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Abdominal CT findings in HIV-infected patients presenting with acute abdomen

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Abdominal CT Findings in HIV-infected Patients Presenting with Acute Abdomen

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Diagnostic Radiology.

Johannesburg, 2016

Declaration

I, Tshiwela Phumudzo Pilar Singo, declare that this research report is my own work. It is being submitted for the degree of MMed (RadD) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

DR TPP Singo

On this 31ST MAY 2016.



For my brothers Nndi, Fulu and Ndavhe... My love for you has no bounds

Publications and presentations

This work has never been published.

It has never been presented at a congress.

Abstract

INTRODUCTION: Clinicians have often been faced with the dilemma of whether to manage HIV-positive patients presenting with an acute abdomen surgically or conservatively. Since poorer outcomes have been associated with surgery, CT scan has been an important tool in clinical decision-making.

AIM: The aim of the study was to evaluate the abdominal CT findings of HIV-positive patients that presented with an acute abdomen, with specific interest in abdominal TB.

METHOD: A retrospective and quantitative study was conducted on HIV-positive adults (50) referred for diagnosis of "acute abdomen"

RESULTS: Fifty percent the patients had a radiological emergency diagnosis, of which only 18% needed surgery, and 44% had a TB related diagnosis on discharge. CT scan had a **sensitivity of 73%** and a **specificity of 64%** (PPV 36%, NPV 89%) in the diagnosis of abdominal TB when compared to laboratory diagnostic tests. When CT scan was compared to a "probable diagnosis" of TB the **sensitivity** and **specificity,** increased to **81%** and **83%** respectively (PPV 77%, NPV 86%).The inter-reader agreement ranged from moderate to almost perfect.

CONCLUSIONS: CT scan was found to be a very useful tool in the management of HIV-positive patients who presented with an acute abdomen. Not only did CT scan identify TB of the abdomen, when surgical management could have been avoided, it frequently **excluded** TB as a cause and assisted in the further surgical management of the patient. **The HIV-positive patient with acute abdomen should receive a contrasted CT scan as part of their work-up not only to diagnose surgical emergencies but also to avoid unnecessary surgery**.

Acknowledgements

This was a very long journey and I am most grateful that I did not have to walk it alone. I would like to take this time to thank all the people who helped me make this possible.

- First and foremost, Thanks Be To God.
- My Supervisors –
    - Dr Susan Lucas, words are not enough. For always helping me find my way when I got lost in my own words.
    - Professor Savvas Andronikou, for your passion in research. One cannot help but to feel inspired in the presence of such spirit.
    - Professor Julien Oettle, for your encouraging words and making me feel that this small effort would move mountains.
- Professor Victor Mngomezulu, for making research a priority in our department.
- Dr Louise Keating and Dr Ronel Swartz, for diving into the deep with me. I could not have done this without you. My sincerest thanks to you both.
- Dr Mbulaheni Nthangeni, My Godfather. For helping me with my statistics. You are a "Godfather" in every sense of the word – Godsend to my brothers and I.
- Drs Wendy & Titus Singo, my parents, who planted the seed in me, the love of writing, research and discovery in those days – a lifetime ago. I love you with all my heart.
- Ndivhuho Singo, My brother, our number one - know you are looking down on me. "See you at the crossroads".
- Fulufhelo and Ndavhelelo Singo, Warriors in my corner. The best brothers any sister could have asked for – *anytime, anyplace, anywhere*...
- Last but not least: To the Lions in my life who remind me to always "Stay Hungry"

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List of Abbreviations

ARV	Antiretroviral treatment
AXR	Abdominal x-ray
CD4	Cluster of Differential 4
CMV	Cytomegalovirus
CRP	C-reactive protein
CT	Computer tomography
FASH	Focused assessment with sonography for HIV-associated tuberculosis
HIV	Human immunodeficiency virus
IBD	Inflammatory/infective bowel disease
NPV	Negative predictive value
PID	Pelvic inflammatory disease
PPV	Positive predictive value
TB	Tuberculosis
WCC	White cell count
WHO	World health organisation

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1. Introduction

1.1. Rationale

Infection with the Human Immunodeficiency Virus (HIV) causes an immune suppressive condition that often presents with abdominal symptoms including the "acute abdomen". This may be caused by infections, bowel perforation related to malignancies, viral infections, or vascular obstruction.

HIV predisposes patients to infections including tuberculosis (TB) with an increased prevalence of extra-pulmonary forms of this disease, such as abdominal TB. Diagnostic imaging findings in patients with abdominal TB are well described and commonly include ascites and lymphadenopathy. These findings, which are optimally demonstrated with Computed Tomography (CT), reflect the immune response of the host to the organism. However, HIV may dampen the host response due to immune suppression, affecting the imaging appearances.

The aim of the study was to evaluate the abdominal CT findings of HIV-positive patients that presented with an acute abdomen, with specific reference to the presence of features ascribed to abdominal TB.

1.2. Background

Clinicians are often faced with the dilemma of whether to manage HIV-positive patients presenting with an acute abdomen surgically or conservatively, particularly since poorer

outcomes have been associated with inappropriate surgical intervention (1, 2). Surgical intervention should therefore be reserved for complications such as bowel perforation. Although investigations like plain films and ultrasound can provide useful information, CT scan of the abdomen is the primary modality for diagnosis and determining management of these patients (2).

1.3. Acute abdomen: Definition and clinical findings

1.3.1. Definition

According to Squires et al the term "acute abdomen" refers to "signs and symptoms of abdominal pain and tenderness, a clinical presentation that often requires emergency surgical therapy" (1). The causes of acute abdomen are numerous and can be medical or surgical; this only emphasises the importance and urgency of identifying the cause and instituting appropriate treatment immediately (1).

Non-surgical causes can be endocrine, metabolic, haematological or related to toxins and drugs. Surgical causes range from haemorrhage due to trauma or other causes, infection involving any intra-abdominal structure, bowel obstruction, perforation or ischaemia (1).

An understanding of peritoneal anatomy can aid in the understanding of the clinical presentations of the conditions that cause acute abdomen. Three types of abdominal pain are described, visceral, parietal and referred pain. Visceral pain is usually vague and localizes poorly depending on its origin. Commonly, for an example, acute appendicitis, will present with vague peri-umbilical pain. Later the pain localises to the right iliac fossa

and this represents parietal peritoneal irritation. Parietal pain is sharp and better localized because it corresponds to the segmental nerve root innervating a specific portion of the peritoneum, while referred pain is felt at a site distant from the origin of the pain (1, 3). Clinical history and physical examination are paramount in establishing the nature of pain present.

Peritoneal inflammation, or peritonitis, results from any irritation in the peritoneal cavity. This usually causes an increase of blood flow and permeability and formation of fibrinous exudate from its surface. This results in a localised ileus and causes adjacent bowel loops to adhere to each other, the omentum or the abdominal wall in an effort to contain the infective process. In such a case, the patient will present with localised parietal type of pain. In contrast, a diffuse process such as a hollow viscus perforation will cause diffuse and general abdominal pain and decreased bowel sounds (1).

1.3.2. Clinical findings

On physical examination, peritonitis is detected by extreme pain on palpation of the abdomen in the presence or absence of rebound tenderness and guarding of the abdomen. Inspection can reveal a rigid, distended abdomen or visible distress on movement in a patient in severe abdominal pain. A hypertympanic abdomen suggests distended bowel or free air, while absence of bowel sounds can be associated with severe peritonitis or advanced mechanical obstruction or paralytic ileus (1, 3).

1.3.3. Laboratory findings

Several different laboratory tests can be performed in patients presenting with acute abdomen to aid in the diagnosis. These include a full blood count (FBC), serum urea and creatinine levels , C-reactive protein (CRP) and serum amylase (3). A decreasing haemoglobin level may suggest acute blood loss. Inflammatory markers such as white cell count (WCC) and CRP, when increased are indicative of inflammatory or infective processes (3). An elevated serum or urine amylase could indicate acute pancreatitis(3).

A lower cluster of differential 4 (CD4) lymphocyte count is associated with a poor outcome in HIV-positive patients. It is, however, not a test specifically done in patients with presenting with acute abdomen, with the purpose of obtaining a diagnosis. Its purpose in this case would be to assess the degree of immune suppression in the HIV positive patient (1). In our setting CD4 count results may only be available a few days after the presentation to the emergency department.

1.3.4. The immune compromised patient

In the immune compromised patient such as HIV, diabetes, steroid therapy or malnutrition, the clinical presentation of the acute abdomen may be unusual. This greatly depends on the level of immune suppression. Patients with mild immune suppression or high CD4 counts generally present with a similar spectrum of abdominal illnesses as immune competent patients (1). Severely immune suppressed patients may lack the ability to mount an adequate immune response evident in the absence of fever, leukocytosis or abdominal pain (1). They are also more prone to opportunistic infections with unusual bacteria, fungi or viruses such as Cytomegalovirus (CMV) (1).

1.4. HIV epidemiology

HIV continues to thrive globally even with the advent of antiretroviral drugs. The majority of new infections as well as the morbidity associated with the disease are most felt in the developing countries where diagnosis and commencement of treatment are delayed due to misinformation and the lack of resources (4).

According to the Joint United Nations Programme on HIV/AIDS (UNAIDS) there were 34 million people living with HIV in the world in 2011 (5). Sub-Saharan Africa was most heavily affected by the pandemic with 1 in 20 adults infected, which constitutes 69% of the global HIV-positive population. There are an estimated 5.6 million people living with HIV in South Africa (6).

Global trends show an overall decline in the incidence of HIV and an accompanying decrease in the mortality rate of AIDS related diseases. Despite the overall decline in new HIV infections and deaths in most regions, sub-Saharan Africa (with a 25% decline since 2001) accounts for 71% of new infections in adults and children, highlighting the enormity of the pandemic in this region (5).

South Africa has shown stabilisation in infection rates, with only a small decrease in prevalence rates in the 15-24 age categories (1.3%) (7). Prevention of mother to child transmission (PTMTC) programmes have resulted in a decrease of prevalence in children 2-14 years of age (6). The Middle East, parts of North Africa, Eastern Europe and Central Asia have seen an increase in the number of new HIV infections after enjoying stability for almost a decade (5).

1.4.1. Classification of severity of disease

In 2007 WHO redefined HIV- stating that patients with CD4 count < 350 cells/μL should be classified as "advanced HIV" moving away from the previous classification of "AIDS defining" with CD4 count < 200 cells/μL. This WHO classification is the classification used in this study (8).

South African national policies on clinical practices in the management of HIV are dynamic. These guidelines are continually updated as new research and developments are made in the treatment of HIV. The goal continues to be the decrease in the HIV burden of disease; and to increase the number of people of antiretroviral (ARV) treatment (9). In the more recent revised adult antiretroviral therapy guidelines of 2014, Meintjies et al have recommended that ARVs be started on all patients with CD4 counts less than 350 cells/μL, moving away from the traditional "AIDS defining" threshold of 200 cells/μL(9). They stated that patients with CD4 counts between 350 – 500 cells/μL should be initiated on ARV treatment when the patient is ready and motivated to start lifelong treatment (9). The Minister of Health has, however, announced that the threshold in South Africa for ARV initiation would be increased to 500 cells/μL in all patients from January 2015 (10).

1.5. HIV and the abdomen

HIV has had a global impact on the burden and the spectrum of diseases that clinicians are faced with. It has also had an effect on the modes of presentation of diseases that cause acute abdomen (11). Although HIV-positive patients suffer from similar abdominal

complaints to those patients who are immune competent, the level of immune suppression, increases the likelihood of certain opportunistic infections that should be considered as the cause for abdominal symptoms (12, 13).

Prompt diagnosis in these patients is essential. This makes CT an indispensible tool in distinguishing those patients that would benefit from surgical intervention, from those that would have a better outcome with conservative treatment (2). CT also has the ability to evaluate the entire abdomen including the solid organs, mesentery and omentum, lymph nodes and the gastrointestinal system, which are all common sites of involvement in the HIV-positive patient (11).

1.6. TB and the abdomen

Abdominal involvement in TB can at times present as acute abdomen. This is evident by the presence of necrotic lymphadenopathy, hepatic and/or splenic micro-abscesses, and omental inflammation and thickening on CT scan but these findings on their own are not indications for surgery (2, 14). Their presence usually encourages the surgeon to commence anti-TB treatment rather than opt for laparotomy. Surgery is generally reserved for patients with bowel obstruction or perforation of a hollow viscus (2).

1.6.1. TB epidemiology

Tuberculosis is caused by *Mycobacterium tuberculosis* infection. This disease is one of the leading infectious causes of death globally, and it is responsible for significant global morbidity and mortality (15). It commonly affects the respiratory system but meningeal

infection (TB meningitis), visceral, nodal, bony, peritoneal and gastrointestinal involvement may also occur (i.e. extra-pulmonary TB) (15). There were approximately 8.7 million new cases and 1.4 million deaths attributed to TB in 2011 (15). The highest incidence of TB was found in Asia and Africa. India, China, Indonesia, Pakistan and South Africa are the five countries with the highest burden of the disease (15). South Africa accounts not only for 24% of the world incidence of TB, but also for the most cases of multi-drug resistant TB and the highest death rate related to TB (15).

The coexistence of TB and HIV in the South African population is approximately 60% (7). Greater efforts are made to actively look for one infection when the other is found (5, 7, 15). After TB exposure an HIV-positive individual has a greater chance of contracting TB than an individual without HIV (15). Antiretroviral therapy (ART) has been shown to greatly reduce the morbidity and mortality of TB in these patients and even reduces the risk of active TB infection by 65% (15).

1.6.2. Pathophysiology of TB Abdomen

Although TB usually has a pulmonary presentation, it can occur and involve any part of the body (16). The abdomen is a common site for extra pulmonary tuberculosis. It has several manifestations which include lymphadenopathy, TB peritonitis, bowel involvement, and abdominal visceral infection which can involve the liver, spleen and the adrenal glands (16). Each of these features will be discussed below.

The pathophysiology of abdominal TB is centred on the exposure to large doses of TB bacilli, which pass though the gut. The glands of the intestinal mucosa, upon exposure,

produce an inflammatory exudate that is sloughed off and either heals with a fibrotic scar, or spreads to adjacent bowel mucosa (17). The lymph nodes providing lymphatic drainage to these areas are subsequently involved from mucosal spread resulting in caseous necrotic nodes and possibly abscess formation (17, 18). Haematogenous spread with subsequent lymph node involvement is the most commonly implicated method of spread (18). When these infected nodes rupture in the abdominal cavity TB peritonitis can ensue.

In 1982 a paper was published by Epstein et al that described three types of TB peritonitis, viz. the wet, the dry and the omental type (17). More recent publications e.g. Burrill et al (16) in 2007 classify TB peritonitis as wet, dry and fibrotic; this is also the classification adopted for the rest of this text. The wet type is associated with ascites or loculated fluid, while the hallmark of the dry type is caseous necrotic lymph nodes and adhesions, which result in a "plastic abdomen". The fibrotic (omental) form is associated with a thickened and fibrotic omentum that forms a triangular mass that hangs from the transverse colon. This mass is often palpable and is often mistaken for a neoplastic process (17).

1.6.3. Clinical diagnosis of TB Abdomen

TB of the abdomen is difficult to diagnose due to the absence of coughing or any specific symptoms which results in delayed diagnosis (16, 17). It usually presents with abdominal pain and/or non-specific constitutional symptoms of weight loss, anorexia, pyrexia and night sweats, malaise, diarrhoea or constipation; and may occur in the absence of acid fast bacilli (AFBs) in the sputum (14). TB abdomen may present in an acute or a chronic

manner. Acute presentation is associated with abdominal pain and distension that can mimic other surgical conditions and emergencies especially if it complicates with ulcer formation, perforation, or obstruction (14).

Abdominal TB can involve any part of the GIT and can mimic several gastrointestinal disorders such as ulcerative colitis, Crohn's disease, peptic ulcer disease and even gastric malignancy. The ileocaecal region is most commonly affected, and this is often associated with abdominal pain, nausea, vomiting as well as features of malabsorption (18). TB affects the colon in either a focal or a patchy distribution. These patients usually present with pain, constitutional symptoms and most notably, derangement of bowel habits. Haematochezia, constipation and multiple peri-anal fistulae are not uncommon in patients with rectal involvement (18).

There is also a direct correlation between patients with AIDS (severe immune deficiency) and the severity of symptoms and gastrointestinal involvement (18). Complications of abdominal tuberculosis will depend on which part of the abdomen is involved. Ulcer formation, fistulae formation, perforation, stenosis, adhesions with obstruction, or bleeding may occur (18).

1.6.4. Laboratory diagnosis of TB

Inflammatory markers such as WCC and CRP are non-specific for the diagnosis of TB but abnormal values in conjunction with other laboratory tests could heighten the index of suspicion for TB (19). In the immuno-compromised patient, a lower CD4 count makes the diagnosis of TB more likely (20).

Acid fast bacilli (AFB), fluid adenosine deaminase activity (ADA), culture, GeneXpert Mycobacterium TB and Rifampicin (MTB/RIF) assay or histology of any specimen or sample may be used to confirm the diagnosis (13, 14, 21). Laboratory tests for the diagnosis of TB can be performed on almost any type of specimen. Pulmonary specimens include sputum, bronchoscopic aspiration, bronchoalveolar lavage, post bronchoscopic sputum, and gastric lavage (21). In contrast, extra-pulmonary specimens include pleural fluid, lymph node and skin biopsy samples, intevertebral disc material, urine, cerebrospinal fluid (CSF), pericardial fluid and ascitic fluid (21).

The tuberculin skin test (Mantoux) has a low sensitivity and specificity and is hardly used nowadays. Acid fast bacilli (AFBs) are visualized on the sputum or fluid on direct microscopy using Ziehl Neelsen or Auramine fluorescence staining (22).

Culture is the standard in the diagnosis of TB but this is a lengthy process that will delay diagnosis and treatment, since it can take up to eight weeks for the results to be finalized (21, 22).

In patients without liver disease, Adenosine Deaminase Activity (ADA) greater than 33 U/L in the ascitic fluid has shown to be sensitive (97%) with a specificity of (100%) in diagnosing TB peritonitis (18).

Histology of any of the above mentioned biopsy specimens could reveal granulomas with caseating necrosis. Polymerase Chain Reactions (PCR) of biopsy samples have shown a

higher sensitivity and specificity than culture alone (18). TB PCR can also be performed on urine specimens (18).

GeneXpert MTB/RIF assay is relatively new diagnostic test that not only provides rapid diagnosis of TB but also gives information on the presence or absence of Rifampicin resistance (21). This expedited diagnosis rapidly identifies those at risk for multidrug resistant TB (MDR-TB) (21).

1.6.5. Imaging findings of TB Abdomen

Plain film and Fluoroscopy

The imaging findings of TB abdomen vary from non-specific signs of acute abdomen to features diagnostic of TB. Plain abdominal x-rays (AXR), fluoroscopy, and CT scan are some of the modalities used in the detection of abdominal TB. Fluoroscopy has no role in the acute setting, but is useful as a diagnostic tool in stomach, bowel and renal involvement (16).

AXR can be valuable in the diagnosis of complications of abdominal TB such as bowel obstruction or pneumoperitoneum from perforated hollow viscus (2, 23). MRI shows similar features of abdominal TB as CT scan and has no real role in the acute setting or in the diagnosis of abdominal TB (23).Renal TB does not often present acutely but AXR features include calcifications of various patterns that may be cortical, medullary or within the calyceal system; and destruction of the kidney from renal auto-nephrectomy may be evident (24). On fluoroscopy, intravenous pyelogram may show decreased

function of the kidney, stone formation or filling defects within the collecting system. This could lead to stricturing and distortion of the collecting system (24).

Ultrasound

Ultrasound readily demonstrates ascites, lymphadenopathy and nodal masses. The ascites is often complex with multiple fibrin strands or septations due the exudative nature of fluid. Omental caking, peritoneal nodularity and thickening are other sonographic features of TB (23). The sonographic features of TB are non-specific, but depending on the patient's clinical picture appropriate investigations should be done. (23, 25).

Visceral involvement in the form of splenic and hepatic microabscesses is a very important sonographic finding in HIV-positive patients (18, 26).The kidneys may appear normal in early TB of the kidneys (24). In progressive disease sonar may show papillary destruction evident by echogenic ill-defined cortical lesions (24).

Ultrasound is also an excellent tool to visualise and characterise lymphadenopathy. Nodes affected by TB are numerous and have hypoechoic necrotic centres. Ultrasound can also show concentric bowel wall thickening and dilatation and on rare occasion mucosal ulceration but these are non-specific findings (25, 26).

Ultrasound is instrumental in excluding other causes of acute abdomen such as acute appendicitis, cholecystitis, free fluid associated with a perforated viscus, TB peritonitis, and pelvic inflammatory disease (27) .

Focus assessment with sonography for HIV-associated tuberculosis (FASH) is an emerging ultrasound technique designed for the emergency clinicians or the inexperienced user (28). FASH aims to assist the clinician to identify features in the chest and abdomen that, in conjunction with the clinical findings, are suggestive of TB. These include pleural and pericardial effusions, ascites and splenic microabscesses(28). This is advantageous in countries such as South Africa where the burden of both HIV and TB is high and may expedite patient management while the results of definitive diagnostic tests such as microscopy and culture are pending (28).

CT scan

CT is the modality of choice to visualise the entire abdomen and identifying features of abdominal TB, as described below.

Lymphadenopathy

The most common feature of abdominal TB is lymphadenopathy. According to Burrill et al (16) and Sood (23), mesenteric, peri-portal and peri-pancreatic nodes are more commonly enlarged but all nodes may be affected. Tuberculous lymph nodes usually have hypoattenuating centres representing central necrosis, while the outer rim enhances on CT scan (16). These features are highly suggestive of TB but are nonspecific and do not always represent caseous necrosis. It is important to note that tuberculous lymph nodes are very rarely a cause of bowel, biliary or genitourinary obstruction.

TB Peritonitis

TB peritonitis is present in one third of patients with abdominal TB and is a cause for an acute abdominal presentation (16). It is postulated to result from haematogenous spread but may also be caused by ruptured lymph nodes with spillage of caseous contents into the abdominal cavity, direct extension of local disease or fallopian tube involvement (16, 17). TB peritonitis has been described as wet, fibrotic, or dry. Wet TB peritonitis is characterised by massive, simple or complex ascites that usually enhances on contrast enhanced CT scan because of its exudative nature (16). Fibrotic TB peritonitis is identified by omental and mesenteric masses, described as cake-like. They exhibit a low mottled attenuation and are associated with matted thickened loops of bowel. The features of dry TB peritonitis include mesenteric thickening, fibrous adhesions, as well as caseous adenopathy. Omental thickening can also occur in dry type of TB peritonitis.

Bowel Involvement

Tuberculosis affects the ileocaecal region and the caecum most commonly by marked concentric thickening of the entire bowel wall, ulceration or a nodular appearance (2, 26, 29). It can also present as skip lesions with concentric mural thickening in other parts of the bowel and in the presence of ileocaecal involvement is highly suggestive of TB (29). It is not uncommon to find large necrotic nodes in the adjacent area (2).

Hepatosplenic and adrenal TB

Hepatosplenic and adrenal involvement is a common finding in patients with disseminated TB. They present with multiple hypoattenuating nodules measuring 0.5 - 2.0mm, that are best appreciated on ultrasound. Larger nodules may also be present.

Tuberculomas may be found in the liver. These are characterised by hypoattenuating masses with areas of calcifications within them (16, 25). Enlarged adrenal glands are seen in patients with active disease (16).

Genitourinary involvement

Most cases of extra pulmonary TB occur within the genitourinary system (16). The kidneys, seminal vesicles and prostate are usually infected as a result of haematogenous spread of disease (16), while infection of the bladder and epipidymis are involved by direct extension of disease (16). Most of the genitourinary tact manifestations generally do not cause acute abdomen, but the gynaecological manifestations of TB my present in the tubo-ovarian abscesses, salpingitis, cervicitis or peritonitis causing acute abdominal symptoms (30, 31).

The kidneys are often involved unilaterally. Non-contrasted CT most commonly shows renal calcifications while CT intravenous pyelogram shows abnormal calyces due to erosion in the early stages. Advanced disease will show features of papillary necrosis evident by hydronephrosis with irregular margins and areas of filing defect from the caseous debris, Infundibular strictures result in dilated calyces; the hallmark of end-stage disease is tuberculous auto-nephrectomy (16, 24). When there is ureteric involvement, the ureteric walls are usually thickened. Strictures also form with an affinity to the pelviureteric junction, at the pelvic brim and at the vesicoureteric junction (16). Involvement of the bladder, seminal vesicles and prostate may occur. Prostate involvement can result in areas of necrosis within the prostate on imaging (16).

Bowel perforation

Direct evidence of perforation includes pneumoperitoneum, fluid collections, extravasation of oral contrast from bowel, and bowel wall pneumatosis from bowel wall ischaemia (11). Near the site of perforation, an abscess or an inflammatory mass (phlegmon) with adjacent fatty stranding may be found. There may also be bowel wall enhancement (11). Kuhlman and Fishman (11) highlighted bowel perforation and unremitting bowel obstruction (48 hours without response to conservative measures) as absolute indications for surgery (11).

The CT findings may help to identify which patients require surgery vs. those that would benefit from conservative management (2, 11, 13). Abdominal CT is therefore an important modality in differentiating patients that require surgical treatment for acute abdomen from those with abdominal TB that should not undergo laparotomy.

1.6.6. Surgical diagnosis

Several features of abdominal TB can be directly visualised during laparoscopy or laparotomy. The presences of necrotic and caseous adenopathy, ascites, splenic and liver macro-abscesses (white tubercules), bowel wall thickening, omental caking and peritoneal thickening are very suspicious for TB (25). These findings are nonspecific, but an expert diagnosis can confidently be made by the surgeon when correlated with patient history and clinical, and imaging features (25). Proximal and distal endoscopy can also be instrumental in the diagnosis of ulcerating bowel lesion that mimic ulcers and provide an opportunity to obtain a tissue sample (18).

1.7. This project in context

It has become clear that HIV-positive patients deserve special consideration when it comes to management of the acute abdomen (13). The focus should be in actively pursuing a diagnosis in a non-invasive manner rather than exploring the abdomen, or excluding other surgical causes, with surgery reserved for patients with perforation of a hollow viscus, confirmed bowel ischaemia and necrosis or non-remitting bowel obstruction (2, 11, 13, 32).

Smit and Du Toit (33) showed that patients with advanced HIV and acute abdomen suffered from a host of disorders quite different from their immune competent counterparts. They also concluded that there was an unacceptably high mortality rate associated with inappropriate surgical intervention in these patients (33). The reason was that conditions such as TB peritonitis, abdominal TB and cytomegalovirus (CMV) related gastrointestinal inflammation or ulceration, in the absence of perforation, are better managed conservatively than with laparotomy. Such patients have been found to respond very well to drug therapy whereas the complications from surgery can be fatal (11). These complications include anastomotic breakdown, entero-cutaneous fistula formation, delayed wound healing, stricture formation, as well as continued abdominal sepsis in the form of collections (11, 13).

More recent publications, however, showed that earlier research failed to distinguish between patients who were merely HIV-positive and those with full-blown AIDS, and therefore painted a poor prognosis for all patients with the virus regardless of stage of disease (12). They also disregarded the impact of antiretroviral therapy on patient

outcome. Furthermore, there is a general lack of consensus in the literature on the outcomes of HIV-positive patients who require emergency surgery. Authors such as Madiba and colleagues (12) maintain that HIV-positive patients have similar outcomes to those who are not infected when compared to those with AIDS (12).

Our research has attempted to provide information to assist in surgical decision making for HIV-infected patients who present with **acute abdominal complaints**. CT scan of the abdomen is the modality of choice when patients present with an acute abdomen as it allows examination of the entire abdomen and can be of great help in localising the pathology, distinguishing important entities such as TB and identifying any complications that may require surgery.

1.8. Aim

The aim of the study was to describe the CT findings in HIV-infected patients with acute abdomen and categorised and compared patients with and without proven abdominal TB.

1.9. Objectives

The objectives of the study were:

- To describe the CT findings in HIV-positive patients that present to a tertiary health care facility with an acute abdomen and to correlate the CT findings with the clinico-pathological findings in these patients

- To determine the value of CT scan in the diagnosis of abdominal TB in this patient population
- To determine the inter-observer agreement between three radiologists reading the CT scans

2. Materials and Methods

2.1. Research paradigm

This was a descriptive, observational, cross sectional, quantitative study, that used data retrospectively obtained from patients' records.

2.2. Sample

The sample population for this study consisted of HIV-positive adults with a referral diagnosis of "acute abdomen" that presented for CT of the abdomen to the Radiology department of Helen Joseph Hospital, a tertiary care hospital in Gauteng. The study commenced after ethics clearance was obtained. A sample size of 50 patients was selected on the likely prevalence of this clinical referral scenario determined from a pilot study of the two year period sampled (January 2012 - January 2014). The number of patients included was severely limited by the inefficient storing facilities and physical obstructions to accessing data. The imaging data was collected at the Diagnostic Radiology department of Helen Joseph Hospital in Auckland Park, Johannesburg, South Africa from; laboratory results from the National Health Laboratory Services (NHLS) database and clinical /surgical data from patients' clinical / surgical notes from their files.

2.2.1. Inclusion criteria

All adult HIV-positive patients who presented with features of acute abdomen and underwent an abdominal CT scan were included in the study.

2.2.2. Exclusion criteria

Patients in whom the CT scan and the clinical information were not retrievable from the archives for review were excluded from the study. Patients who had a discrepancy in their patient identification details at radiology, NHLS and filing department that could not be rectified were also excluded.

2.3. Materials and Methods

All scans from this institution were performed on a 16 slice Brilliance CT scan (Phillips, Eindhoven, Netherlands). The standard abdominal scan protocol employed 120KV and 400 mAs with 1mm reconstructions using an abdominal soft tissue window. Routine CT scans of the abdomen were performed with 100ml of intravenous contrast injected into an antecubital vein using an auto-injector at 3ml per second injection rate (depending on the calibre of the intravenous access line). The scans were mostly performed in the portovenous phase and the pelvis was routinely included. The use of oral contrast or a delayed scan varied depending on the specific indication for the scan.

Fifty CT scans of patients that fulfilled the inclusion and exclusion criteria were saved on a digital storage device and transferred to a laptop. A DICOM viewer was used to read the scans. Each CT scan was read by three readers: a senior radiology registrar and two consultant radiologists, all blinded to each other's findings and blinded to the clinical, surgical or laboratory diagnosis.

The NHLS database was used to access the relevant laboratory results and the clinical notes from the patients' files were used to obtain the findings at surgery and final / discharge / treatment diagnosis.

2.4. Data collection

Data for these three parameters (radiology, clinical and pathology) were collected on a data collection sheet that is shown in Appendix A.

The CT scan findings recorded were those relating to conditions that could result in acute abdomen, HIV or TB: free intra-peritoneal air, appendicitis and tubo-ovarian abscesses (related to acute abdomen); lymphadenopathy (related to HIV).

The readers were also instructed to consider lymph nodes with a short axis diameter of more than 1cm as positive or CT significant.

As these findings can be attributed to a number of conditions that would result in a patient presenting with an acute abdomen, the readers were asked to formulate a final diagnosis from the CT findings and categorise them into the following: Normal/no abnormality, surgical, TB related, Inflammatory/infective bowel disease, gynaecological and 'Other'.

The final CT decision for each CT variable was determined based on a majority principle i.e. two or three 'yes' recordings for a parameter was converted to a final 'yes' decision

while two/three 'no' recordings was converted to a 'no' final decision. These were used for comparison against the standard of surgical, laboratory or clinical diagnosis.

The primary investigator collected the laboratory and clinical variables using the 'clinical data collection sheet' [Appendix A].

Laboratory results were deemed 'definite' for TB if there were acid-fast bacilli (AFB) on smear, positive culture for TB, granulomatous disease on biopsy specimen or positive gene Xpert of a sample. In the absence of 'definite' TB, 'Probable' TB was recorded when the following were present: Patient on TB treatment; or clinical diagnosis of TB; or two or more of the following - night sweats; TB contact; chronic cough; weight loss - obtained from the patient notes. White cell counts (WCC) greater than 10×10^9, C-reactive protein (CRP) greater than 5mg/L were considered abnormal.

CD4 count was collected as a continuous variable, but was categorised according to the WHO classification as mentioned in section 1.4.1 above as either$CD4 \leq 350$cells/µL or CD4 > 350cells/µL and reported as such - CD4 counts below this level were considered indicative of advanced HIV infection (8).

2.5. Reliability and validity

Three observers reviewed each scan independently and noted their findings blinded to each other in order to improve the reliability of the data collected. The patient's clinical

and laboratory information was withheld from the observers. The Fleiss'-Kappa score was used to calculate inter-observer agreement.

2.6. Bias

The fact that all the patients in the study were HIV-positive was known to the readers and created an inherent bias, which was unavoidable. The rest of the patients' clinical history (e.g. if TB was diagnosed) was withheld from the CT readers to minimise further bias in their findings. The patient request forms dictated which patients were included in the study. Variations in the description of an 'acute abdomen' required further inquiry into the patient notes for decision to include the patient into the study.

Investigation of HIV-positive patients with acute abdomen usually starts with an ultrasound of the abdomen which introduces another bias - if signs of TB abdomen were found at ultrasound; the patients might not have had a CT scan.

2.7. Statistical analysis

Descriptive statistics, mostly frequency tables and graphs were utilised to analyse the data using the 'final' decision for each variable determined from the majority decision of the three readers. Sensitivity, specificity, positive and negative predictive values were calculated for the CT scans ability to predict the surgical diagnoses, presence of TB (definitive / probable) and final / discharge / surgical/ treatment diagnosis of inflammatory bowel disease, gynaecological pathology or 'other'.

The inter-reader agreement was initially measured with Fleiss' Kappa score. However, this test is very unstable and highly dependent on the prevalence (34). It is most accurate if the prevalence is approximately 50%. The test therefore results in inaccurate kappa scores if the prevalence is either very high or very low. The free-marginal multi-rater kappa score was created by Randolph to overcome this problem because it is not dependent on prevalence and accommodates the presence of multiple readers (34).

2.8. Ethics

The study was approved by the Human Research Ethics Committee of the University of the Witwatersrand, approval number M131151. This certificate is attached as Appendix B. No additional investigations were performed; this was purely a retrospective record review.

2.8.1. Data safety

The scans were anonymised using an assigned study number. The key to 'decipher' the number coding was kept in a secure location that was known only to the primary investigator and the supervisor. Several back-up versions of the data were kept at all times to prevent loss of information due to data corruption and these were kept on storage devices with password protection.

3. Results

3.1. Demographics

The total number of patients meeting the inclusion criteria was 50. Of these, 36 were female and 14 were male. The youngest patient was 21 years of age and the oldest was 63 years. The mean age of the patients was 37.5 years; standard deviation was 9.5 years, while the median age was 37.5 years.

3.2. Clinical data

A summary of the presenting complaints is tabulated below in table 3.1. Six patients were on TB treatment at the time of presentation.

Table 3.1. Summary of frequencies of the presenting complaints according to the patients' clinical notes.

Presenting Complaint N=50 (%)			
Abdominal Pain	37 (74%)	Fever/Rigors	8 (16%)
Vomiting	15 (30%)	Epigastric Pain	5 (10%)
Abdominal distention	13 (26%)	Diarrhoea	4 (8%)
Malaise	10 (20%)	Melaena Stools	4 (8%)
Abdominal mass	10 (20%)	Sepsis	3 (6%)
Constipation	10 (20%)	Burning on Micturition	3 (6%)
RIF pain	9 (18%)	Haematuria	2 (4%)

Note: Some patients had more than one complaint and therefore totals do not add up to 50

Table 3.2 depicts symptoms obtained by the clinician on history as well as the pertinent clinical signs found on clinical examination of the patient.

Table 3.2. Summary of the frequencies of important clinical signs and symptoms

Clinical N=50 (%)	
Night Sweats	14 (28%)
Generalised lymphadenopathy	10 (20%)
Ascites	6 (6%)
Chronic cough	4 (8%)
TB Contact	3 (6%)

Note: Some patients had more than one sign or symptom and totals therefore do not add up to 50

The laboratory findings, which include the septic markers CRP and WCC, confirmatory tests for TB, blood cultures and histology results were collected from the NHLS database and the patients' files. The CD4 count and whether the patient was on ARV treatment were also noted.

Table 3.3. Summary of the frequencies of relevant abnormal laboratory results

Abnormal Laboratory Results N=50 (%)	
Elevated WCC	21 (42%)
Elevated CRP	44 (88%)
AFB/Gene Xpert positive	**10 (20%)**
CD4 count ≤ 350 cells/μL	39 (96 78%)
TB Culture positive	**4 (8%)**
Blood Culture positive for organism other than TB	2 (4%)
Definitive diagnosis on histology • **Definitive diagnosis of TB on histology**	8 (16%) **2 (4%)**

Note: Patients had more than one abnormal result and therefore the totals do not add up to 50.
WCC- white cell count, CRP – C-reactive protein, ARV – antiretroviral and TB - tuberculosis

Of the fifty patients, 44 (88%) had an elevation of the non-specific infective marker CRP, while 21 patients (42%) had an elevated WCC. Thirty-nine patients (78%) had a CD4 count less than 350 cells/μL thus qualifying for ARV treatment according to the policy at that time, but only 17 patients (34%) were on ARVs at the time of presentation with an acute abdomen. Of the eight patients that had their final diagnosis made on histology, two had TB confirmed on histology.

Ten patients (20%) were diagnosed with TB on microscopy (AFB) or GeneXpert. Four (8%) had positive TB cultures on the specimen tested and two patients (4%) had a TB diagnosis made on histology. One patient was AFB positive, but culture showed *Mycobacterium avium complex*; that could give a positive AFB without TB infection. The final number of patients with TB diagnosed on laboratory tests was **eleven**, as some patients had TB diagnosed on more than one modality.

A summary of the clinical diagnoses according the patient notes/discharge summaries are summarised above in table 3.4 and is used as the 'final diagnosis' in this research. Only one patient (2%) was discharged as normal i.e. no pathology.

Table 3.4. Summary of frequency of the diagnoses made upon discharge of the patient, according to the clinical notes

Final Diagnosis As Written in Discharge Notes N=50 (%)	
Normal	1 (2%)
Surgical final diagnosis Perforated viscus Appendicitis Bowel obstruction Abscess Other	 2 (4%) 6 (12%) 6 (12%) 8 (16%) 15 (30%)
Definitive TB diagnosis	11 (22%)
Probable TB	**9 (18%)**
Final diagnosis of IBD	2 (4%)
Final diagnosis of gynaecological pathology	8 (16%)
Final diagnosis 'other'	11 (22%)

Note: Some patients had more than one diagnosis and therefore the totals do not add up to 50
TB –tuberculosis, IBD –Inflammatory / infective bowel disease

The rest of the forty-nine patients had a final diagnosis. Out of fifty patients, thirty-seven (74%) had a surgical diagnosis. These comprised eight patients (16%) who had intra-abdominal abscesses, six with bowel obstruction (12%), six with appendicitis (12%) and two (4%) with a perforated viscus. The large majority of these patients had 'other' surgical conditions (15 patients, 30%).

Eleven patients (22%) had a definite diagnosis of TB confirmed on positive TB culture, AFB smear or Gene Xpert, while nine had a probable diagnosis of TB, (based on a combination of clinical symptoms such as the presence of weight loss or night sweats or anyone already on TB treatment). This adds up to twenty patients (40%) who were discharged with a TB related diagnosis.

Gynaecological conditions comprised 16% (eight patients) of the final diagnoses, while the rest of the diagnoses included inflammatory/infective bowel diseases (eight patients, 16%) and "other" conditions (eleven patients, 22%).

3.3. CT Data

Review of the CT scan reports by the three readers showed that the commonest finding was lymphadenopathy in forty-five subjects (90%) followed by abdominal collections, in twenty-one subjects (42%). Table 3.5 summarises the frequencies of CT findings and table 3.6 the frequency of lymphadenopathy according to lymph node site.

Table 3.5. Summary of the frequencies of the CT scan findings.

CT Findings N=50 (%)	
Lymphadenopathy	45 (90%)
Abdominal Collections	21 (42%)
Pneumoperitoneum	17 (34%)
Visceral abscesses	16 (32%)
Bowel Wall Thickening	16 (32%)
Ascites	10 (20%)
Complex Mass	8 (16%)
Mesenteric Thickening	6 (12%)
Omental Thickening	3 (6%)
Mesenteric Ischaemia	1 (2%)
Pneumatosis	0 (0%)
Contrast Extravasation From Bowel	0 (0%)

Note: Some patients had more than one CT finding and therefore the totals do not add up to 50

Forty-five patients (90%) of the fifty had lymphadenopathy involving one or more groups on CT scan. Only five patients (10%) had no lymphadenopathy. One patient (2%) had all lymph node groups involved.

Table 3.6. Summary of the frequency of lymphadenopathy found on CT scans overall and according to lymph node group location

Lymphadenopathy sites N= 50 (%)	
Total number of patients with lymphadenopathy	**45 (90%)**
Para Aortic	30 (60%)
Inguinal	29 (58%)
Mesenteric	28 (56%)
Coeliac	16 (32%)
Pelvic	14 (28%)
Perisplenic	7 (14%)
Periappendiceal	6 (12%)
Porta-hepatis	3 (6%)
No lymphadenopathy	5 (10%)

Note: Some patients had more than one group of lymph nodes involved and therefore the totals do not add up to 50

The CT scan diagnoses are summarised in table 3 7. No patients were diagnosed as normal on CT scan. Half of the patients had a surgical emergency diagnosis (total of 25 patients). Thirteen of these patients (26%) had an intra-abdominal abscess, nine (18%) had bowel obstruction and two (4%) had appendicitis. Forty–four percent (22 patients) had a diagnosis related to TB as described in section 2.4 and defined on the data collection sheet [Appendix A].

Table 3.7. Summary of the frequencies of final CT scan diagnoses

CT diagnosis	**N= 50 (%)**
Normal	0 (0%)
Surgical emergency - Perforated viscus - Appendicitis - Bowel obstruction - Abscess - Other	**25 (50%)** 0 (0%) 2 (4%) 9 (18%) 13 (26%) 1 (2%)
TB Related	22 (44%)
Inflammation/Infective bowel disease	7 (14%)
Gynaecological	12 (24%)
Other	15 (30%)

Figures 3.1 and 3.2 represent imaging of patient that underwent surgery that had a discrepancy on CT and discharge diagnosis. Only one patient had only ascites and lymphadenopathy on CT, with no other documented abnormality on CT. The discharge diagnosis of this patient was gastric carcinoma. Figure 3.1 shows representative images of the CT scan of this patient. The patient had no features of gastric carcinoma on CT scan.

Table 3.8 summarises the CT scan and the final diagnoses of the nine patients that had an operation.

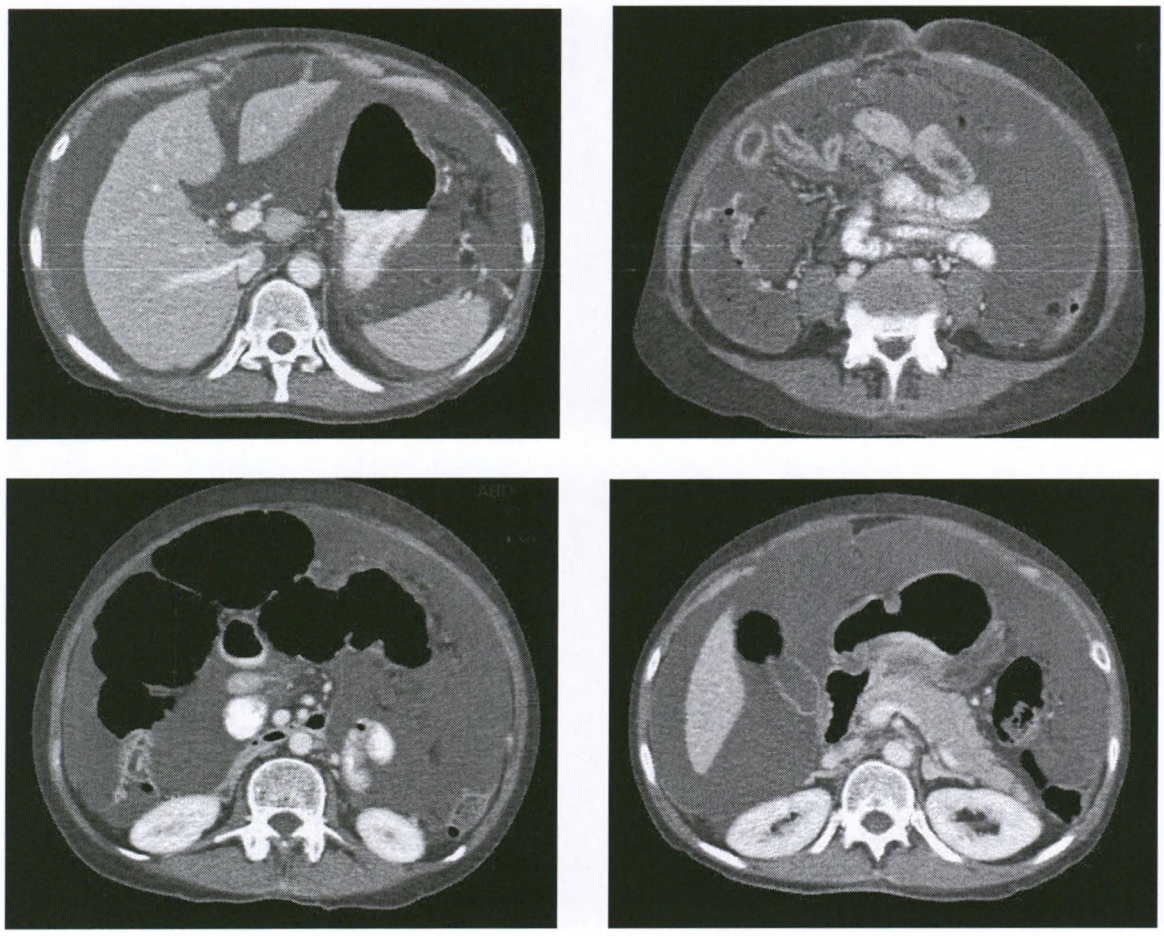
Table 3.8. Summary of CT scan and discharge diagnoses for patients that had surgery

CT scan and discharge diagnosis for the patients that had surgery (N=9)	
CT Findings	**Discharge Diagnosis**
Bowel obstruction, evidence of TB Renal pathology	Nephrectomy for xanthogranulomatous pyelonephritis
Abscess, with perforation	Gangrenous appendix
Ascites, adenopathy	Gastric adenocarcinoma*
Bowel obstruction, TB related, with appendiceal abscess	Appendiceal abscess, MDR –TB cultured on sputum
Bowel obstruction, with perforated viscus (appendix perforation)	Perforated gangrenous appendix with Klebsiella sepsis
Abscess, TB related	Pancreatitis, TB of the pancreas
Bowel obstruction, TB related	RIF mass, lymphoma
Bowel wall thickening	Bowel ischaemia
Abscess, TB related	TB related abscess

* See figure 3.2

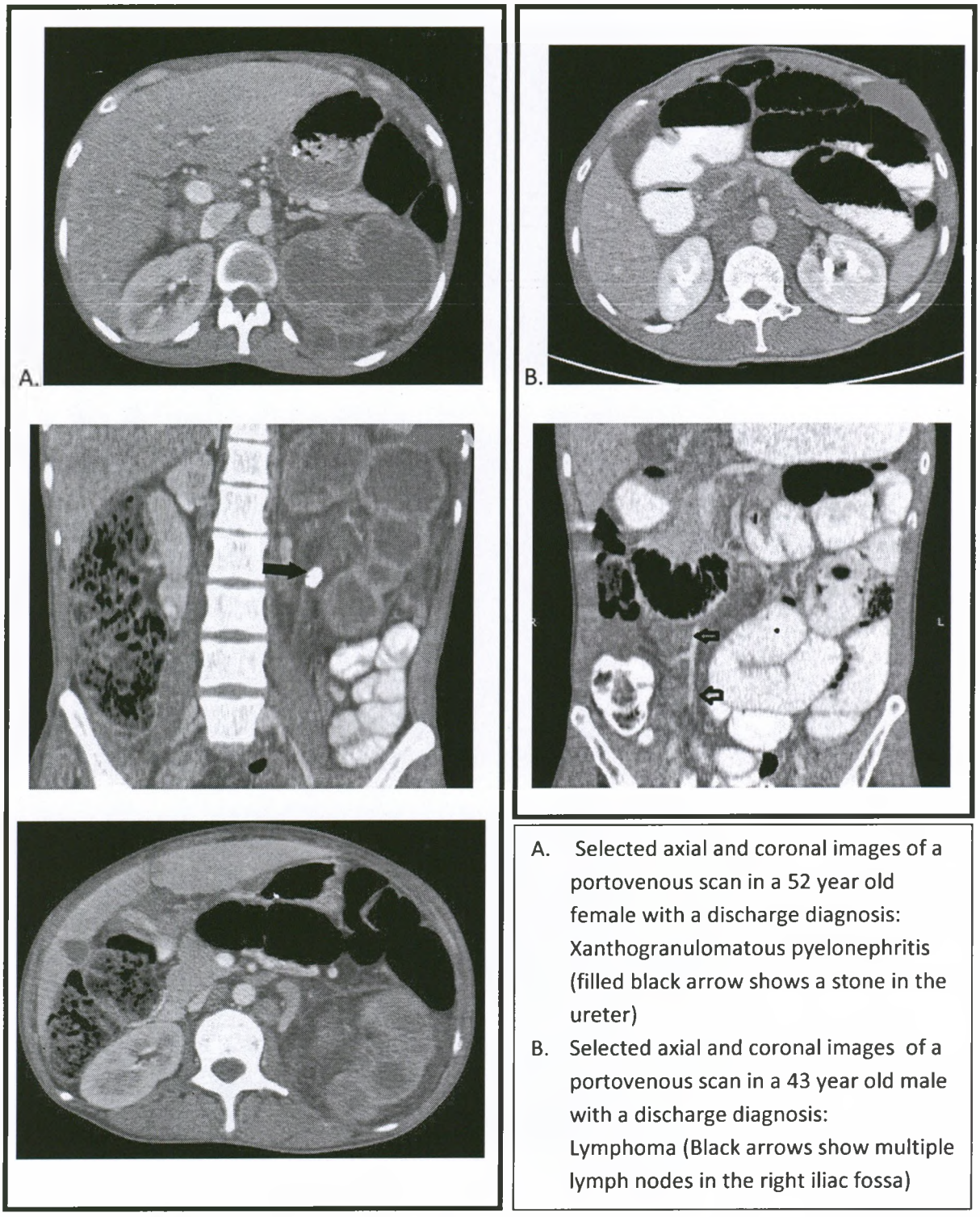
Of the nine patients that had surgery, CT showed an indication for emergency surgery in eight (78%): bowel obstruction in four patients (44%), abscess formation in three (33%) and bowel wall ischaemia in one (11%).

Five of the patients that went for surgery (56%) had features of TB on CT scan. However, only three (33%) of these patients had proven TB as a discharge diagnosis. The other two patients with TB diagnosed on CT, had granulomatous pyelonephritis and lymphoma in the RIF respectively. See figure 3.2 for representative images of the CT scans of these patients.



39 year old male patient presenting with abdominal pain, distention and constipation. The above images demonstrate contrast and air in the stomach. There are no obvious abnormalities of the stomach or focal liver lesions. There is marked ascites present. Discharge diagnosis of gastric carcinoma

Figure 3.1. Selected post contrast axial CT images in a patient with a discharge diagnosis of gastric carcinoma.



A. Selected axial and coronal images of a portovenous scan in a 52 year old female with a discharge diagnosis: Xanthogranulomatous pyelonephritis (filled black arrow shows a stone in the ureter)

B. Selected axial and coronal images of a portovenous scan in a 43 year old male with a discharge diagnosis: Lymphoma (Black arrows show multiple lymph nodes in the right iliac fossa)

Figure 3.2. Selected post contrast axial and coronal CT images of two patients that had laparotomy whose CT scan showed features suggestive of abdominal TB but had a different discharge diagnosis

Table 3.9 illustrates the high frequency of surgical and gynaecological conditions that include not only the emergencies previously discussed but conditions such as cholecystitis, pancreatitis, pyelonephritis or pelvic inflammatory disease. Sixty percent were identified on CT scan and clinical correlation increased this to 66%.

Table 3.9. Summary of CT and discharge diagnoses for all patients in the study

CT findings	N= 50 (%)	Discharge diagnosis	N = 50 (%)
Surgical or gynaecological conditions	30 (60%)	Surgical or gynaecological conditions	33 (66%)
TB related	22 (44%)	TB related	20 (40%)
Malignancy	1 (2%)	Malignancy	4 (8%)
Inflammation/Infective bowel disease	7 (14%)	Inflammation/Infective bowel disease	2 (4%)
Other (unspecified/undetermined)	8 (16%)	Medical (Drug induced hepatitis & Idiopathic thrombocytopenic purpura)	3 (6%)

3.4. TB Sensitivity and Specificity

Table 3.10 summarises and compares CT scan and clinical findings. From this table the sensitivity and specificity of CT scan for diagnosing TB against a definitive and combined definitive and probable diagnosis were calculated.

Table 3.10 is a 2x2 table of CT diagnosis against the definitive diagnosis of TB (confirmed on AFB, culture or Gene Xpert).

Table 3.10. Sensitivity and specificity of CT scan against the definitive TB diagnosis

		CT DIAGNOSIS	
		TB +	**TB -**
DEFINITIVE TB DIAGNOSIS	**TB +**	8 (16%)	3 (6%)
	TB -	14 (28%)	25 (50%)

The **sensitivity** of CT scan (the ability to detect the presence of TB) in our patient population was **73%**. The **specificity** of CT scan (the ability to identify the absence of TB) was **64%**, while the accuracy was 66%. The positive predictive value (PPV) was 36%. The negative predictive value (NPV) was 89%.The prevalence was 22%.

To create the Table 3.11, the definitive diagnosis patients were combined with those that had a clinical suspicion of TB and both groups were treated as having the disease.

Table 3.11. Sensitivity and specificity of CT scan against the definitive and probable diagnosis of TB

		CT DIAGNOSIS	
		TB +	**TB -**
COMBINED DEFINITIVE AND PROBABLE TB DIAGNOSIS	**TB +**	17 (34%)	4 (8%)
	TB -	5 (10%)	24 (48%)

The **sensitivity** of CT scan in confirming a strongly suspicious diagnosis of **TB was 81%.** The **specificity was 83%,** while the accuracy was 82%. The positive predictive value was 77% and the negative predictive value was 86%. The prevalence was calculated to be 42%.

3.5. Inter-reader agreement

Inter-observer agreement is tested using a Kappa score. Multiple kappa scores have been developed to determine the degree of agreement between observers. The ranges of possible scores when using any kappa, as well as the interpretation of these scores, are represented in table 3.12 (34).

Table 3.12. Interpretation of kappa (ranges)

Agreement	Range
Perfect	1
Almost perfect	0.81 -1.0
Substantial	0.61 – 0.80
Moderate	0.41 – 0.60
Fair	0.21 – 0.40
Slight	0.01 – 0.20
Poor	< 0

Fleiss' Kappa is the kappa test most commonly used for multiple observers, but it is known to be unreliable if the frequency of a finding is either very high or very low. Randolph's kappa is a free-marginal multirater Kappa that was developed specifically to address free-marginal data (34). It is not dependent on the prevalence of a finding and is considered to be more stable than Fleiss' kappa for frequencies of findings that are either very high or very low. The tables below compare the two kappa values for each variable and demonstrate the difference in agreement between the readers using the two different kappa score types.

Table 3.13 summarises the Randolph's kappa score for inter-reader agreement of the CT findings in this study, as well as Fleiss' kappa for comparison. No variables showed perfect agreement. The variables showed significantly higher agreement when Randolph's kappa was used, especially when incidence of the variable was very low. Contrast extravasation from bowel is a good example. In reality, only one reader reported

contrast extravasation in only two cases. Randolph's kappa reflects this as an almost perfect agreement, while Fleiss' kappa indicated poor agreement.

Table 3.13. Randolph's kappa score for CT findings in HIV-positive patients with acute abdomen, with Fleiss' kappa for comparison

CT Finding	N=50 (%)	Randolph's kappa	Inter-reader agreement	Fleiss' kappa	Inter-reader agreement
Contrast Extravasation From Bowel	0 (0%)	0.95	Almost Perfect	-0.01	Poor
Mesenteric Ischaemia	1 (2%)	0.92	Almost Perfect	0.23	Fair
Pneumoperitoneum	17 (34%)	0.89	Almost Perfect	-0.03	Poor
Pneumatosis	0 (0%)	0.89	Almost perfect	-0.03	Poor
Omental Thickening	3 (6%)	0.87	Almost Perfect	.46	Moderate
Liver Macroabscesses	5 (10%)	0.79	Substantial	0.47	Moderate
Splenic Microabscesses	7 (14%)	0.71	Substantial	0.31	Fair
Splenic Macroabscesses	5 (10%)	0.63	Substantial	0.28	Fair
Abdominal Collections	21 (42%)	0.55	Moderate	0.53	Moderate
Complex Mass	8 (16%)	0.52	Moderate	0.27	Fair
Ascites Complex	6 (12%)	0.44	Moderate	-0.05	Poor
Ascites Simple	4 (8%)	0.36	Fair	0.36	Fair
Mesenteric Thickening	6 (12%)	0.31	Fair	-0.03	Poor
Bowel Wall Thickening	16 (32%)	0.07	Slight	0.02	Slight

For the detection of lymphadenopathy, the inter-reader agreement ranged from moderate to slight with Randolph's kappa and fair to poor with Fleiss' kappa, with the majority of the lymph node groups receiving a fair agreement with both scores (Table 3.14).

Table 3. 14. Randolph's kappa scores for lymphadenopathy on CT, with Fleiss' kappa for comparison

Lymphadenopathy	N=50	Randolph's kappa	Inter-reader agreement	Fleiss' kappa	Inter-reader agreement
Periappendicial	6 (12%)	0.55	Moderate	0.13	Slight
Perisplenic	7 (14%)	0.44	Moderate	0.15	Slight
Pelvic	14 (28%)	0.37	Fair	0.25	Fair
Porta Hepatis	3 (6%)	0.37	Fair	-0.07	Poor
Coeliac	16 (32%)	0.36	Fair	0.28	Fair
Inguinal	29 (58%)	0.31	Fair	0.25	Fair
Para Aortic	30 (60%)	0.25	Fair	0.23	Fair
Mesenteric	28 (56%)	0.15	Slight	0.14	Slight

In general, the variables showed significant better agreement when the Randolph's kappa was used instead of the Fleiss' kappa. This is best demonstrated in the infrequent findings like contrast extravasation, mesenteric ischemia, pneumatosis and omental thickening, i.e. the free-marginal variables. These variables showed poor agreement when using Fleiss' kappa, but almost perfect agreement when using Randolph's kappa. The two kappas showed similar results when the frequency of the finding was approximately 50%, e.g. inguinal, para-aortic and mesenteric adenopathy.

The readers' final CT scan diagnosis showed a substantial agreement with regards to gynaecological diagnoses and other surgical emergencies with Randolph's kappa, compared to the moderate and fair agreement respectively with the Fleiss' kappa. Readers' final decision for 'Normal' scans and 'perforated viscus, had a poor agreement with Fleiss' kappa and an almost perfect agreement of Randolph's kappa (Table 3.15).

Table 3.15. Randolph's kappa score for inter-reader agreement of the final CT diagnosis, with Fleiss' kappa for comparison

Final CT Diagnosis	Incidence	Randolph's kappa	Inter-reader agreement	Fleiss' kappa	Inter-reader agreement
Normal	0(0%)	0.87	Almost Perfect	-0.03	Poor
Surgical emergencies	25 (50%)				
- Perforated viscus	0 (0%)	0.97	Almost Perfect	-0.01	Poor
- Appendicitis	2 (4%)	0.81	Almost Perfect	0.17	Slight
- Bowel obstruction	9 (18%)	0.52	Moderate	0.35	Fair
- Abscess	13 (26%)	0.47	Moderate	0.33	Fair
- Other	1 (2%)	0.79	Substantial	0.22	Fair
TB Related	22 (44%)	0.19	Slight	0.19	Slight
Inflammatory / Infective Bowel Disease	7 (14%)	0.55	Moderate	0.25	Fair
Gynaecological	11 (22%)	0.63	Substantial	0.46	Moderate
Other	15 (30%)	0.28	Fair	0.12	Slight

Table 3.16 below shows the total number of the types of agreement as a frequency and a percentage for the Fleiss kappa and Randolph's kappa.

Table 3.16. Comparison of frequencies of agreement for Randolph's kappa and Fleiss' kappa inter-reader agreement of the CT scan findings for three readers

Inter-reader agreement	Ranges	Randolph's kappa Frequency (%)	Fleiss' kappa Frequency (%)
Perfect	1	0 (0%)	0 (0%)
Almost perfect	0.81 -1.0	8 (25%)	0 (0%)
Substantial	0.61 – 0.80	5 (16%)	0 (0%)
Moderate	0.41 – 0.60	8 (25%)	4 (12%)
Fair	0.21 – 0.40	8 (25%)	13 (41%)
Slight	0.01 – 0.20	3 (9%)	7 (22%)
Poor	< 0	0 (0%)	8 (25%)

4. Discussion

The HIV-infected patient with an acute abdomen has always posed a dilemma in diagnosis and management (13). The literature has shown that the number of unnecessary operations and possible morbidity and mortality can be prevented with the use of cross-sectional imaging (35) .This study attempted to establish the role of imaging in the management of HIV-positive patients that present with acute abdomen to guide the clinicians as to which patients should have surgery, and in which patients it should be avoided.

4.1. Clinico-pathological correlates

The majority of the patients in our study presented with various abdominal complaints – abdominal pain (74%) and vomiting (30%) were the most common complaints. Abdominal distension, abdominal masses, constipation and specifically RIF masses were also amongst the presenting complaints. These are very nonspecific complaints and can be attributed to other illnesses. The clinicians rely on a good history from the patient, their immediate presenting complaints, clinical examination as well as adjunct laboratory and imaging findings in determining the best management for each patient.

On questioning by the attending clinician, 28% of patients in our study admitted to suffering from night sweats, while 8% had a chronic cough. There are important symptoms that can be ascribed to both HIV infection and TB. On clinical examination of the patients, 20% had non-specific generalised lymph adenopathy and 6% were suspected of having ascites.

Forty-two percent of the patients in the current study had a raised WCC which is a general marker for infection. In HIV/AIDS, this immune response is usually diminished and the WCC may be normal as it was in the majority of the patients in our study (36).

The CD4 count is an important marker of immune suppression and can be a predictor of the presence of opportunistic infection (36). In patients with high CD4 counts (>200 cells/μL), the focus should be to exclude general surgical conditions such as acute appendicitis or viral gastritis in patient presenting with abdominal complaints (36). Conversely, patients with very low CD4 counts , opportunistic infections, such as TB and CMV, should actively be excluded (36). Our study showed that thirty-nine patients (78%) had CD4 counts less than 350 cells/μL indicating that they should have been on ARV treatment (8). We found that only 34% of our patient cohort was on ARV treatment.

4.2. CT Findings in HIV-infected patients presenting with acute abdomen

The 50 patients in our study all had abnormal CT scans. All these findings were significant enough to impact on the management of the patient. Only one of the CT scans showed only ascites and adenopathy. This shows that HIV-positive patients **with acute abdomen can benefit from being imaged by urgent CT scan**. Of the nine patients in our study that went for surgery, CT scan correctly showed an indication for emergency surgery in eight patients. Even though the CT scan might not necessarily show pathology requiring immediate surgery, the findings on CT are significant enough to impact on the management of the patient. The following were found: pyelonephritis, cholecystitis,

pancreatitis and pelvic inflammatory disease in 11 patients (22 %) that, while it does not warrant emergency surgery, convey a definitive diagnosis that can be managed appropriately without the need for surgery.

Abdominal CT is a useful tool to identify the **presence** of features of abdominal TB, as well as the **absence** of abdominal TB. In our study, CT scan was able to diagnose TB with a sensitivity of 81% when compared to clinical and laboratory parameters. This means that CT scan could identify patients with abdominal TB in the cohort that presented with acute abdomen 81% of the time, thereby identifying those patients in whom surgery was ill advised. This would have a direct impact on mortality and morbidity in the form of post operative complications. This is demonstrated by a study done by Islam in 2014 (35). He showed significant post operative complications in patients with suspected HIV and abdominal TB. Out of a patient cohort of 49, 19 patients (38%) in that study died, while 22 patients (45%) had significant complications such as fistulae (35). These findings support the premise of a more conservative approach to acute abdomen in patients with HIV and abdominal TB.

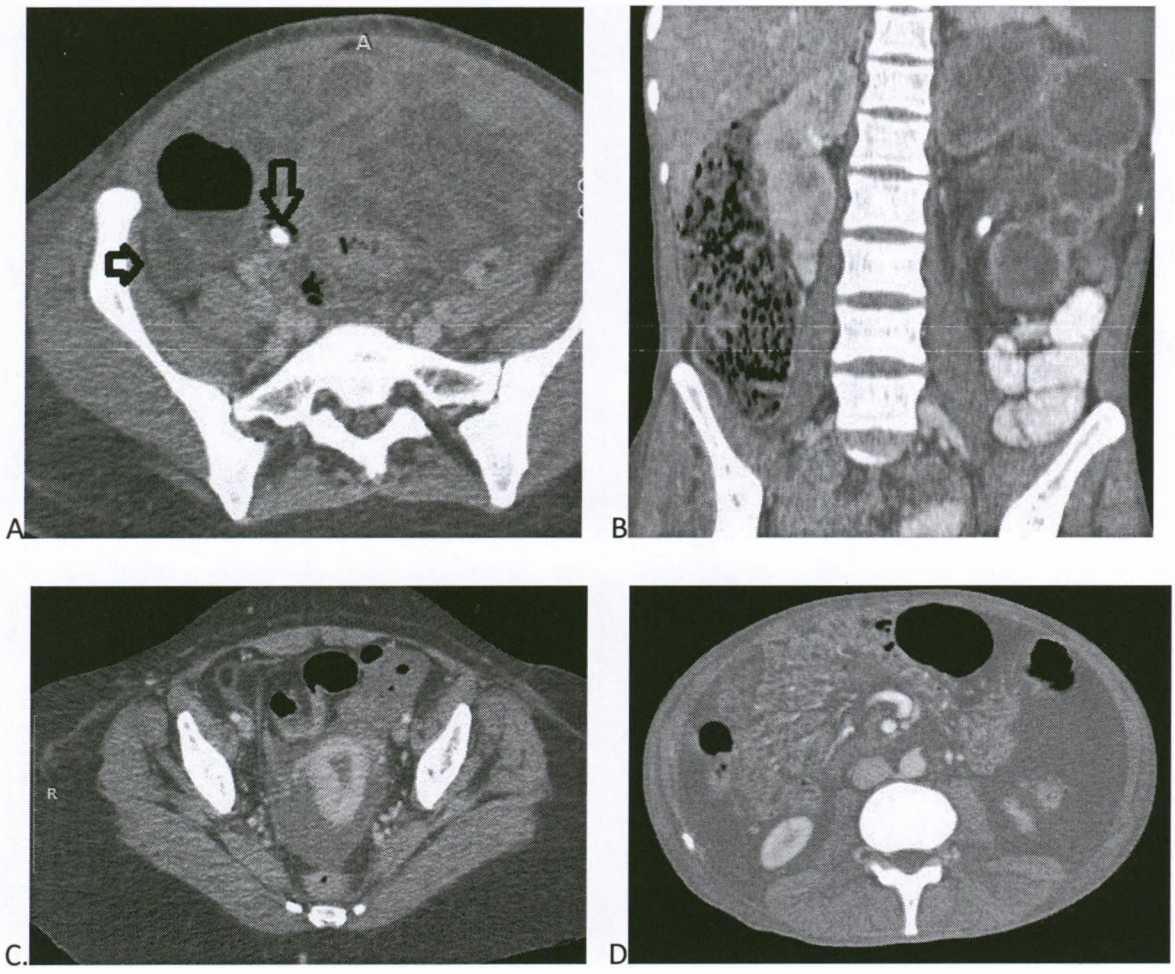
There was a negative predictive value of 86%. This means that when CT **did not find evidence of abdominal TB**, this was supported by the laboratory and clinical tests. This, in fact, is a very important finding of this study. With the use of CT scan, we were able to resolve diagnostic doubt in 86% of HIV-positive patients that presented with acute abdomen. We confirmed that they **definitely did not have abdominal TB.** We were able to show that other surgical emergencies such as acute appendicitis, abscesses or unremitting bowel obstruction were the cause of the acute abdomen. The clinician's

decision to take a patient for explorative laparotomy was not compounded by the possibility of finding features of abdominal TB, and its resulting associated post-operative complications as described by Islam (35).

The importance of excluding abdominal TB cannot be overemphasised because, barring bowel perforation, patients with abdominal TB should be treated non-surgically (2, 11, 13, 32). The diagnosis of TB on CT can prevent unnecessary surgery in these patients and will have a positive influence on the mortality and morbidity of these patients.

The images in Figure 4.1 show some examples of the surgical emergencies in the HIV-positive patients that presented with acute abdomen. They include acute complicated appendicitis with appendiculolith and abscess collection, xanthogranulomatous pyelonephritis with a visible stone in the ureter, pelvic inflammatory disease (PID) and mesenteric ischaemia.

Figure 4.2 demonstrates some of the features consistent with abdominal TB found in our patient cohort. These included psoas abscesses, generalised, necrotic lymphadenopathy, visceral (splenic) micro -abscesses, and ascites.



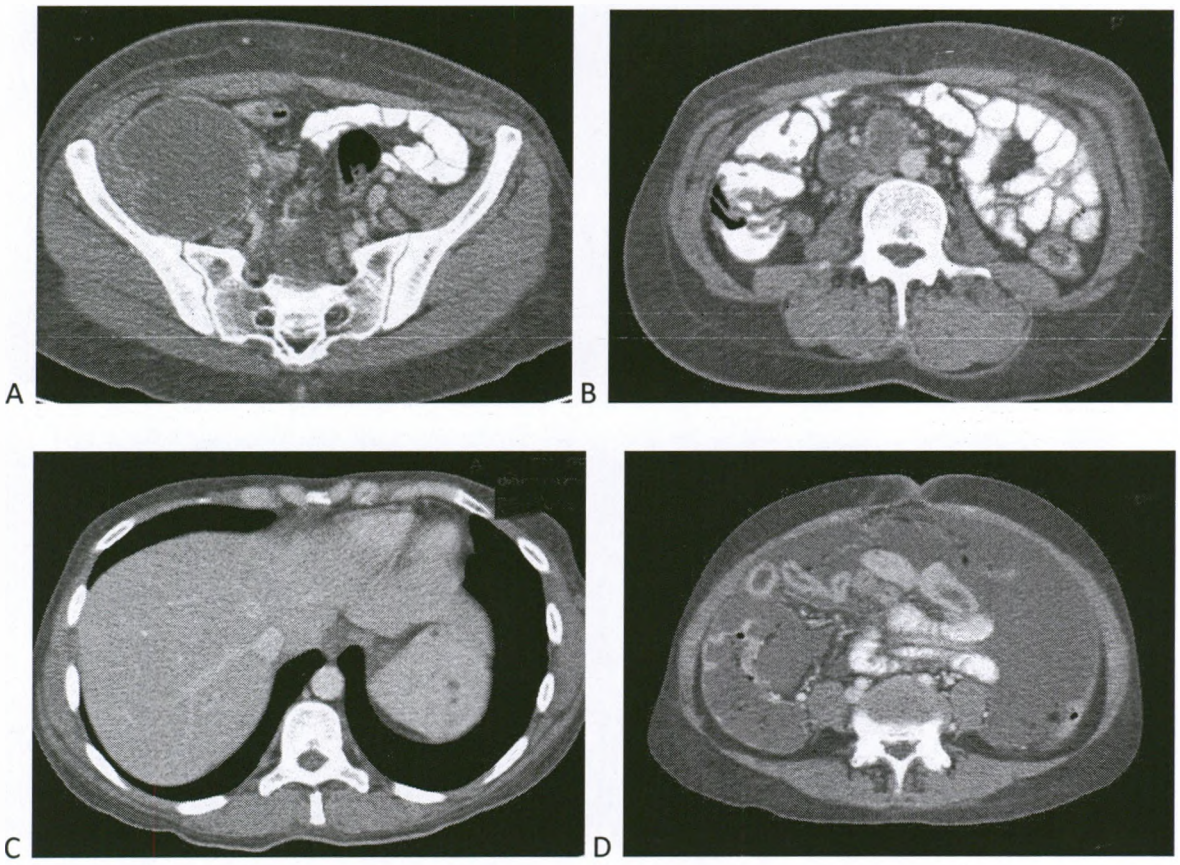
A. Axial image in portovenous phase of a 37 year old male with appendiceal abscess (smaller open arrow) with an appendiculolith (larger open arrow)

B. Coronal image (portovenous phase) in a 39 year old female patient with pyelonephritis of left kidney with calculus in left ureter

C. Axial image (portovenous phase) in a 49 year old female with pelvic inflammatory disease, fluid in uterine cavity and free fluid in the pelvis

D. Axial image (portovenous phase) in a 39 year old male patient with mesenteric ischaemia showing abnormal enhancement of the bowel and ascites

Figure 4.1. Selected axial and coronal post contrast CT images in HIV-infected patients presenting with acute abdomen, demonstrating examples of surgical emergencies



A. Axial image (portovenous phase) in a 31 year old female with a right psoas abscess

B. Axial image (portovenous phase) – 29 year old male showing necrotic para aortic lymphadenopathy

C. Axial image (portovenous phase) – 44 year old female patient with splenic micro-abscesses

D. Axial image (portovenous phase) of a 41 year old male with ascites

Figure 4.2. Selected axial and coronal post contrast CT images in HIV-infected patients presenting with acute abdomen, demonstrating examples of abdominal TB

4.3. Inter-reader agreement on CT scan

Traditionally Fleiss' kappa score is used to analyse the inter reader agreement on the CT scans of the patient cohort. This score is known to be heavily influenced by prevalence of the conditions being reviewed (34). When using this statistical test it resulted in an overall poor agreement between readers because of the low prevalence values of the variables in this study. The free-marginal multi-rater kappa described by Randolph was able to address the abovementioned problem (34). It is a more reliable test that is not influenced by prevalence (34). Randolph's kappa showed much better agreement between readers, with ratings of moderate, fair, and almost perfect predominating. These findings indicate an overall good agreement amongst the readers.

Generally, the variables showed significantly better agreement when the Randolph's kappa was used instead of the Fleiss' kappa. Randolph's kappa was consistently higher or at least equal to the Fleiss kappa. The results of the two tests were similar when the prevalence of the finding was between 40% and 60%.

Although the 'pneumatosis' and 'contrast extravasation' variables reflected a 0% prevalence in our study, there were a few instances (four for pneumoperitoneum and two for contrast extravasation) where one reader disagreed with the other two readers. Randolph's kappa accurately reflected this as "near perfect" agreement, while Fleiss' kappa interpreted this as "poor".

4.4. Results in context

This study focuses on the HIV-positive patients presenting with acute abdomen to a tertiary institution with a specific focus on the diagnosis of TB abdomen. We found no similar studies in the literature for comparison. The radiological literature is focuses on describing the imaging findings of abdominal TB, while the clinically based literature has focused on unusual clinical presentations of TB and precautions in the HIV-positive patients as well as surgical outcomes, with a paucity of imaging findings (17, 35, 37).

A case series from a teaching hospital in Ghana by Ohene-Yeboah in 2006 documented the acute presentation and the surgical findings of abdominal TB. They assessed patients presenting with acute abdomen and included patients that had positive TB culture or histology on specimens obtained during surgery (38). Patients with confirmed TB had their presenting complaints retrospectively assessed. Unlike the current study, there was no specific mention of the HIV status of the patients or other laboratory findings like the septic markers. Imaging was also not a feature of the study. The findings of this study are summarised in table 4.1. below.

Its relevance to our study lies in the documented **clinical** findings. Their focus was on the acute presentation of abdominal TB, like the current study. The commonest presenting complaint was bowel obstruction (72.9%) that was associated with abdominal pain and distention, vomiting, and constipation (38). Our study similarly found that abdominal pain (74%), distention (26%), and vomiting (30%) were the most common findings. Twelve percent of our patients were also discharged with a final diagnosis of bowel obstruction.

Table 4.1. Summary of study by Ohene-Yeboah of patients with acute abdomen and confirmed TB

	Ohene-Yeboah (2006) (38)
Sample size	96 patients
Country	Ghana
Inclusion criteria	Acute abdomen with TB positive surgically obtained histological specimens
Exclusion criteria	
Study design	Prospective study
Focus	To determine the presentation and outcome of acute abdominal TB for general surgeons
Contrast with current study	No correlation with HIV status No focus on CT scan
HIV/TB co infection	Not mentioned
Clinical data available	TB culture, Histology
CT protocol	CT scan was not mentioned – the focus was on surgical findings
Clinical findings / diagnosis	Pre-operative Clinical diagnosis Acute intestinal obstruction (72.9%) Acute diffused peritonitis (23.9%) Acute appendicitis (4%) Surgical Findings Ileocaecal hypertrophied mass (31.3%) Small bowel pathology (42.7%) Peritonitis with tubercules (12%) Inflamed appendix wit ileocaecal mass (4.2%)
Surgery done	100%
CT Findings	Nil

Twenty-two percent of the patients in Ohene-Yeboah's study had acute diffuse peritonitis while, 4% had acute appendicitis. While all patients in both the studies presented with acute abdomen, we had a higher number of patients with acute appendicitis (12%) and

other surgical emergencies e.g. intra-abdominal abscesses (26%). The explanation for this difference lies in the fact that all the patients in Ohene-Yeboah's study had proven TB, while only 22% of the patients in the current study had proven TB.

Two studies that documented **imaging** findings of TB abdomen were found and compared to the current study. These are summarised in table 4.2.

In 2014 Islam (35) conducted a prospective study in a South African hospital in Kwa-Zulu Natal. Although this was a surgical study its focus was on patients with abdominal TB and the surgical complications thereof. While HIV infection was not an inclusion criterion as in the current study, 80% of the participants were HIV-positive (35).The study focused on using clinical parameters such as haemoglobin levels, albumin levels and the presence of acidosis to determine the level of illness. They also looked at ICU admission and whether patient required total parenteral nutrition (TPN) (35). Only six of their patients had CT of the abdomen, of which 50% had bowel perforation and the other 50% where found to have ascites, lymphadenopathy and bowel wall thickening (35). Although the number of scanned patients is significantly lower than the current study, the CT scan findings of the patients in the study by Islam were quite similar to ours (35). Table 4.2 summarises these findings and compares them to this study.

The patients in the Islam study had a significant mortality and morbidity associated with surgery. Nineteen patients (38%) died.
Significant morbidity was attributed to entero-cutaneous fistulae that resulted (35). The recommendation from that study was that the use of CT at **presentation** could improve

outcome of these patients and guide clinical management in the cases where surgery might be contra-indicated. This is paramount in clinical decision-making and to prevent inappropriate laparotomy (35). The current study also advocates the judicious use of CT in the HIV positive patient presenting with an acute abdomen for these reasons.

Table 4.2. Comparison between the current study and related studies

	Randin (1995) (39)	Shaukat (2010)(37)	Islam (2014) (35)	Singo (2015) (The current study)
Sample size	259 patients	58 patients	49 patients	50 patients
Country	United States of America	Pakistan	South Africa	South Africa
Inclusion criteria	HIV-positive patients with abnormal CT scan findings	Suspicion of Abdominal TB	Patients with suspected and confirmed abdominal TB that had emergency laparotomy (includes HIV-infected patients – 80%)	HIV-positive Acute Abdomen
Exclusion criteria	Patients who refused HIV testing	On TB treatment, urogenital TB	Nil	
Study design	Prospective study	Retrospective record review	Prospective study	Retrospective record review
Focus	To evaluate abdominal computed tomographic (CT) findings in patients with HIV infection	Descriptive. Common findings of abdominal TB on CT scan	Surgical complication of patients with TB of the abdomen that underwent emergency laparotomy	CT findings of HIV-infected patients with acute abdomen
Contrast with current study	Patients did not specifically present with an acute abdomen	No correlation with clinical outcome No correlation with HIV status or immune deficiency	Not all patients were HIV-positive Focus on complications of surgery No specific focus on CT scan	
HIV/TB co infection	22%	Not mentioned	80%	50%
Clinical data	TB culture, Histology	Nil	Hb, Albumin, Acidosis, ICU	WCC, CRP, AFB, TB culture, Histology

available			admission, TPN required	
CT protocol	Mostly post contrast +/- delay +/- oral contrast	Post contrast with IV and oral contrast	Not specified Only 6 patients had CTs	Mostly post contrast +/- delay +/- oral contrast
Clinical findings / diagnosis	Correlation with biopsy, culture and histology results	No clinical focus, descriptive only	Used clinical parameters to rate illness severity (see clinical data above)	Normal 2%* Surgical emergency 74% TB related 50% Inflammatory Bowel 4% Gynaecology related 16% Other 22%
Surgery done	Not mentioned	Not mentioned	100%	18%
CT Findings	Normal 0% Surgical emergency - Appendicitis 1% - Abscess 2% - Other 2% TB Related 22% - Lymphadenopathy 61% - Bowel wall thickening 24% - Visceral abscesses 41% Malignancy 38%	Ascites 75% Lymphadenopathy 55% Omental thickening 57% Bowel wall thickening 28% Visceral abscesses 6%	Bowel perforation 50% Ascites (free fluid) Lymphadenopathy - 50% Bowel wall thickening -	Normal 0% Surgical emergency 50% - Perforated viscus 0% - Appendicitis 4% - Bowel obstruction 18% - Abscesses 26% TB related 44% - Ascites 20% - Lymphadenopathy 90% - Omental thickening 0% - Bowel wall thickening 32% - Visceral abscesses 32% Inflammatory Bowel conditions 14% Gynaecology related 22% Other 30%

*One patient's discharge diagnosis was normal, or no abnormality was found. The CT scan findings were consistent with lymphadenopathy and gynaecological pathology.

Shaukat (37) conducted a descriptive study of CT findings of 58 patients with suspected abdominal TB, with CT protocols very similar to the current study. However, this study, in contradistinction to the current study and to the study by Islam (35), focused solely on CT scan findings and did not comment on HIV status, the clinical presentation (e.g. acute abdomen) or clinical sequelae such as surgery.

In the study by Shaukat (37) the most common imaging finding was ascites (75%) followed by omental thickening (57%) and lymphadenopathy (55%). In our study the most common finding was lymphadenopathy, found in 90% of the patients while bowel wall thickening and visceral abscesses were found more often in our study. Omental thickening was only found in 6% of our patients.

Of the 58 patients in the study by Shaukat, two had normal scans and nine had other surgical diagnoses not related to TB which included appendicitis, diverticulitis and bowel wall lymphoma (37). This was similar to the patients in our study who also had a high incidence of surgical conditions.

A study of CT findings of patients with HIV by Randin (39) showed that the majority of the patients had HIV related conditions (78%). The commonest findings were of lymph adenopathy (61%), hepatomegaly (39%) and splenomegaly (24%). Gastric masses or wall thickening (24%) and hepatic (19%) and splenic (21%) microabscesses were also found. Thirty-four percent of patients in that study had TB while 24% had evidence suggestive of lymphoproliferative disease. Both of these conditions were confirmed histologically (39).

In the current study the readers were not asked to comment on the size of the visceral organs but noted the presence of hepatic (10%) and splenic (10%) microabscesses. The major similarity with the study by Randin was the findings of lymphadenopathy, which was found in 90% of our patient population and 61% of the patients in Randin's study. Forty-two percent of patients in our study had a diagnosis of TB, which was also more than the study by Randin (22%). Neither of these studies characterised the adenopathy.

Our study showed a larger number of patients with bowel wall thickening (32%) and other pertinent findings of acute abdomen such as pneumoperitoneum (34%) and abdominal collections (42%). Although the study by Randin focused on HIV-positive patients, the patients in that study did not present with acute abdomen. This could account for these differences.

The abovementioned studies demonstrate the importance of CT scan in HIV positive patients presenting with acute abdomen. CT can assist with identifying features of abdominal TB as well as the detection of other surgical conditions and the associated complications in these patients (35, 37). CT can be used to plan surgical management or radiological intervention (35). It is clear that CT scan is essential in HIV-infected individuals with acute abdomen to diagnose surgical emergencies and to identify TB of the abdomen that would negate the need for surgery. CT scan in HIV-positive patients with acute abdomen was correct for diagnoses other than TB in 86% of cases (NPV – 86%).

4.5. Limitations of the current study

This study did not include patients that had a sonographic diagnosis of TB. These patients did not have a CT scan and were treated based on their sonographic findings. Our recommendations, however, advocate that all HIV-positive patients presenting with clinical evidence of an **acute abdomen** should have a CT scan in the emergency situation, as a high number of patients in this study had a surgical diagnosis (84%).

The retrospective nature of this study created an inherent bias with regards to the discharge diagnosis of probable TB. The diagnosis of "probable TB" could have been made after the CT scan results suggested abdominal TB.

This study did not look at the post surgical complications of the patients that did undergo laparotomy or any other long-term complications.

4.6. Application of this knowledge

The fact that CT scan can readily differentiate those patients who require emergency surgical intervention from those who would benefit from conservative management compels us to advocate that these patients undergo CT as an emergency procedure.

CT scan provides a good roadmap for surgery but more importantly, it can confidently exclude abdominal TB and its complications.

4.7. Future Research

There are still several aspects of this topic that have not been fully explored by this study or the reviewed literature.

The lack of evidence with regards to the surgical outcome of the HIV-infected patient can be further explored by a prospective study that will follow these patients up longitudinally with reference to complication rates of operative or non-operative management of HIV-infected patients that present with an acute abdomen. A further study should also look at radiological intervention in patients that present with collections.

5. Conclusion

The HIV-infected patient with acute abdomen presents a diagnostic dilemma for surgeons and physicians alike.

This study has shown CT scan to be a very useful tool in the management HIV-positive patients that present with acute abdomen. CT not only identified and excluded TB of the abdomen; it very frequently accurately diagnosed other surgical and gynaecological conditions that presented in our patient population. This was paramount in planning further management of the patients.

CT was found to be a reliable tool as readers showed good agreement in the findings.

The HIV-positive patient with acute abdomen should undergo a contrasted CT scan as part of their work-up not only to diagnose surgical emergencies but also to avoid unnecessary surgery.

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Appendix A: Data Collection Sheets

CT SCAN DATA COLLECTION SHEET		
Study Number		
Age	Gender M F	Date Of Study
Presenting Complaint		
Tb Related	Ascites Complex	Bowel Wall Thinkening
	Ascites Simple	Liver Microabsecces
	Abdominal Collections	Splenic Macroabscesses
	Omental Thickening	Splenic Microabscesses
	Mesenteric Thickening	Contrast Extravasation From Bowel
	Mesenteric Ischaemia	Pneumoperitonuem
	Complex Mass	
	Pneumotosis	
Lymphadenopathy	Coeliac	Porta Hepatis
	Para Aortic	Perisplenic
	Mesenteric	Pelvic
	Periappendiceal	Inguinal

CT SCAN DATA COLLECTION SHEET		
Study Number		
Date of Study:	**GENDER: M F**	**Age**
CT Findings	**YES**	**NO**
Normal / No Abnormality		
Surgical Emergency: - Perforated viscus [ ] - Appendicitis [ ] - Bowel obstruction [ ] - Abscess [ ] - Other [ ]		
TB		
Inflammatory/Infective Bowel Disease		
Gynaecological		
Other		

CLINCAL DATA COLLECTION SHEET

Study Number

Age	Gender M F		Date Of Study
Presenting Complaints			
Clinical	Night Sweats		
	TB Contact		
	Chronic cough		
	Generalized lymphadenopathy		
	Ascites		
Laboratory Results	WCC		TB Culture
	CRP		Blood Culture
	AFB		Histology
Lymphadenopathy At Surgery	Coeliac		Porta Hepatis
	Para Aortic		Perisplenic
	Mesenteric		Pelvic
	Periappendiceal		Inguinal

CLINICAL DATA COLLECTION SHEET		
Study Number		
Date of Study:	**GENDER:** M F	**Age**
Gold standard clinical parameters	**YES**	**NO**
Final / discharge / surgical/ treatment diagnosis of 'Normal / No Abnormality'		
Surgical final diagnosis - Perforated viscus [ ] - Appendicitis [ ] - Bowel obstruction [ ] - Abscess [ ] - Other [ ]		
'Definite TB': (Culture positive or AFB smear positive or Xpert positive)		
'Probable TB' (in absence of 'definite TB' features): - On TB treatment or... - Clinical diagnosis of TB or..... - 2 or more of the following [night sweats; TB contact; chronic cough; weight loss]		
Final / discharge / surgical/ treatment diagnosis of IBD		
Final / discharge / surgical/ treatment diagnosis of Gynaecological pathology		
Final / discharge / surgical/ treatment diagnosis of 'other'		

Appendix B: Ethics Clearance Certificate



HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M131151

NAME: (Principal Investigator)	Dr Tshiwela Phumudzo Pilar Singo
DEPARTMENT:	Radiation Sciences Helen Joseph Hospital
PROJECT TITLE:	Abdominal Computer Tomographic Findings in HIV Infected Patients Presenting with Acute Abdomen
DATE CONSIDERED:	29/11/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Su Lucas
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 10/01/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**

Principal Investigator Signature M131151 Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES