obtain CD4 or HIV viral load testing.

CONCLUSION

Among patients with acute, uncomplicated appendicitis, being HIV/AIDS positive negatively affects the likelihood

of undergoing surgical intervention. However, given the fact that patients who do undergo appendectomy have no demonstrable post-operative differences in complications, we contend that HIV-positive status should not deter surgeons from offering definitive care for acute, uncomplicated appendicitis.

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