COMPARISON OF EMPYEMA THORACIS PRESENTATION BETWEEN HIV INFECTED AND NON HIV INFECTED PATIENTS AS SEEN AT A TERTIARY HOSPITAL IN KENYA.

A dissertation submitted in partial fulfillment of the requirement of the University of Nairobi for the award of the degree of Master of Medicine (M.Med) in General Surgery.

By

Dr Nyamohanga Marwa Patrick

2013.
DECLARATION

I hereby declare that this research proposal is my own original work and has not been presented for a degree in any other University.

Sign…………………………… Date……………………..

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H58/76510/09

MBChB (U.O.N).
APPROVAL

This dissertation has been submitted for examination with our approval as university supervisors.

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DEDICATION

To my dear wife Carolyne, daughter Vanessa and son Warren who endured the long hours of absence as I undertook this study.

To my late mother Esther Mokami, for teaching me how to walk and shaping my thinking.

My guardian and special mentors Mr. and Mrs. Shadrack Manga, for teaching me how to walk again after the demise of my parents. You will always be a source of inspiration.
ACKNOWLEDGEMENT

I would like to offer my sincere gratitude to the following people, without whose input, this work would not have been complete;

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LIST OF ABBREVIATIONS

CDC - Center for Disease Control
UK - United Kingdom
VCT - Voluntary Counseling and Testing
PITC - Provider Initiated Testing and Counseling
PTB - Pulmonary Tuberculosis
HIV - Human Immunodeficiency Virus
KNH - Kenyatta National Hospital
LDH - Lactate Dehydrogenase

DEFINITION OF OPERATIONAL TERMS

EMPYEMA; was defined as presence of pleural fluid level on chest radiograph, whose aspiration or drainage revealed frank pus.
ABSTRACT

Background:

Emphysema thoracis accounts for 23% of chest related complications in Human Immunodeficiency Virus-Acquired immunodeficiency Syndrome (HIV/ AIDS) and is a frequent complication of pneumonia in patients with HIV. Patients infected with HIV developing empyema thoracis tend to present late and are sometimes subjected to different management modalities with a lot of complications. Existing literature shows that this results in long hospital stay, high morbidity and mortality and that HIV infection has changed the pattern of presentation of many diseases. A clear understanding of symptoms, signs and microbial causes will help bridge the knowledge gap leading to early diagnosis and shortened hospital stay among these patients.

Objective: To compare the symptoms, signs and microbial causes of empyema thoracis between HIV and non HIV infected patients.

Study design: Cross-sectional comparative study at Kenyatta National Hospital over 4 month’s duration between December 2012 and April 2013.

Methods and materials: We recruited 32 HIV infected patients and 32 non HIV infected patients making up a total of 64 subjects using convenient sampling method. Independent variables were presence or absence of HIV infection. The dependent variables were signs, symptoms and microbiology of empyema thoracis.

Statistical analysis: Graph Pad Instat ™ version 2.04 statistical software was used for analysis of data. The p value of equal or less than 0.05 was considered significant.
Results: Thirty six males (56.25%) and 28 females (43.75%) participated. Chest pain was the most common and consistent symptom in both HIV infected and non-HIV infected patients, 100% and 97% respectively. Cough was the second commonest symptom seen in 97% of HIV and 84% of non-HIV infected. Weight loss was noted in 81.3% of HIV and 53.1% of non-HIV infected patients. Patients without HIV infection presented with massive pleural pus with midline shift in 43.8%, while those with HIV infection only 15% had a noticeable midline shift. Whereas 81.3% of HIV infected patients reported fever prior to hospital admission only 68% had clinically demonstrable fever. Among the non-HIV infected, 66.4% reported febrile illness but only 59% had demonstrable fever. The commonest etiological factor among the HIV infected patients was TB (50%) and Para pneumonia (47%). In non-HIV infected patient’s malignancies (34%) and iatrogenic causes mainly chest tube insertions (32%) were the main etiological factors. The most common cultured organism in HIV infected were pseudomonas spp (25%) while Staphylococcus aureus were the most common isolates among non HIV infected at 34%.

Conclusion: Chest pain is the most common and consistent symptom in both HIV and non-HIV infected patients presenting with empyema thoracis. Aseptic technique should be observed during chest tube insertion at all times.
INTRODUCTION

Empyema thoracis is the accumulation of pus in the pleural space also defined as pleural fluid with a pH less than 7.1 and either lactate dehydrogenase (LDH) level more than 1000 i.u/l or glucose level less than 40 mg/dl. The management of empyema thoracis remains a challenge to physicians and surgeons\(^1\).\(^2\). The condition presents in three sequential stages namely; initial exudation stage, fibrino-purulent stage and organization stage\(^3\).

Human Immunodeficiency Virus-Acquired Immunodeficiency Syndrome is an immunosuppressive condition that occurs in human beings infected with HIV and presents in 4 stages as per the Center for Disease Control (C.D.C) classification. Stages 1 and 2 are mild without opportunistic infections while Stage 3 and 4 have a variety of HIV/AIDS related problems and opportunistic infections.

The emergence of HIV has changed the pattern of presentation of many diseases and the pattern of change is different when compared between developing and developed countries\(^4\). Despite the advances in antibiotics therapy during the last decades, thoracic empyema remains a common clinical entity with significant associated morbidity and mortality.

Empyema thoracis accounts for about 23% of chest related complications in HIV/AIDS and is a more frequent complication of pneumonia in patients with HIV, with an incidence of 5.4% \(^1\).\(^2\). Different studies have shown that empyema thoracis in HIV has an indolent presentation therefore the diagnosis is usually delayed. In this regard patients have an associated long hospital stay even after surgical management such as chest tube insertion, thoracotomy or decortication\(^5\). Pleural effusions occur in as many as 27% of hospitalized HIV infected patients, of which 40-61% are associated with bacterial infections\(^1\).\(^3\). The prevalence of different causative organisms responsible for pleural infection varies from country to country\(^4\).\(^6\). Pneumococcal infection remains the most common cause of empyema in developed countries while *Staphylococcus aureus* is the most common cause of thoracic
empyema in developing countries among non HIV patients \(^6\). Literature has paucity of local data on the above hence the need for local epidemiological study in order to give a guide on antibiotic choices. This study aims to elucidate the symptoms of empyema thoracis as seen in a HIV background and compare them with those of non HIV infected patients.
LITERATURE REVIEW

Empyema thoracis was first described by Hippocrates who defined drainage of the pleural space as the cornerstone of its management. Empyema thoracis can either be total or loculated and is invariably a secondary disease, never primary and is almost always unilateral\textsuperscript{7,8}.

In Kenya, in the pre-HIV era, a 1978 study, reported non-tuberculous pulmonary diseases as the commonest cause of empyema thoracis at 27.2\%, followed by trauma at 18.7\% and tuberculosis at 16.6\%; while in 1981 it was reported that pyogenic pneumonia was the most common cause accounting for 39.3\%, tuberculosis at 38.8\%, malignant tumours at 2.2\% and thoracotomies 0.5\% \textsuperscript{9,10}. Later, in 1999, a 10 year retrospective study by Kinyanjui\textsuperscript{11} of 224 subjects, found post pneumonic complications to account for 39\%, pulmonary tuberculosis at 38\% and thoracotomy at 0.5\% of empyema thoracis.

This changing pattern on the etiologies of empyema thoracis from previous studies \textsuperscript{9,10} shows that there is need to find out the changes that have taken place over the last 13 years. The two studies (by Oburra and later Kinyanjui) had anticipated an increase in empyema thoracis at Kenyatta National Hospital due to increasing prevalence of poverty and HIV respectively \textsuperscript{9,11}. However, there is no current data indicating whether the anticipated changes ever took place. In the U.K-based Multicentre Intrapleural Sepsis Trial (M.I.S.T) of 430 patients with empyema thoracis, the median duration of symptoms prior to recruitment was 14(8-28) days. Acute febrile illness with localized pleurisy was seen in aerobic infection, while anaerobic infections had insidious symptoms with poor appetite, weight loss and less prominent fever \textsuperscript{12}.

In HIV negative patients the following symptoms have been documented in empyema thoracis; fever as a symptom in 68\% of patients, cough 62\%, dyspnoea 38\%, chest pains 60\%, abdominal pains 17\%, diarrhea, fever and vomiting 17\% \textsuperscript{13}. A study in Zambia \textsuperscript{5} showed that patients with HIV and tuberculosis on treatment for thoracic empyema were found to have symptoms of cough in 37\%, chest pains in 74\% and lymphadenopathy in 72\%. However these symptoms are also common in patients with tuberculosis and \textit{Pneumocystis}
and are unlikely to guide towards the diagnosis of empyema thoracis. Chest pains, cough, and dyspnoea were reported to be the main and commonest symptoms of empyema thoracis in Kenya.  

**Microbial causes**

The prevalence of causative organisms of pleural infection varies among countries for example in United States of America (USA) empyema thoracis occurs mainly in tuberculosis patients. In developing countries it occurs both as complications of tuberculosis and community acquired pneumonia. In non-HIV patients, *Staphylococcus aureus* and *Streptococcus pneumoniae*, combined causes 70% of empyema thoracis. In HIV infected patients, data is deficient yet this is key in arriving at appropriate antibiotic choice albeit empirically. Studies from the U.K, Canada and New Zealand demonstrate that *Streptococcus milleri* is the most common isolate in adults with community acquired empyema. The proportion ranges between 32 to 50% of cases. Some reports suggest that patients with *Streptococcus milleri* related empyema thoracis more commonly have co-morbidities, such as underlying malignancies or diabetes mellitus. In pediatric empyema, *Streptococcus pneumoniae* is the most common organism and account for up to 51% of cases. Oburra found that *Mycobacterium tuberculosis* accounted for 25%, and *Staphylococcus aureus* 42.1%, being the most common cause of empyema thoracis in non HIV patients. Negative cultures were noted in 21% of all empyema thoracis while *Pseudomonas* accounted for 10.5% and *E. coli* 5.5%. Currently there is scarce data available among those with HIV.
STUDY JUSTIFICATION

Empyema thoracis is a disease of historical importance and is still a modern menace. Incidences of empyema are rising in both developed and developing countries, including in pediatric populations. In Scotland, the incidence of empyema has risen up to 10 times in 1-4 year old children since 1998. Similar reports have been published from the USA, Canada and elsewhere in Europe; the trend is mirrored in adults with a significant mortality in the latter group.

Pulmonary complications in patients infected with HIV are common and are associated with high rates of morbidity and mortality. Twenty three percent of HIV infected patients present with empyema thoracis yet there is little data available in Kenya and Africa in general on symptoms and presentation, and an unresolved debate rages on especially on the ideal management approach.

Failure to understand the presentation patterns of empyema thoracis in HIV by clinicians, results in delayed diagnosis. There is paucity of data on causative organisms of empyema thoracis in HIV to guide the clinicians on appropriate antibiotic choice. The prevalence of HIV/AIDS, wider use of immunosuppressants and organ transplantation, and increasing age of the population means that pleural infection will continue to remain a common and significant illness.

HYPOTHESIS

Symptoms, microbiology and etiology of empyema thoracis in HIV infected and non HIV infected patients are the same.
BROAD OBJECTIVE
To compare the presentation of empyema thoracis between HIV infected and non HIV infected patients.

SPECIFIC OBJECTIVES
1. Determine the signs and symptoms of empyema thoracis in HIV and non HIV infected patients.
2. Determine the duration of symptoms at time of hospital presentation in HIV and non HIV infected patients.
3. Determine the microbial profile in HIV and non HIV infected patients.

STUDY DESIGN
STUDY DESIGN: A cross-sectional comparative study

STUDY SETTING: The accident and emergency department, surgical and medical units of Kenyatta National Hospital.

STUDY POPULATION: Patients admitted to Kenyatta National Hospital with empyema thoracis, Case group being HIV +ve and controls HIV –ve patients.

STUDY DURATION: Four months (December 2012 to 18th March 2013).
MATERIALS AND METHODS

SAMPLE SIZE
To determine the number of patients required in each category (Non-HIV infected and HIV infected) patients. Lehr’s equation of sample size determination for two groups was used as follows:

\[ n = \frac{16}{\Delta^2} \]

Where

\[ \mu_0 - \mu_1 \]

\[ \Delta = \frac{\delta}{\Delta} \]

Assuming a standardized difference, \( \Delta \), is expected to be 0.5.

Then \( 16 / 0.5^2 = 64 \) patients

Therefore a minimum of 64 subjects were sampled.

To compare HIV infected and non HIV infected empyema thoracis patients, in each group 32(HIV) infected patients were recruited while the other 32(non HIV) infected patients were also recruited through convenient sampling. Whether 32 subjects in each group were to provide sufficient statistical power was determined using the online power and sample size calculator (http://www.statisticalsolutions.net/pss_calc.php) ²⁹. Using the default values for alpha (\( \alpha \)) (0.05) and sigma (\( \delta \)) (0.5) a sample size of 32 gave a power of 1.000 which was
higher than the default value of 0.8. Therefore, a minimum of 32 HIV infected and 32 non HIV infected subjects per group provided sufficient sample size for the study.

**INCLUSION CRITERIA**

All patients with empyema thoracis admitted at KNH and consented to participate in the study.

Diagnosis of empyema thoracis was defined by presence of pleural fluid level on Chest radiograph, whose aspiration or drainage revealed frank pus.

**EXCLUSION CRITERIA**

Those who did not consent to the study or were unable to consent such as the mentally ill patients

**SAMPLING PLAN:** All consecutive patients were recruited through convenient sampling method.

**DATA COLLECTION:** At admission data was collected by the principal researcher and two trained research assistants with MBChB, using predesigned questionnaires. The data collected included the patient biodata, duration and type of symptoms, signs, etiological and co-morbid factors, culture and sensitivity.

**Specimen collection:** Pleural fluid (volume of 4 mls) was collected from patients with empyema thoracis across the spectrum (irrespective of the stage) under aseptic technique using a syringe and needle through the anatomically recognized safe triangles at the time of chest tube insertion by a trained medical doctor to minimize risk of bleeding or pneumothorax. Specimens were placed in standard KNH sterile bottles and 2 mls taken to the laboratory by the principal researcher or assistants within 30 minutes for microbiology (gram stain, ZN stain and culture and sensitivity). Another 2 mls of pleural fluid was submitted for
biochemistry (LDH, Glucose and pH). Microbiology and biochemistry studies were undertaken at the KNH laboratories. Microbiological analysis was by a team of four sensitized medical laboratory technologist with diplomas in medical laboratory technology working in different shifts. Biochemical analyses were undertaken at the KNH biochemistry laboratory, a team of four sensitized medical laboratory technologist who are holders of diplomas in medical laboratory technology handled and processed the specimen. To ensure that quality and standards are maintained the in-charge of biochemistry laboratory supervised the handling of specimen.

Trained HIV counselors were involved in the counseling and testing of patients whose HIV status was unknown. The pre-test counseling was performed by sensitized ward-attached trained VCT counselors who strictly followed the protocol of the National AIDS and STI Control Programme, Ministry of Public Health and Sanitation, Kenya.Nairobi:NASCOP:2008. For the purpose of this study, the model of Provider Initiated Testing and Counseling (PITC) was used. The principal researcher or the research assistants would explain the procedure and the reasons for requesting the test to the patient. If the patient agreed, then the VCT counselor would take the patient through the pre-test session where basic HIV information would be provided. The patient would be given time to ask questions and received personalized information. The information given was beneficial to knowing ones HIV status, an explanation of the HIV testing process, and the need for consent for HIV test and availability of support, as well as care and treatment for those who tested positive. Therefore the licensed rapid test kits were used. Blood samples for HIV test would be collected using the pin prick method by the HIV counselor. All positive test results had to be confirmed by at least one other test, using the serial testing algorithm.
DATA MANAGEMENT AND ANALYSIS
All data was recorded in MS Excel data sheets saved under password protection only accessed by personnel involved in the project. Hard copy back-ups were securely locked in a cabinet only accessed by personnel involved in the project.
The independent variables were presence and absence of HIV infection. The dependent variables were signs, symptoms and microbiological findings. Student T-test was used for comparison of mean differences of biochemical parameters between HIV and non HIV infected patients.
Chi square or Fisher’s exact test was used as appropriate to determine any association of HIV and non HIV data that was then put into tables with mutually exclusive and exhaustive cells.
Graph Pad Instat™ Version 2.04 statistical software was used for analysis of the data. A p value of less than 0.05 was considered significant.

DATA PRESENTATION
Data Frequencies were presented in tables, graphs and pie-charts.

STUDY LIMITATIONS
A few patients had been started on antibiotics prior to specimen collection.
In 21% of the patients in both HIV and non-HIV infected the cultures were negative.
The biochemistry machine was unable to analyze the thick pus despite dilution.

DELIMITATIONS
Prompt specimen collection at or on admission
Use of HIV counselor and ensuring patient’s confidentiality
Dilution of the thick purulent material in 1:10 ratio made it possible to analyze biochemically.
ETHICAL CONSIDERATIONS AND APPROVAL

The study commenced upon approval by the department of surgery (UON) and KNH Ethics and Research committee.

An informed consent was obtained from each of the participant prior to enrolment in the study. The guardian was required to sign consent on behalf of participants who were unable to do so and an assent form in addition to the consent was signed for minor’s ages 13 to 17 years while a guardian signed consent was considered sufficient for children below 13 years of age. Counseling of the participants was carried out sensitizing the patients that the specimen collection would be associated with some discomfort and bearable pain.

Those who declined participation were not denied treatment that they deserved because of their decision not to participate since participation was voluntary.

There was no extra cost incurred for participating in the study, confidentiality and privacy were observed.

Data collected will be destroyed upon completion of dissertation.
RESULTS

A total of 64 patients with empyema thoracis who met the inclusion criteria were recruited.

Demographic characteristics of the general study population

Study participants were aged between 5 years and 69 years. Most were adults with only 3 patients being children. Males were 36 (56.25%) and females 28 (43.75%).

The analyzed data is as presented below.

1. Signs and symptoms of empyema thoracis in HIV and non HIV infected patients.

Figure 1: Presenting symptoms for HIV positive and negative patients

Other presenting symptoms which were observed at least once in none HIV infected patient included draining of pus from the surgical site, nocturnal breathlessness and orthopnoea, leg swelling, coma, easy fatigability, oral thrush, reduced appetite and pus oozing from the chest stab wound. Three patients who were HIV infected also presented with the following
symptoms each; inability to walk without support, bilateral oedema of the lower limbs and one gave a history of trauma/stab wound into the chest.

Weight loss was significantly higher in HIV positive (81.3%) compared to HIV negative patients (53.1%) (p < 0.05, by Fisher’s Exact test). Lymph node enlargement was also more frequent in HIV infected patients (Table 1 below).

Table 1: Symptoms of empyema thoracis in HIV positive and negative patients

<table>
<thead>
<tr>
<th></th>
<th>Number of HIV negative</th>
<th>Number of HIV positive</th>
<th>p Value(^a)</th>
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<tr>
<td>Cough</td>
<td>27</td>
<td>31</td>
<td>=0.1961</td>
</tr>
<tr>
<td>Chest pain</td>
<td>31</td>
<td>32</td>
<td>=1.0000</td>
</tr>
<tr>
<td>Fever</td>
<td>21</td>
<td>26</td>
<td>=0.2574</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>9</td>
<td>=0.7735</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>14</td>
<td>16</td>
<td>=0.8025</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4</td>
<td>5</td>
<td>=1.0000</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>3</td>
<td>5</td>
<td>=0.7070</td>
</tr>
<tr>
<td>Weight loss</td>
<td>17</td>
<td>26</td>
<td>=0.0319</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>4</td>
<td>=0.1132</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>8</td>
<td>16</td>
<td>=0.0697</td>
</tr>
<tr>
<td>General malaise</td>
<td>12</td>
<td>13</td>
<td>=1.0000</td>
</tr>
</tbody>
</table>

\(^a\)p Value obtained by Fisher’s Exact test.

p Value < 0.05 considered significant
Co-morbidities

Diabetes mellitus was not observed in any patient. Malnutrition was observed in both HIV positive (3.1%) and negative (9.4%) patients (Figure 2 below). Though more frequent in HIV negative patients the difference was not significant (p > 0.05, Fisher’s Exact test).

**Figure 2**: Co-morbidities in HIV positive and negative patients

![Figure 2](image)

Other co-morbidities observed among HIV negative patients included pulmonary tuberculosis, acute decompensated heart failure, heart disease, severe head injury and a tissued central line, peptic ulcer disease, valvular heart disease, rheumatoid arthritis and chest stab wound. One patient with HIV infection was also found to have valvular heart disease.

Most significant co-morbidity observed in women was breast cancer. Among sixteen women without HIV, seven (43.8%) had breast cancer while none of the HIV positive women had breast cancer.
Signs of Empyema thoracis

Presence of fever and pallor was higher among the HIV infected patients than the non-HIV infected patients while cyanosis was higher in HIV negative though the differences are not significant (p > 0.05, Fisher’s Exact test) (Figure 3 below).

Figure 3: Signs of empyema thoracis in HIV positive and negative patients

Respiratory system findings

Mediastinal shift was significantly higher among the HIV negative patients (43.8%) compared to the HIV infected (15.6%) (p < 0.05 [p=0.0272], Fisher’s Exact test). Other respiratory system findings were not significantly different between the two groups (p > 0.05) (Figure 4 below).
Among four HIV negative patients we observed swelling of the surgical site, tracheal deviation, reduced chest expansion and joint deformity. Two patients with HIV infection had orthopnoea and oral thrush.

**Etiology of empyema thoracis**

Etiology of empyema thoracis differed between HIV negative and positive patients. Parapneumonic and PTB were higher in HIV positive while chest trauma, malignancies and iatrogenic causes were higher in HIV negative patients (Figure 5 below).
**Figure 5:** Aetiology of empyema thoracis in HIV positive and negative patients

The difference observed in parapneumonic, PTB and malignancies were significant ($p < 0.05$, Fisher’s Exact test). Iatrogenic causes though higher in HIV negative patients it was not significant ($p > 0.05$) as shown in Table 2 below.

**Table 2: Aetiology of empyema thoracis**

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>HIV negative</th>
<th>HIV positive</th>
<th>p Value$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Para pneumonic</td>
<td>4</td>
<td>15</td>
<td>=0.0054</td>
</tr>
<tr>
<td>PTB</td>
<td>7</td>
<td>16</td>
<td>=0.0360</td>
</tr>
<tr>
<td>Chest trauma</td>
<td>5</td>
<td>1</td>
<td>=0.1961</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>0</td>
<td>0</td>
<td>ND$^b$</td>
</tr>
<tr>
<td>Lung abscess</td>
<td>1</td>
<td>1</td>
<td>=1.5079</td>
</tr>
<tr>
<td>Malignancies</td>
<td>11</td>
<td>1</td>
<td>=0.0027</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>10</td>
<td>3</td>
<td>=0.0596</td>
</tr>
</tbody>
</table>

$^a$ p Value obtained by Fisher’s Exact test  
$^b$ ND – Not done  

p Value < 0.05 considered significant
2. Duration of symptoms at time of hospital presentation in HIV and non HIV infected patients.

Figure 6: Duration of symptoms prior to hospital presentation

Patients not infected with HIV had a varying range of days within which symptoms were present before presentation to hospital (Figure 6). They had extremes ranging from (1 day) to (728 days). The mean days of duration of symptoms at presentation in HIV infected were 44 days while non-HIV infected were 84 days (Table 3).

Table 3: Duration of symptoms in days

<table>
<thead>
<tr>
<th></th>
<th>HIV Negative</th>
<th>HIV Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean days</td>
<td>84.3</td>
<td>44.0</td>
</tr>
<tr>
<td>Median days</td>
<td>25.5</td>
<td>30.0</td>
</tr>
<tr>
<td>Minimum days</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Maximum days</td>
<td>728</td>
<td>210</td>
</tr>
<tr>
<td>Standard Dev.</td>
<td>140.9</td>
<td>47.0</td>
</tr>
</tbody>
</table>

Comparison of the two categories of HIV positive versus HIV negative using Mann-Whitney U test shows that there is no significant difference in duration of symptoms at presentation (p = 0.8140).
3. **The microbial profile in HIV and non HIV infected patients.**

Acinetobacter spp and Citrobacter were isolated only in patients without HIV infection (Figure 7 below).

**Figure 7:** Microbial profile in HIV positive and negative patients

Although more isolates of *Pseudomonas spp* were isolated in HIV positive (25%) than in HIV negative (6.3%) the difference is not significant (p >0.05, Fisher’s Exact test). On the other hand more isolates of *Staphylococcus aureus* were isolated in HIV negative (34.4%) than HIV positive (15.6%) and likewise the difference is not significant (p > 0.05, Fisher’s Exact test) as shown in table 4 below.
Table 4: Microbial profile

<table>
<thead>
<tr>
<th>Organisms Isolated</th>
<th>HIV Negative</th>
<th>HIV Positive</th>
<th>p Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count</td>
<td>%</td>
<td>Count</td>
</tr>
<tr>
<td>Acinetobacter spp</td>
<td>1</td>
<td>3.1</td>
<td>0</td>
</tr>
<tr>
<td>Citrobacter</td>
<td>1</td>
<td>3.1</td>
<td>0</td>
</tr>
<tr>
<td>E. coli</td>
<td>4</td>
<td>12.5</td>
<td>3</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>1</td>
<td>3.1</td>
<td>0</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>4</td>
<td>12.5</td>
<td>2</td>
</tr>
<tr>
<td>Pseudomonas spp</td>
<td>2</td>
<td>6.3</td>
<td>8</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>11</td>
<td>34.4</td>
<td>5</td>
</tr>
<tr>
<td>Staphylococcus aureus and E.coli</td>
<td>1</td>
<td>3.1</td>
<td>0</td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td>3</td>
<td>9.4</td>
<td>6</td>
</tr>
<tr>
<td>Pseudomonas spp and Staphylococcus aureus</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
</tr>
<tr>
<td>Staphylococcus aureus and streptococcus pneumonia</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
</tr>
<tr>
<td>No bacteria isolated</td>
<td>4</td>
<td>12.5</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>100.0</td>
<td>32</td>
</tr>
</tbody>
</table>

a p Value obtained by Fisher’s Exact test
p Value < 0.05 considered significant

Antibiotic susceptibility

Susceptibility of the bacteria to antibiotics did not differ significantly between HIV positive and negative with the exception of Imipenem to which resistance was higher in isolates from HIV negative patients (p < 0.05) (Table 5 below).
Table 5: Antibiotic sensitivity for bacterial isolates in HIV positive and negative patients

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>HIV Negative</th>
<th>Total tested</th>
<th>% Resistant</th>
<th>HIV Positive</th>
<th>Total tested</th>
<th>% Resistant</th>
<th>p Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Augmentin</td>
<td>8</td>
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<td>13</td>
<td>8</td>
<td>10</td>
<td>18</td>
<td>55.6</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>6</td>
<td>11</td>
<td>17</td>
<td>4</td>
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<td>17</td>
<td>76.5</td>
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<td>Ceftriazone</td>
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<td>13</td>
<td>26</td>
<td>11</td>
<td>12</td>
<td>23</td>
<td>52.2</td>
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<td>Ciprofloxacin</td>
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<td>9</td>
<td>13</td>
<td>8</td>
<td>7</td>
<td>15</td>
<td>46.7</td>
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<td>Levofloxacin</td>
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<td>2</td>
<td>50.0</td>
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<tr>
<td>Cefotaxime</td>
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<td>4</td>
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<td>Meropenem</td>
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<td>0.0</td>
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<td>Amikacin</td>
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<td>6</td>
<td>1</td>
<td>7</td>
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<td>0.0</td>
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<td>4</td>
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<td>Vancomycin</td>
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<td>ND</td>
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<td>ND</td>
</tr>
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<td><strong>Clotrimazole</strong></td>
<td><strong>ND</strong></td>
<td><strong>ND</strong></td>
<td><strong>ND</strong></td>
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<td>1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*a* p Value obtained by Fisher’s Exact test  
p Value < 0.05 considered significant  
ND – Test not done  
- Statistics not done because the numbers were too low  

Multidrug resistance (defined as organisms resistant to more than two antibiotics) was observed in bacteria isolates from both HIV positive and negative patients (Table 6 and Table 7)
Biochemical analysis

Glucose, pH and LDH levels were measured and the levels for pH were below 7.1, LDH was greater than 1000 while glucose was below 40mg/dl. Nine pleural fluid samples from the none-HIV patients and ten from HIV infected were not analyzable since they were too thick.

**Table 6: Antibiotic sensitivity for bacterial isolates in HIV negative patients**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Citrobacter</th>
<th>P. aeruginosa</th>
<th>E. coli</th>
<th>S. aureus</th>
<th>Acinetobacter</th>
<th>S. aureus</th>
<th>E. coli</th>
<th>E. coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Augmentin</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>R</td>
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<tr>
<td>Cefuroxime</td>
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<td>R</td>
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<td>R</td>
<td>S</td>
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<tr>
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<td>R</td>
<td>R</td>
<td>R</td>
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<td>S</td>
<td>R</td>
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</tr>
<tr>
<td>Ciprofloxacin</td>
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<td>R</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Imipenem</td>
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<td></td>
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<td><strong>Resistant total</strong></td>
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</tr>
</tbody>
</table>
**Table 7:** Antibiotic sensitivity for bacterial isolates in HIV positive patients

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Pseudomonas spp</th>
<th>P. aeruginosa</th>
<th>Pseudomonas spp</th>
<th>Pseudomonas spp</th>
<th>E. coli</th>
<th>S. aureus</th>
<th>Pseudomonas spp</th>
<th>S. aureus</th>
<th>Pseudomonas spp</th>
<th>E. coli</th>
<th>Pseudomonas spp</th>
<th>E. coli</th>
<th>P. aeruginosa</th>
</tr>
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<tbody>
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DISCUSSION

It is true that the emergence of HIV has changed the pattern of presentation of many diseases and that the pattern of change is different between developing and developed countries \(^4\). Our study conducted in a developing country shows that this statement has been validated. In our study, among the HIV positive patients the most consistent symptoms were weight loss in 81.3% which was significantly higher compared to 53.1% among the non-HIV infected patients. This differs from the Zambian study by Desai, and Mugalla \(^5\). Lymphadenopathy was also higher in HIV infected patients although the difference was not statistically significant. Lymphadenopathy may occur in other conditions such as PTB and lymphoma therefore may not be considered a specific symptom of empyema thoracis.

In our study chest pain was a symptom in 100% and 97% of HIV and non HIV infected patients respectively. Cough was the second commonest symptom in 97% of HIV and 84% non-HIV infected patients. Weight loss was third in the HIV infected (81.3%) and 53.1% in HIV negative patients. The chronic nature of HIV-AIDS may have contributed to the weight loss in patients with empyema thoracis, however the long duration of symptom prior to hospital presentation witnessed in HIV infected patients and the prolonged catabolic phase is a possible cause of the weight loss. Just like the Zambian \(^5\) study, chest pain still remains the most common symptom in both HIV and non-HIV infected patients. While 97% of HIV infected patients presented with cough in our study, only 37% of HIV infected patients had cough in previous studies \(^5,9,10\).

A noticeable symptom in this study among the HIV infected group was vomiting which was reported in 13%. None of the HIV negative patients presented with vomiting. It is worth noting that some HIV infected patients were already on highly active anti-retroviral therapy that are also known to cause nausea and vomiting, therefore this may not be a reliable symptom.

Unlike previous studies \(^13\), this study shows that none of the HIV negative patients presented with vomiting or abdominal pains and the most common symptoms in this group were chest pains, cough and fever. This observation clearly demonstrates a changing pattern of presentation in both HIV and non-HIV infected patients.
In this study fever and pallor were the commonest signs recorded among HIV infected patients (68% compared to 59%) and (35% compared to 19%) respectively. Despite some patients reporting hotness of body they had normal temperature. A number of them had been started on analgesics such as acetaminophen which have antipyretic effects. The anemia was probably as a result of chronic nature of the disease, late presentation and nutritional deficiency. Tachypnoea was the most consistent sign in both non-HIV and HIV infected patients in our study and this was comparable to previous studies\textsuperscript{5,9,13}.

Mediastinal shift was significantly higher (43.8%) among non-HIV patients compared to HIV infected patients (15%). The volume of pus was massive in non-HIV compared to HIV infected patients and this did explain the mediastinal shift. Cyanosis was commonly demonstrated among non-HIV infected patients. The cause of cyanosis is likely to have been the distress resulting from massive pleural fluid that was demonstrable in this group. Non-HIV infected patients have a stronger immunity and are likely to mount a significant immunological or inflammatory response following chest infection or neoplastic irritation of the pleural space. This may be the sole reason why they had voluminous pus.

In this study, the median duration of symptoms prior to hospital presentation in HIV and non-HIV infected groups were 30 days and 25.5 days respectively. Though not statistically significant, it is clear that HIV infected patients tended to present late by almost double that which had been reported in the U.K-based MIST study\textsuperscript{12}. The late presentation may be explained by the poor health seeking behavior in our population, self-medication and indolent nature of empyema thoracis in HIV.

Our study shows that the commonest causative organism in non-HIV infected patients were \textit{Staphylococcus aureus} in 34.5%. This is in tandem with reports in other studies, where Pneumococcal infection remains the commonest cause of empyema thoracis in developed countries while \textit{Staphylococcus aureus} is the leading cause in developing countries among non-HIV infected patients\textsuperscript{6}. Escherichia coli were reported in 12.5%, \textit{Pseudomonas aeruginosa} in 12.5%, \textit{Streptococcus pneumoniae} in 9.4% and \textit{Pseudomonas spp} in 6.3%. \textit{Klebsiella}, \textit{Citrobacter} and \textit{Acinetobacter} each
accounted for 3.1% of the empyema thoracis in the non-HIV infected group. This pattern of microbial infectivity is not unique to empyema thoracis but has also been reported in other conditions where there is good host immunity. This shows that a more virulent organism is needed to cause an infection if an individual’s immune system is competent.

In HIV infected group *Pseudomonas spp* were the commonest causative agents (25%) followed by *Streptococcus pneumoniae* (18.8%) and *Staphylococcus aureus* (15.6%). Though the difference may not be significant statistically, we were able to demonstrate a totally different picture in the microbial pattern when you compare between HIV infected and non HIV infected patients. This study shows that compromised immunity predisposes patients to infections by organisms that are less virulent and those that will otherwise not cause infection except in very sick patients in intensive care units or in a nosocomial pattern. *Acinetobacter spp* and *Citrobacter* were isolated only in patients who were non-HIV infected. Most patients with polymicrobial infections were those whose empyema resulted from iatrogenic causes especially after chest tube insertion, thus a breach in aseptic technique predisposed patients to polymicrobial empyema thoracis.

Negative cultures were reported in 12.5% of both HIV and non-HIV infected patients in our study, whereas previous studies in Kenya had reported negative cultures in 21% of empyema thoracis. The negativity range with conventional methods has been reported to be as high as 40%. Different postulations have been made to explain the negative cultures (sterile pus). It may simply represent effective antibiotic treatment prior to sample collection or alternatively, it may suggest that continual presence of bacteria is not necessary to sustain the ongoing inflammatory response after the initial bacterial invasion. It may also be due to lack of sensitivity of conventional cultural techniques. Molecular techniques have been used elsewhere to improve detection of bacteria, but these facilities are expensive and are not yet available or utilizable in our set up. The prompt submission of collected specimens to the laboratory for culture may have improved our culture yield compared to previous studies.
While *Streptococcus milleri* is the most common isolate in adults with community acquired empyema. Our study shows that among HIV infected patients *Pseudomonas spp* were the commonest causative agents while *Staphylococcus aureus* caused most of the empyema in the non-HIV infected patients. Our findings compares favorably with those of previous studies especially in empyema thoracis among non-HIV infected patients.

In pediatric age group, *Streptococcus pneumoniae* has been reported to be commonest causative agent accounting for up to 51% of empyema thoracis. In our study only 3 recruits were below the age of 12 years. One was a five years old HIV negative male in whom we cultured *Staphylococcus aureus* and *Escherichia coli*, the second was a 9 years old HIV negative male in whom we had negative cultures and a 7 years old HIV positive female in whom we cultured *Streptococcus pneumoniae*. Given the small number of children involved in our study it would be inappropriate to make a comparison or any inference on the commonest causative organism. The incidence of empyema thoracis has risen up to 10 times in children between the age of 1-4 years in Scotland, USA and Canada. In this study no one was below the age of 4 years, therefore we can conclude that the global trend of pediatric empyema is not mirrored in our set up.

The high incidence of empyema in the productive age group of 15 to 50 years in this study is consistent with the findings in the earlier study by Behra and Tandon. This is the same age bracket that has the highest HIV affliction rates in our set up, a trend that may impact negatively in our economic performance considering that these are the most productive members of our society.

In this study, susceptibility of the isolated organisms to antibiotics did not differ significantly between HIV infected and no-HIV infected patients. Imipenem resistance was higher in isolates from HIV negative patients than HIV infected and this difference was statistically significant. This Imipenem resistance may be explained by the nosocomial pattern of empyema thoracis noted in the non-HIV infected group. A number of these patients had been on multiple antibiotics prior to specimen collection. Multidrug resistance was observed in bacterial isolates from both HIV infected and non-HIV infected patients almost in equal proportions.
The biochemical analysis of pleural fluid demonstrated pH levels consistently below 7.1, LDH greater than 1000 and glucose below 40 mg/dl. This goes to show that the patients recruited into the study met the diagnostic criteria for empyema thoracis both clinically and biochemically as described in the methodology. A few samples from non-HIV and HIV infected patients were not analyzable since they were reported to be too thick despite attempts to dilute them. Most patients were beyond stage 1 (the exudative stage) because in stage 2 the biochemical findings usually are; pH less than 7.2 , glucose lower than 60 mg/dl and LDH is usually increased beyond 1000, consistent with the fibrinopurulent stage. The few patients whose pleural fluid was too thick to analyze were in the organizational stage. In this stage when treatment is delayed the pleural fluid may drain spontaneously through the chest wall, a well documented clinical condition called empyema thoracis necessitans as reported in one of our patients. The advanced stage of the disease at the time of hospital presentation is in keeping with poor health seeking behavior, poverty, attempt to seek alternative care and the missed diagnosis due to the non-specific symptoms especially in the HIV infected group.

Although other studies show that diabetes mellitus and malignancies are associated with Streptococcus milleri empyema thoracis 21. In this study diabetes mellitus was not observed in any of the patients. Malnutrition was a common co-morbid factor in both HIV and non HIV infected patients. However we did not attempt to match causative organisms with the co-morbid factor.

The prevalence of different etiological factors for pleural infection varies from country to country. An example is in the USA where empyema thoracis mainly occur in patient with tuberculosis, whereas in the developing countries it occurs both as a complication of tuberculosis and community acquired pneumonia 14, 15. Our study established that among HIV positive patients the most common etiological factor was pulmonary tuberculosis (50%) and only 22% of non-HIV infected patients had PTB. This is a likely pointer on how the rising incidence of tuberculosis is impacting negatively among HIV infected patients. Para pneumonia was a factor in 47% and 13% of HIV and non-HIV infected respectively. The most common etiological factor among non-HIV infected patients
were malignancies in 35% and only 4% in HIV infected. The most significant co-morbid factor observed in female patients in our study was breast cancer. Among the 16 women without HIV infection who participated in the study, seven (43.8%) had breast cancer while none of the HIV infected females had breast cancer. A number of these women had initially presented with malignant pleural effusion, for which chest tubes were inserted only to present later with empyema thoracis. This study raises concerns regarding malignant pleural effusions that progressed to empyema thoracis, and critically questions whether strict aseptic technique and adherence to protocol is being observed during chest tube insertion. Iatrogenic causes mainly post chest tube insertion was an important factor in 32% of non-HIV infected patients. Iatrogenic causes mainly post chest tube insertion was an important factor in 32% of non-HIV infected patients. In contrast the findings in the previous studies showed this only accounted for less than 0.5% of empyema thoracis 9,10.
CONCLUSION AND RECOMMENDATION

CONCLUSION

Chest pain is the most common and consistent symptom in both HIV and non-HIV infected patients presenting with empyema thoracis.

Weight loss and lymph node enlargement are important and common symptoms of empyema thoracis among the HIV infected patients and empyema thoracis tends to be massive with associated mediastinal shift in the non-HIV infected patients.

Pulmonary tuberculosis and para pneumonia were the commonest etiological factors causing empyema thoracis in HIV infected patients. While malignancies and iatrogenic causes such as chest tube insertion played a major role in the non-HIV infected, there was no significant difference in the duration of symptoms prior to hospital admission between these two groups. Pseudomonas spp were the most common causative organisms in the HIV infected patients while Staphylococcus aureus caused most of empyema thoracis in non-HIV infected patients. Susceptibility to antibiotics by isolated organisms did not differ significantly between the two groups of the study population. And Imipenem resistance was noted to be higher in the isolates from non-HIV infected group. Most patients presented late in stages 2 and 3 disease. It is indeed true that HIV has changed the pattern of presentation of empyema thoracis as it has probably done for many other diseases.

RECOMMENDATION

We recommend that a higher level of professionalism and aseptic technique be adopted and practiced in the minor theatre at KNH and elsewhere during chest tube insertion. This will minimize the risk of iatrogenic empyema thoracis.

We recommend that all patients suspected or confirmed to have HIV infection who present with chest pains and lymphadenopathy be evaluated for empyema thoracis.

We also recommend a follow up study to establish the role played by the level of CD4 count in HIV infected patients in development of empyema thoracis in future.
REFERENCES


APPENDIX 1

DATA COLLECTION SHEET

Study number……………………………………………..Hospital Number……………………………………………..

Date of Recruitment…………………………

Date of admission…………………………

1. Patient personal details.

(A)Sex Male □ Female □
(B)Age ……………………………
(C)Duration of symptoms before admission to hospital……………………………………………..

2. Presenting symptoms (code No=0, yes=1)

I. Cough □
II. Chest pains □
III. Fever □
IV. Nausea □
V. Dyspnoea □
VI. Abdominal pains □
VII. Diarrhea □
VIII. Weight loss □
IX. Vomiting □
X. Lymphadenopathy □
XI. General malaise □
XII. Others (specify)……………………………………………………………………

3. Have you used antibiotics before admission to hospital? (Code No=0, yes=1)
4. Co-morbidities (code no=0, yes=1).

I. HIV/AIDS

II. DIABETES MELLITUS

III. CHRONIC LUNG DISEASE

IV. CHRONIC LIVER DISEASE

V. MALNUTRITION

VI. OTHERS (SPECIFY) ..........................................................................................................................

5. Signs present (code No=0, yes=1)

a) General signs.

I. Fever........recorded.........

II. Cyanosis

III. Pallor

IV. Others (specify)

b) Respiratory system findings (code No=0, yes=1)

I. Tachypnoea

II. Mediastinal shift

III. Stony dullness

IV. Loss of breath sounds

V. Chest wall deformity

VI. Pleural cutaneous fistula

VII. Bronchopleural fistula

VIII. Others (specify) ..........................................................................................................................
6. Etiology of the empyema

I. Parapneumonic
II. P.T.B
III. Chest trauma
IV. Bronchiectasis
V. Lung abscess
VI. Malignancies
VII. Iatrogenic
VIII. Others (specify)………………………………

7. Culture and sensitivity of the pus (code NO=0, YES=1)

i. No growth obtained
ii. Growth isolated……………..
iii. If positive (specify name of organism)……………………………………

iv. List the antibiotic sensitivity
   a. ………………………………………………………
   b. ………………………………………………………
   c. ………………………………………………………
   d. ………………………………………………………
   e. ………………………………………………………

Biochemistry results

LDH……………………………………

pH……………………………………

Glucose………………………………

8. HIV Test Results (CODE: NEGATIVE=0, POSITIVE=1) ☐
Appendix II - Consent form

Comparison of empyema thoracis presentation between HIV infected and Non HIV infected patients as seen at a tertiary hospital in Kenya

English version

This Informed Consent form is for patients of all ages hospitalized at the Kenyatta National Hospital with empyema thoracis. We are requesting these patients to participate in this research project whose title is “Comparison of empyema thoracis presentation between HIV infected and Non-HIV infected patients as seen at a tertiary hospital in Kenya“.

Principal investigator: Dr. Nyamohanga Marwa Patrick

Institution: School of Medicine, Department of surgery- University of Nairobi

Supervisors: Dr Peter L.W Ndaguatha and Professor Stephen W.O. Ogendo.

This informed consent has three parts:
1. Information sheet (to share information about the research with you)
2. Certificate of Consent (for signatures if you agree to take part)
3. Statement by the researcher

You will be given a copy of the full Informed Consent Form.

Part I: Information sheet

My name is Dr. Nyamohanga Marwa Patrick, a post graduate student at the University of Nairobi’s School of Medicine. I am carrying out a study to determine the main features of empyema thoracis (pus in the chest cavity) and microbial profile. This will be determined by data collection through filling of questionnaires, collection of pleural fluid for biochemical analysis, microbiology, culture and sensitivity. Blood specimen will also be collected for HIV testing and the results will not be communicated. The information will help doctors gain new insights into this disease and guide towards rapid recognition of the development of empyema and understand the causative organisms that are crucial to successful treatment and improvement of outcome.
I am inviting you to participate in my study and you are free to either agree immediately after receiving this information or later after thinking about it. You will be given the opportunity to ask questions before you decide and you may talk to anyone you are comfortable with about the research before making a decision. After receiving this information concerning the study, please seek for clarification from either myself or my assistant if there are words or details which you do not understand.

If you agree to participate, you will be asked to provide personal information and other details related to Empyema thoracis. All the information which you provide will be kept confidential and no one but the researchers will see it. Your name will not appear in any document or any specimen container. The information about you will be identified by a number and only the researchers can relate the number to you as a person. Your information will not be shared with anyone else unless authorized by the Kenyatta National Hospital/University of Nairobi – Ethics and Research Committee (KNH/UoN-ERC).

Your involvement in this research will be through an interview and clinical evaluation and you will not expose yourself to any risks if you consent to participate. You will experience bearable pain during the pin prick sample collection for HIV testing. There will be no extra cost incurred for participating in the study. Participation in this study is out of your own free will, you will not be denied medical care incase you refuse to participate in the study. You may stop participating at any time with no consequences whatsoever. All the information that you give us will be used for this research only.

This proposal has been reviewed and approved by the KNH/UoN-ERC which is a committee whose work is to make sure research participants like your self are protected from harm. The contact information is given below if you wish to contact any of them for whatever reason;

- Secretary, KNH/UoN-ERC
  P.O. Box 20723 KNH, Nairobi 00202
  Tel 726300-9
  Email: uonknh_erc@uonbi.ac.ke
• University of Nairobi research supervisors

Professor Peter L.W Ndaguatha
MBChB, M.Med F.C.S (ECSA) Fellow of Urology (U.K)
Department of Surgery, School of Medicine, University of Nairobi
P.O. Box 19676 KNH, Nairobi 00202
Tel # 0202726300

Professor Stephen W.O. Ogendo,
MBChB (U.O.N), M.Med Surgery (U.O.N), F.C.S (ECSA), PGDRM
Department of Surgery, School of Medicine, University of Nairobi
P.O. Box 19676 KNH, Nairobi 00202
Tel # 0202726300

• Principal researcher:

Dr. Nyamohanga Marwa Patrick
Department of Surgery, School of Medicine, University of Nairobi
P.O. Box 19676 KNH, Nairobi 00202
Mobile phone 0722485324
Part ii: Consent certificate by patient

I……………………………………………………..freely give consent of myself or for my proxy (Name……………………………………………………..) to take part in the study conducted by Dr. Nyamohanga Marwa Patrick, the nature of which has been explained to me by him/his research assistant. I have been informed and have understood that my participation is entirely voluntary and I understand that I am free to withdraw my consent at any time if I so wish and this will not in any way alter the care being given to me or my proxy. The results of the study may directly be of benefit to me or my proxy and other patients and more significantly to the Medical professionals to better understand the Disease namely empyema thoracis that finally translate to early diagnosis and better management of patients who will in future present with this disease.

..........................................................................................
Signature/left thumb print (Participant/Next of kin)
Date……………………………………………………………………

Day/Month/Year

Statement by the witness if participant is illiterate
I have witnessed the accurate reading of the consent form to the participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness……………………………………………………………………
Signature of witness……………………………………………………………………
Date……………………………………………………………………

Day/Month/Year

Thumb print of participant if Unable to sign due to illiteracy
Part iii: Statement by the researcher

I have accurately read out the information sheet to the participant, and to the best of my ability made sure that the participant understands the following:

- Refusal to participate or withdrawal from the study will not in any ways compromise the quality of care and treatment given to the patient.
- All information given will be treated with confidentiality.
- The results of this study might be published to enhance knowledge and to help improve the quality of diagnosis, treatment and improve the outcome of empyema thoracis in both HIV and non-HIV patients.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the participant.

Name of researcher taking consent……………………………………………………………………

Signature of researcher taking the consent…………………………………………………………

Date……………………………………………………………………………………………………

Day/Month/Year
2 (b) Kiswahili version

Fomu ya idhini

(i) Sehemu ya kwanza – Maelezo ya Daktari mtafiti.

Mimi ni Dkt Nyamohanga Marwa Patrick, kutoka shule ya Elimu ya Afya idara ya upasuaji Chuo Kikuu cha Nairobi (University of Nairobi). Ninafanya utafiti wa kuangalia dalili, wadudu husika, sababisho na muda wa kukaa hospitalini kwa wagonjwa walio na maradhi yanayosababisha usaa kuwepo ndani ya kifua cha mwanadamu nikiwahusisha walio na madhara ya ukimwi na wale wasio na ukimwi. Ningependa kuchagua wewe ama mgonjwa wako katika utafiti huu wangu ninafanya hivyo kwa kuuliza maswali fulani ya afya, kupima usaa huo katika maabara na pia damu. Katika utafiti huu utatakiwa kutoa taarifa yako binafsi Habari zote zitakazo kusanywa zitashughulikiwa kwa siri na hazitasambazwa ila tu kwa ruhusa kutoka kwa mkurugenzi mkuu wa utafiti wa chuo kikuu cha Nairobi na hospitali kuu ya Kenyatta.

Utafiti huu utawasaidia madaktari kuulewa ugonjwa huu kwa undani zaidi hivyo basi kuweza kuangalia kwa wagonjwa wao kwa ubora zaidi na kuwapa mbinu ya kuutambua hivyo ugonjwa haraka iwezekanavyo, kupatiana tiba inayo faraa kulingana na wadudu husika na kufupisha zile siku wagonjwa wanazwa katika hospitali na kuzuia wengi wao kutokana na vifo. Kutakua na uchungu kidogo wakati wa kudungwa sindano kutoa damu ya kupima. Kuhusika kwako kwenye utafiti huu hao maafisa yeye yake yasiyotaka kufaa kuhusika kwako kwenye utafiti huu hauna malipo yeyote ila ni kwa hiari.

Unaweza kuuliza maswali yeyote kuhusu utafiti huu na ukiridhika tafadhali 1 jaze simu ya idhini iliyopo hapa chini. Unaweza pia kuuliza swali lolote baadaye kwa kupiga simu ya mtafiti mkuu ama mkuu wa idara ya upasuaji katika chuo kikuu cha Nairobi ama walimu wasimamizi wa utafiti ukitumia nambari za simu zifuatazo:

Walimu wakuu wa Chuo kikuu cha Nairobi:

1. Profesa Peter L.W Ndaguatha,
   MBChB, M.Med, F.C.S (ECSA) Fellow of Urology (U.K)
   Sanduku la Posta 19676 KNH, Nairobi 00202. Nambari ya simu: 0202726300

2. Profesa Stephen Ogendo,
   Sanduku la Posta 19676 KNH, Nairobi 00202. Nambari ya simu: 0202726300

   • Mtafari: Daktari Nyamohanga Marwa Patrick,
   Idara ya Upasuaji ya Shule ya Afya – Chuo kikuu cha Nairobi,
   Sanduku la Posta 2678 KNH Nairobi 00202. Nambari ya simu ya mkononi 0722485324
(ii) Sehemu ya pili – Idhini ya mgonjwa.
Mimi (Jina)…………………………………………………………kwa hiari yangu ama kwa hiari ya mgonjwa wangu (Jina la Mgonjwa)………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………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My name is Dr Nyamohanga Marwa Patrick. I am trying to learn about a medical condition that cause accumulation of pus in the chest cavity because this particular condition causes a lot of deaths in our set up and the aim of this study is to compare the symptoms, signs and causative organisms between patients who have HIV infections and those without HIV infection, this will help create a knowledge base and help doctors understand this condition better and with this knowledge improve on patient care and early diagnosis which translates to improvement of treatment outcome. If you would like, you can be in my study.

If you decide you want to be in my study, you will be asked some personal questions and a sample of pus from your chest and blood specimen will be collected for laboratory testing with bearable pain.

There are no risks involved in this study; you will not incur any extra costs for participating in this study. Other people will not know if you are in my study. I will put things I learn about you together with things I learn about other children/teens, so no one can tell what things came from you. When I tell other people about my research, I will not use your name, so no one can tell who I am talking about.

Your parents or guardian have to say it’s OK for you to be in the study. After they decide, you get to choose if you want to do it too. If you don’t want to be in the study, no one will be mad at you. If you want to be in the study now and change your mind later, that’s OK. You can stop at any time.

My telephone number is 0722485324. You can call me if you have questions about the study or if you decide you don’t want to be in the study any more.
I will give you a copy of this form in case you want to ask questions later.

**Agreement**

I have decided to be in the study even though I know that I don’t have to do it. Dr Nyamohanga Marwa Patrick has answered all my questions.

______________________________  
Signature of Study Participant  
______________________________

Signature of Researcher  

______________________________  
Date  

______________________________  
Date
APPENDIX IV

DECLARATION OF ORIGINALITY FORM

This form must be completed and signed for all works submitted to the University for Examination

Name of Student: Dr. Nyamohanga Marwa Patrick

Registration Number: H58/76510/09

College of: Health Sciences

Faculty/School/Institute of: Medicine

Department of: General Surgery

Course Name: Master of Medicine (M.Med) in General Surgery

Title of the work: Comparison of empyema thoracis presentation between HIV infected and non-HIV infected patients as seen at a tertiary hospital in Kenya.

DECLARATION

1. I understand what Plagiarism is and I am aware of the University’s policy in this regard

2. I declare that this thesis is my original work and has not been submitted elsewhere for examination, award of a degree or publication. Where other people’s work or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi’s requirements.

3. I have not sought or used the services of any professional agencies to produce this work

4. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work

5. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

Signature ________________________________________________
Declaration Form for Staff
UNIVERSITY OF NAIROBI

Declaration of Originality Form

This form must be completed and signed for all scholarly works produced.

Name of Staff ___Professor Peter L.W. Ndaguatha_____________________________
Payroll Number _____________________________________________________
College ___________ Health Sciences____________________________________
Faculty/School/Institute_ of Medicine____________________________________
Department _________ of Surgery____________________________________
Title and bibliographic details of the work: “Comparison of empyema thoracis presentation between HIV infected and non HIV infected patients as seen at a tertiary hospital in Kenya”.

DECLARATION
1. I understand what plagiarism is and I am aware of the University’s policy in this regard.
2. I declare that this _____ Dissertation ___________ scholarly work (Paper, book chapter, Monograph, review, etc) is my original work. Where other people’s work or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi’s requirements.
3. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work.
4. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

Signature ____________________________________________

Date ________________________________________________
Declaration Form for Staff  
UNIVERSITY OF NAIROBI  

Declaration of Originality Form  

This form must be completed and signed for all scholarly works produced.

Name of Staff ______ Professor Stephen W. O. Ogendo__________________________
Payroll Number _____________________________________________________
College ______ Health Sciences___________________________________________
Faculty/School/Institute of Medicine________________________________________
Department ______ Surgery_______________________________________________

Title and bibliographic details of the work: “Comparison of empyema thoracis presentation between HIV infected and non HIV infected patients as seen at a tertiary hospital in Kenya”.

DECLARATION  
1. I understand what plagiarism is and I am aware of the University’s policy in this regard.  
2. I declare that this __Dissertation_________ scholarly work (Paper, book chapter, monograph, review, etc) is my original work. Where other people’s work or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi’s requirements.
3. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work.  
4. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

Signature ________________________________

Date ________________________________
APPENDIX V

KNH/UON-ERC APPROVAL LETTER

Dr. Nyamohanga Marwa Patrick
Dept. of Surgery
School of Medicine
University of Nairobi

Dear Dr. Nyamohanga

RESEARCH PROPOSAL: COMPARISON OF EMPYEMA THORACIS PRESENTATION BETWEEN HIV INFECTED AND NON HIV INFECTED PATIENTS AS SEEN IN A TERTIARY HOSPITAL IN KENYA (P073/06/2012)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and approved your above revised proposal. The approval periods are 13th December 2012 to 12th December 2013.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 80 days prior to expiry of the approval period.
   (Attach a comprehensive progress report to support the renewal).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an executive summary report within 90 days upon completion of the study
   This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website www.uonbi.ac.ke/activities/KNHuoN

13 December 2012
Yours sincerely

[Signature]

PROF. A.N. GUANTAI
SECRETARY, KNH/UON-ERC

c.c. The Deputy Director CS, KNH
    The Principal, College of Health Sciences, UoN
    The Dean, School of Medicine, UoN
    The Chairman, Dept. of Surgery, UoN
    The HOD, Records, KNH
    Supervisors: Dr. Peter L. Ndaguatha, Dept. of Surgery, UoN
               Prof. S.W.O. Ogendo, Dept. of Surgery, UoN