# HUMAN IMMUNODEFICIENCY VIRUS AND TUBERCULOSIS COINFECTION AT FORT PORTAL REGIONAL REFERRAL HOSPITAL

**BY**

**AMINU SULAIMAN YUSUF.**

**BMS/0119/133/DF**

**A RESEARCH DISSERTATION SUBMITTED TO THE FACULTY OF CLINICAL MEDICINE AND DENTISTRY IN PARTIAL FULFILMENT FOR THE AWARD OF BACHELOR OF MEDICINE AND SURGERY AT KAMPALA INTERNATIONAL UNIVERSITY**

**APRIL, 2019**

**ABSTRACT**

**Background;** Worldwide, tuberculosis (TB) is one of the top 10 causes of death, and the principal cause from a single infectious agent (above HIV/AIDS); millions of people continue to fall sick with the disease to each year, HIV and TB alone or as coinfections, are a significant public health problem in the world with the biggest contribution to morbidity and mortality felt in sub-Saharan Africa. The immunosuppressive state caused by the decline in immunity as a result of HIV enables TB transmission, infection, reactivation and spread to extra-pulmonary sites making tuberculosis a major opportunistic infection in HIV patients. This study aimed to assess the prevalence of TB/HIV infection, EPTB and any adverse effects it might have on treatment adherence and overall outcome

**Method;** A review of records retrospective study design was employed that made use of both qualitative and quantitative approaches. A total of 384 TB cases took part in the study, 12% of whom were also HIV infected. The prevalence of EPTB was 9.90% with no adverse effects on treatment adherence and overall outcome.

**Result;** Records reviewed showed that physician-reported cases of EPTB documented among 384 TB patients. 38 cases of EPTB were reported while the remaining 346 were categorized into PTB. The prevalence of EPTB was thus 9.90% and that of PTB 90.10% with no adverse effects on treatment adherence and overall outcome.

**Conclusion;** The prevalence of TB/HIV coinfection was high at 12% though not as high as estimates from previous studies elsewhere. This notwithstanding, urgent interventions are needed to reverse this. The prevalence of EPTB was low at 9.9%, values far lower than estimates of previous studies. Treatment adherence was not adversely affected by TB/HIV coinfection and for this reason no unfavourable outcomes were reported. 2 case-fatality rates were reported in the patients with a diagnosis of TBM

**DECLARATION**

I do hereby declare that this research dissertation entitled **'HUMAN IMMUNODEFICIENCY VIRUS AND TUBERCULOSIS COINFECTION AT FORT PORTAL REGIONAL REFERRAL HOSPITAL'** is the product of my own efforts and to the best of my knowledge and conviction, has never been presented to any institution for any award or qualification whatsoever. Where the works of other people have been included, due acknowledgement to this has been made in accordance with the appropriate referencing and citations.

Researcher: **AMINU SULAIMAN YUSUF, BMS/0119/133/DF**

Signature ……...Date ……...……...…

**APPROVAL**

This research dissertation entitled **'HUMAN IMMUNODEFICIENCY VIRUS AND TUBERCULOSIS COINFECTION AT FORT PORTAL REGIONAL REFERRAL HOSPITAL'** has been produced under my close supervision and guidance and I therefore recommend that the student should go ahead and hand in a copy for further consideration.

Supervisor: **MR. SA'ID AKINOLA SAHEED, MSc MICROBIOLOGY**

Signed……...…Date……. …..

**ACKNOWLEDGEMENT**

I would like to, first and foremost, acknowledge The Almighty God, The Giver of life and who without Him all is in futility. I would also like to thank my lovely parents, siblings, mentors, teachers and colleagues for moulding me into what I am today and what am bound to become in the future. Special thanks go to my supervisor, **Mr. Sa'id Akinola Saheed,** whose guidance have been instrumental in every step of this piece of work.

**LIST OF FIGURES**

**LIST OF TABLES**

**LIST OF ABBREVIATIONS**

| | | |
|---|---|---|
| **AIDS** | **:** | Acquired Immunodeficiency Syndrome |
| **ART** | **:** | Anti-retroviral Therapy |
| **CDC** | **:** | Centres for Disease Control and Prevention |
| **CYP** | **:** | Cytochrome P |
| **EEAC** | **:** | European Economic Area Countries |
| **EPTB** | **:** | Extra-pulmonary Tuberculosis |
| **EU** | **:** | European Union |
| **FPPRH** | **:** | Fort Portal Regional Referral Hospital |
| **GOU** | **:** | Government of Uganda |
| **HIV** | **:** | Human Immunodeficiency Virus |
| **INH** | **:** | Isoniazid |
| **IREC** | **:** | Institutional Research and Ethics Committee |
| **IRIS** | **:** | Immune Reconstitution Inflammatory Syndrome |
| **KIU** | **:** | Kampala International University |
| **MDR-TB** | **:** | Multi-drug Resistant Tuberculosis |
| **NNRTIs** | **:** | Non-Nucleoside Reverse Transcriptase Inhibitors |
| **OIs** | **:** | Opportunistic Infections |
| **PIs** | **:** | Protease Inhibitors |
| **PLHIV** | **:** | People Living With HIV |
| **PLWHA** | **:** | People Living with HIV / AIDS |
| **PTB** | **:** | Pulmonary Tuberculosis |
| **SSA** | **:** | Sub-Saharan Africa |
| **TB** | **:** | Tuberculosis |
| **UGTB** | **:** | Urogenital Tuberculosis |
| **USA** | **:** | United States of America |
| **WHO** | **:** | World Health Organization |

**OPERATIONAL DEFINITIONS**

**Prevalence** **:** The number of new and relapse cases of TB arising in a given time period, usually 1 year;

**Mortality** **:** The number of deaths in a given time period, usually 1 year

**TABLE OF CONTENTS**

# CHAPTER ONE: INTRODUCTION

## 1.0.Background

Worldwide, tuberculosis (TB) is one of the top 10 causes of death, and the principal cause from a single infectious agent (above HIV/AIDS); millions of people continue to fall sick with the disease to each year. In 2017, TB caused an assessed 1.3 million deaths (range, 1.2–1.4 million) amongst HIV-negative people, and there were a supplementary 300 000 deaths from TB (range, 266 000–335 000) among HIV-positive people. There were an assessed 10.0 million incidence of TB (range, 9.0–11.1 million), corresponding to 133 cases (range, 120–148) per 100 000 population (Ozer et al., 2017).

TB affects all nation state and all age groups. Estimates for 2017 were that 90% of cases were grown-ups (aged ≥15 years), 64% were male, 9% were persons living with HIV (72% of them in Africa) and two thirds stood in eight countries: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). Only 6% of cases were in the WHO European Region and the WHO Region of the Americas, each of which had 3% of cases (Ozer et al., 2017).

Not less than one third of people living with HIV are also diseased with TB. At autopsy, studies have initiate that 30 – 50% 0f patients have evidence of TB. By the year 2013, about a quarter of all TB deaths happened in HIV positive persons and TB was the leading cause of death in those that had HIV. In sub-Saharan Africa (SSA), about 41% of HIV patients have TB.

In 2011 alone, 400,000 of 1.4 million TB deceases occurred in HIV infected individuals and in the United States of America (USA), 10,521 TB cases 7.9% of whom were also HIV positive (World Health Organization, 2014).

The Tuberculosis (TB) epidemic is following the Human Immunodeficiency Virus (HIV) epidemic. This is because as the HIV epidemic ages and people become more and more immunocomprised, TB prevalence rise. Studies have shown that HIV kills TB-specific CD4 T-cells, damages macrophage activation and reduces the numbers of lung-homing CD4 cells. Also, there is a resultant defective granuloma formation with successive loss of control of the infection. HIV infection is the top risk factor for TB; HIV encourages progression of latent or recent infections of Mycobacterium tuberculosis to active disease, and also increases the rate of relapse of TB. People with HIV may also be more vulnerable to TB infection (Stop TB Partnership, 2015).

Other complications that have been seen in HIV/TB coinfection include well studied facts that each disease makes the other further worse! This has been attributed to the misfortune that both diseases deal on the patient's immune defences as well as the synergistic adverse effects

produced by anti-TB and anti-retroviral (ART) pills. For instance, virtually all anti-TB and ART pills are injurious to the liver (Ramappa & Aithal, 2013). It is an eminent fact that, Rifampicin, which together with Isoniazid (INH) make the pillar of anti-TB treatment regimens, is an inducer of liver enzymes and thus will always impose use of ART regimens that don't consist of protease inhibitors (PIs) and Nevirapine or will involve an upward dose modification of these two drugs to achieve effective levels in the blood. Higher doses mean higher probabilities or adverse effects (Gray & Cohn, 2013). Of relevance also, is the weighty issue of ART initiation / continuance in a patient freshly diagnosed with TB (Karakousis & Piggott, 2011). The ever looming threat of the dangerous immune reconstitution inflammatory syndrome (IRIS) is an endless worry to the health provider (Sharma & Soneja, 2011).

It is in the backdrop of all this and the revitalization of TB infection control efforts that inspired the researcher to propose such a study. TB prevalence still being in height, especially amongst the HIV infected and the prevalence of TB/HIV coinfection being largely unidentified, predominantly in developing countries, including Uganda, which fired the need for this study.

### 1.1. Problem Statement

The TB epidemic is growing in tandem with the HIV/AIDS curse. TB remains the principal cause of death among people living with HIV, accounting for around one in three AIDS-related deaths. More TB cases and deaths have been conveyed annually among the HIV infected than in the normal population. The statistics have been mostly contributed by the WHO sub-Saharan region, which has borne most of the scourges brunt (Glaziou, Floyd, & Raviglione, 2018).

It is important that people living with HIV with no TB symptoms get TB preventative treatment, which diminishes the risk of developing TB and cuts TB/HIV death rates by around 40%. This nonetheless, it is estimated that 49% of people living with HIV and tuberculosis are ignorant of their coinfection and are therefore not receiving care (Drummond et al., 2015).

The HIV/AIDS epidemic in Uganda has been conveyed to continue being severe, mature, generalized and heterogeneous with an estimated 1.3 Ugandans infected with the virus (Uganda AIDS Comission, 2017). Tuberculosis remains a major issue for people living with HIV in Uganda. In 2016, HIV prevalence in Uganda was estimated at 7.3%, and 24% of people with TB were co-infected with HIV (WHO, UNAID, 2016).

Fort Portal is found in Kabarole District in the large Western Uganda region. As per newest reports, the region has had the highest number of people infected with HIV contributing a staggering 13.2% of all the HIV cases in the country (Uganda AIDS Comission, 2017). This

by extension would suggest higher HIV/TB coinfection cases, both diagnosed and un-diagnosed within the region.

## 1.2.Study Objectives

### 1.2.1. Main Objective

To assess the prevalence and determinants of TB-HIV coinfection among HIV positive patients attended to at FPRRH.

### 1.2.2. Specific Objectives

1) To determine the prevalence of TB-HIV coinfection among HIV positive patients at FPRRH.
2) To determine the prevalence of extra pulmonary TB (EPTB) among HIV positive patients at FPRRH.
3) To determine the effect of TB-HIV coinfection on treatment adherence and overall outcome at FPRRH.

## 1.3. Research Questions

1) Is the prevalence of TB high in HIV infection?
2) What is the prevalence of extra pulmonary TB in HIV infection?
3) Does TB-HIV co-infection affect the adherence to treatment and overall outcome?

## 1.4. Significance of the Study

The study set out to fill the statistics gap that existed as to the actual prevalence of TB-HIV coinfection at FPRRH. This information will be priceless in informing stakeholders on planning and policy-making towards strategies of eradicating TB. Findings on effects of HIV infection on TB treatment outcomes highlight on the specific facility-based challenges and thus facilitate tailor-made solutions specific for any problems exposed. Challenges that could be contributing to the expansion of multidrug-resistant TB (MDR-TB) due to challenges of TB treatment in HIV coinfection such as non-adherence due to synergistic adverse drug interactions would fuel development of treatments that have minimal of these effects and thus encourage adherence. Lastly, findings from this study were expected to ignite supplementary research on the same or related topic in the same or similar cohort elsewhere and thus deepen the pool of knowledge that already existed on the subject matter.

## 1.5.Study Scope

### 1.5.1. Geographical Scope

The study was conducted at Fort Portal Regional Referral Hospital (FPRRH), commonly known as Fort Portal Hospital, sometimes referred to as Buhinga Hospital, is a hospital in the town of Fort Portal, in Kabarole District, Western Uganda. It is the referral hospital for the districts of Bundibugyo, Kabarole, Kamwenge, Kasese, Ntoroko and Kyenjojo. It is a public hospital, funded by the Uganda Ministry of Health and general care in the hospital is free. It is one of the 13 "Regional Referral Hospitals" in Uganda. The hospital is designated as one of the 15 "Internship Hospitals" where graduates of Ugandan medical schools can serve one year of internship under the supervision of qualified specialists and consultants. The bed capacity of Fort Portal Hospital is quoted as 333.

### 1.5.2. Content Scope

The study was about assessing the prevalence of TB-HIV coinfection, and the impact of HIV infection on treatment adherence and overall patient outcomes.

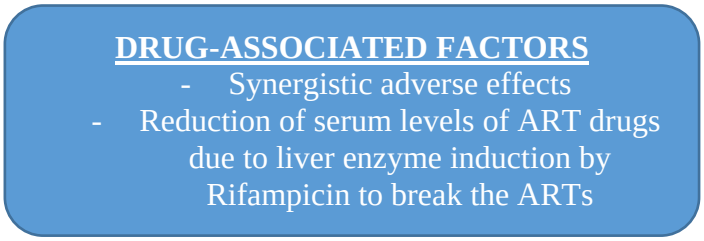
### 1.5.3. Time Scope

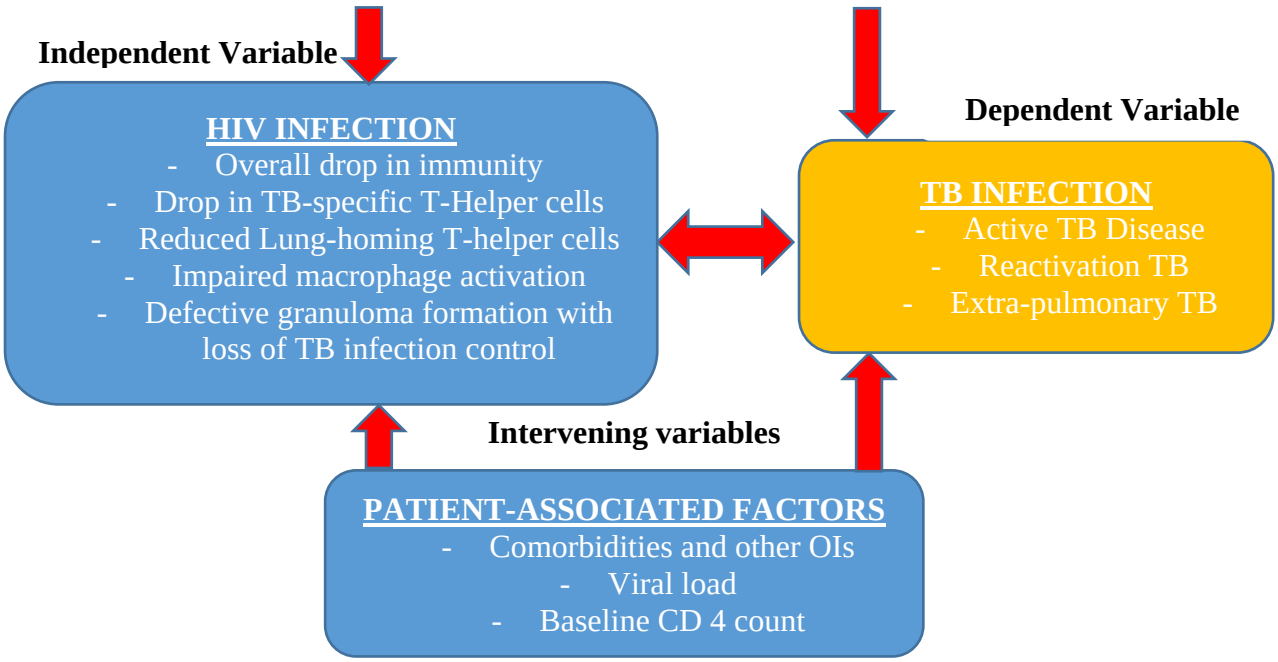
The study was conducted in retrospective fashion for the period running from the months of July 2018 and December 2018.

## 1.6.Conceptual Framework

The conceptual framework implemented for this study was adopted and constructed from researcher's own understanding of literature reviewed. HIV infection will be taken as the independent variable that will determine whether one is co-infected with TB or not (dependent variable). Drug accompanying factors and patient associated factors will be the intervening variables. With HIV-TB co-infection, the result is an increased pill load that might affect patient adherence to treatment which may eventually lead to deteriorating of both conditions in the presence of one another. The red arrows indicate that a factor worsens the one the arrow is pointing to.

*Figure 1: Conceptual Framework on HIV-TB Coinfection (Researcher's Own Views)*




Independent Variable
HIV INFECTION
- Overall drop in immunity
- Drop in TB-specific T-Helper cells
- Reduced Lung-homing T-helper cells
- Impaired macrophage activation
- Defective granuloma formation with loss of TB infection control
Dependent Variable
TB INFECTION
- Active TB Disease
- Reactivation TB
- Extra-pulmonary TB
Intervening variables
PATIENT-ASSOCIATED FACTORS
- Comorbidities and other OIs
- Viral load
- Baseline CD 4 count

# CHAPTER TWO: LITERATURE REVIEW

## 2.0.Introduction

This chapter pacts with the literature reviewed on the prevalence of TB-HIV coinfection, the prevalence of extra-pulmonary TB in HIV infection and the effect of TB-HIV coinfection on complete patient outcome.

## 2.1. Prevalence of TB-HIV Coinfection

Amongst the known risk factors for development of TB, HIV infection is known to be the strongest. On the flipside TB is the commonest HIV-associated opportunistic infection (OI) worldwide (Gray & Cohn, 2013). In 2002, the global estimate of new TB cases was 8.8 million and the global prevalence rate growth was roughly 1.1% per year (WHO, 2015). The scale of the global tuberculosis epidemic indicates the enormous challenge for tuberculosis control, which is complicated by the impact of HIV and drug-resistant tuberculosis (Glaziou et al., 2018). In fact, according to WHO 8% of PLHIV newly enrolled in HIV care in 92 countries were notified with TB in 2017 (WHO, 2017).

A study conducted by (Pimpin et al., 2011) in the European Union (EU) and European Economic Areas Countries (EEAC) initiate that the proportion of HIV-co-infected TB patients varied from 0 to 15% with western and eastern countries having higher levels and increasing trends of infection over time compared with central EU/EEA countries.

India alone accounts for 24 percent of total TB cases making it the world's TB capital. In a cross-sectional study shown in an ART clinic of a district hospital in Pratapgahr India in 2015, the prevalence of HIV/TB co-infection was found to be 18.1% among HIV-positive patients (Tripathi, Tripathi, & Tripathi, 2015).

TB-HIV co-infection is one of the biggest public health challenges in sub-Saharan Africa. The prevalence of TB-HIV co-infection widely varies; the prevalence of HIV among TB patients ranges from 3.8 to 72.3%, whereas the prevalence of TB among HIV-positive patients ranged from 2.9 to 64.5% (Gao, Zheng, & Fu, 2013). The African region accounts for 75% of the estimated number of HIV-positive incident TB cases (Glaziou et al., 2018).

Of all new cases of TB, 1.1 million (13%) befall in HIV-infected patients; of those, 0.35 million (32%) die. In 2010, 26% of all new TB cases befallen in sub-Saharan Africa, but the region bore 82% of the global 1.1 million new TB cases among HIV-positive people (Hermans, 2012).

In South Africa, studies have also forwarded high prevalence values. In 2010 for instance, study findings previously described high prevalence of HIV infection among adults (23%) and rapidly escalating TB notification rates in a peri-urban township, Site-M in Cape Town, South Africa (Bekker & Wood, 2010).

Among the HIV infected individuals of the Amhara region of Ethiopia, a study conducted in 2016 found that out of a total of 517 HIV positive participants, 158 (27.7%) had pulmonary TB (PTB) (Mitku, Dessie, Muluneh, & Workie, 2016).

In a meta-analysis conducted by (Tesfaye et al., 2018) in Ethiopia that included 21 studies with a total of 12,980 participants, the pooled prevalence of TB / HIV Co-infection was found to be 25.59% (95% CI (20.89%–30.29%).

In the principally pastoralist areas of northeast Ethiopia, TB-HIV coinfection was found to be highly prevalent. The 2015 study showed that out of the 325 pulmonary TB suspects, 44 (13.5%) were smear positive, and 105 (32.3%) were culture positive. Among smear-positive patients, five were culture negative and, hence, a total of 110 (33.8%) suspects were bacteriologically confirmed pulmonary TB patients. Out of 287 pulmonary TB suspects who were verified for HIV infection, 82 (28.6%) were HIV positive. A significantly higher proportion of bacteriologically confirmed pulmonary TB patients [40 (40.4%)] were HIV co-infected compared with patients without bacteriological indication for pulmonary TB [42 (22.3%)] (Belay, Bjune, & Abebe, 2015).

A recent study conducted among HIV infected subjects in North-western Tanzania in 2018 showed that TB-HIV coinfection prevalence stood at 11% (Gunda et al., 2018).

According to (WHO, 2017) the HIV prevalence in Uganda is estimated at 7.3%, and approximately 50-60% of TB patients are also co-infected with HIV.

**2.2.Prevalence of Extra pulmonary TB among HIV Patients**

The impaired immunity that HIV infection causes predisposes patients to disseminated/extra-pulmonary TB. This results from defective confinement of infection to the lungs as a result of defective macrophage activation and granuloma formation (Diedrich & Flynn, 2011).

Sandgren and colleagues made a descriptive analysis to assess the burden and trends of EPTB in EU/EEA countries. During 2002 to 2011, 167,652 cases of EPTB were reported by the 30 Member States. EPTB accounted for 19.3% of all notified cases, ranging from 5.8% to 44.4% among Member States. Overall, TB notification rates decreased in 2002–2011 due to a decrease in PTB. Notification rates of EPTB persisted stable at 3.4 per 100,000 in 2002 and 3.2 per 100,000 in 2011. Thus, the proportion of EPTB increased from 16.4% in 2002 to 22.4% in 2011. Of all EPTB cases reported during 2002–2011, 37.9% were foreign-born or citizens of another country, 33.7% were culture-confirmed and the overall treatment success was 81.4%. Thus a significant percentage of notified TB cases are extra-pulmonary, and in contrast to PTB, EPTB rates are not decreasing (Sandgren, Hollo, & van der Werf, 2013). Solovic and colleagues, on the other hand, reported the percentage of EPTB cases among TB in the EU

ranged from 4% to 48% but attributed this difference to differences in risk factors for EPTB or encounters in diagnosis (Solovic et al., 2013).

Mazza-Stalder and colleagues considered the proportion of EPTB was increasing, at 20–40%. In 1984 EPTB was a major health problem in Australia, where 24.3% of all new TB notifications were extra-pulmonary in origin (Mazza-Stalder, Nicod, & Janssens, 2012).

In a retrospective study, Lin and colleagues compared patients with EPTB and PTB in southern Taiwan (Lin et al., 2009). They found that, among a total of 766 TB patients, EPTB was diagnosed in 102 (13.3%) and PTB in 664 (86.7%); 19.6% of EPTB patients also had PTB. The most frequently involved EPTB site is the bone and joints (24.5%).

EPTB had an increasing rate in Turkey in 2001–2007 but the reason remains chiefly unknown (Gunal et al., 2011).

Over the past decade, the spectrum of EPTB in Siberia has changed expressively (Kulchavenya, Zhukova, & Kholtobin, 2013). TB of the central nervous system nearly doubled from 4.9% to 8.7%, mostly due to comorbidity with HIV. Bone and joint TB increased by about half, from 20.3% to 34.5%, and amongst this group TB spondylitis with neurological disorders prevailed – the most debilitating form of the disease. The proportion of UGTB decreased from 42.9% to 31.7%. In contrast, there was a decrease of peripheral lymph node TB from 16.7% in 1999 to 11.2% in 2011, with fistulous disease still common. At the end of the last century ocular TB accounted for 7.4% and in 2008 (in 2009 listed in 'others') for 4.4% of the patients with EPTB. Accordingly, in 1999 'other' formulae of TB accounted for 7.8% and in 2009 for 15.8% (in 2011, 13.9%). The increase is partly due to inclusion of patients with ocular TB in this group, and partly due to better diagnosis of TB of the skin, abdominal organs, breast, etc (Kulchavenya et al., 2013).

In Turkey in 2001–2007 the most commonly seen two types of EPTB were genitourinary TB (27.2%) and meningeal TB (19.4%). TB of bone/joints, pleura, lymph nodes, skin, and peritoneal TB occurred at a frequency ranging from 9.7% to 10.7% (Gunal et al., 2011). Other authors from the same region reported slightly different data. Among 141 EPTB patients in Istanbul over 7 years, meningeal TB accounted for 23%, and TB lymphadenitis 21%. Other types of EPTB were skeletal, miliary, peritoneal, abscess, UGTB, cutaneous and gastrointestinal participation which ranged between 18% and 1%. Mean age was 42 and female/male ratio was nearly equal (Sevgi et al., 2013).

In 2009 almost a fifth of TB cases in the United States were extra-pulmonary; inexplicable slower annual case count decreases have occurred in EPTB compared with annual case count decreases in PTB cases. From 1993 to 2006, among 253,299 cases, 73.6% were PTB and 18.7%

were EPTB, including lymphatic (40.4%), pleural (19.8%), bone and/or joint (11.3%), genitourinary (6.5%), meningeal (5.4%), peritoneal (4.9%) and unclassified EPTB (11.8%) cases (Peto, Pratt, Harrington, LoBue, & Armstrong, 2009).

In France in 2012 the most common clinical presentations of EPTB were lymphadenitis, pleuritis and osteo-articular TB. Peritoneal, urogenital or meningeal TB were less frequent, and their diagnosis was often problematic due to the wide differential diagnosis and the low sensitivity of diagnostic tests including cultures and genetic amplification tests (Mazza-Stalder et al., 2012).

In some countries the rate of growth of bone and joint TB has reached the leading position among EPTB (Kulchavenya et al., 2013). Location of TB on the spine remains the most common form of skeletal TB, representing 62.2% of all osteoarticulary locations (Didilescu & Tanasescu, 2012). The skeletal form was responsible for 3% of the total number of cases, with 50% of these due to spinal tuberculosis (Wiler, Shalev, & Filippone, 2010).

EPTB comprises 20–25% of the total burden of the disease, in which UGTB is 4% according to a report by Singh and colleagues. It has been well described that the urogenital system is a common site of EPTB in adults, but the true prevalence of UGTB is less clear, and reports have varied from 4% to 73% (Singh et al., 2011).

Among 386 patients studied at a TB reference centre in northern Portugal, 260 (67.4%) had pulmonary tuberculosis (PTB) and 126 (32.6%) extra-pulmonary TB (EPTB). HIV infection (OR = 2.72, 95%CI = 1.25–5.93) was an independent risk factor for EPTB. HIV co-infection (OR = 12.97; 95%IC: 1.71–48.42) and the presence of previous TB treatment (OR = 7.62; 95%IC: 1.00–57.9) were found to increase the risk of disseminated disease (Sanches, Carvalho, & Duarte, 2015a).

In a systemic review and meta-analysis that was conducted in sub-Saharan Africa that involved 31 studies and a total of 28,659 PLWAs, it was concluded that the prevalence of EPTB among PLWHA was high. The prevalence estimates of EPTB among PLWHA ranged from 6.4% (95% CI: 3.8, 9.0) to 36.8% (95% CI: 28.6, 45); random-effects pooled prevalence of EPTB among PLWHA was found to be 20% (95% CI: 17, 22; heterogeneity: $\tau 2=0$; $\chi 2=509.09$, degrees of freedom [df]=30, $P<0.00001$; I2=94%). No evidence of publication bias was observed (P=0.44 for Egger's regression analysis and P=0.11 for Begg's rank correlation analysis) (Mohammed, Assefa, & Mengistie, 2018).

Among patients treated for tuberculosis at the Douala General Hospital in Cameroon, the proportion was found to be relatively high with bone and joints being the most affected sites. HIV infection was most strongly associated with neuromeningeal forms. Of total of 749

patients recorded for an anti-TB treatment, the overall prevalence of HIV is 41.5% (95% confidence interval [CI]38-45.1). The prevalence of EPTB was 42.9% (321). HIV infection was present in 33.6% of patients with EPTB. The most affected sites of disease were bones and joints (29.6%), lymph nodes (17.8%), the pleura (15%), peritoneum (14.3%), and the central nervous system and meninges (9%). Neuromeningeal TB however, less common was most strongly associated with HIV infection, odd ratio (OR)2.3 (95% CI 1.1-5.0, $p < 0.05$) (Namme et al., 2013).

In a tertiary care centre in Oman, a total of 260 TB cases were reviewed, of which EPTB comprised 37%, PTB comprised 53%, and disseminated TB comprised 10%. The most common sites of infection in the EPTB group were the lymph nodes and the abdomen (Gaifer, 2017).

Reports from a study conducted in rural Uganda have had EPTB rates of as high as 20% (Ollé-Goig, 2010).

**2.3.Effect of TB-HIV Coinfection on Adherence to Treatment & Outcome**

HIV encourages the progression of infection with Mycobacterium tuberculosis to active TB, both in people with recently acquired infections and those with latent infections. Undeniably, HIV is the main powerful risk factor known for activation of latent M. tuberculosis infection (Raghavan, Alagarasu, & Selvaraj, 2012). For an HIV infected person co-infected with M. tuberculosis, the risk of developing active TB reaches 5–10% annually, instead of the 5–10% lifetime risk for an individual not infected with HIV. This discrepancy is clearly linked to the immunodeficiency caused by HIV (Geldmacher, Zumla, & Hoelscher, 2012). Furthermore, HIV infection increases the rate of recurrent TB, which can be due to either endogenous reactivation or exogenous reinfection.

TB is one of the most mutual infections in HIV-infected people, especially in high TB prevalence areas. HIV critically increases the number of TB patients, which in turn increases TB transmission from family members (the highest TB transmission risk is from household contacts, such as children and HIV-positive partners) and community members (through contact in work-places, schools and hospitals) where there is a risk of nosocomial infections from both patients (whether HIV-positive or -negative) and health care workers. Additionally, the risk of MDR-TB transmission may be increased if effective and uninterrupted TB treatment is not certified (Kompala, Shenoi, & Friedland, 2013).

As HIV infection progresses, CD4 lymphocytes decline by about 50–80 cells/mm3/year, and the immune system becomes less able to prevent the growth and local spread of M. tuberculosis (Schutz, Meintjes, Almajid, Wilkinson, & Pozniak, 2010). Pulmonary TB (PTB) remains,

especially in adults, the commonest form of TB, but its presentation depends on the degree of immunosuppression. The clinical pictures, sputum-smear results and chest X-rays are often different in the early stage of HIV infection (CD4 >350 cells/mm3) and the late stage (CD4 <200 cells/mm3) (Sharma & Mohan, 2013).

The clinical presentation of TB cases in early HIV infection is similar to that of individuals without HIV infection, similar to post-primary PTB, that is, with positive sputum smears (defined as two or more initial smear examinations that are positive for acid-fast bacilli (AFB), or one plus consistent radiographic abnormalities) and often with cavities in the chest X-ray. In contrast, the clinical presentation in late HIV cases resembles primary PTB: the sputum smear is often negative and radiological infiltrates are present instead of cavities. In case of severe immunodeficiency, the rate of extra-pulmonary TB (EPTB) increases in both adults and children. Because of difficulties in diagnosis, disseminated TB may account for a high proportion of misattributed hospital deaths (Davies, Gordon, & Davies, 2014).

Active TB on itself is responsible for minor immune deficiency. In countries with independent epidemics of TB and HIV/AIDS, TB does not always indicate severe deterioration of the immune system in HIV-infected people because it may occur before HIV infection or in its early stages, before the immune system has deteriorated. When active TB occurs in HIV patients, a worsening of the HIV-related deficiency is commonly observed, facilitating the progression of other opportunistic infections such as Candida albicans oesophagitis, Cryptococcus meningitis and, particularly, Pneumocystis jirovecii (formerly P. carinii) pneumonia (Ismail & Bulgiba, 2013). Any of these opportunistic infections may be lethal. If so, TB is indirectly responsible for the death (Shankar et al., 2014).

In addition, TB has been found directly responsible for an average mortality rate of 30% among HIV/AIDS cases in many reports (Scott, Da Silva, Boehme, Stevens, & Gilpin, 2017). These data emphasize the need of early diagnosis and specific treatment of TB in all HIV-infected patients, especially when the clinical pattern of CD4 cells count shows a severe degree of immunodeficiency (National Institute of Health, 2018).

Rifampicin stimulates the activity of the hepatic cytochrome P450 (CYP) enzyme system that metabolizes NNRTIs and PIs (see Annex 2 for ARV classes). This mechanism leads to a reduction in the blood levels of NNRTIs and PIs, and consequently the incomplete suppression of HIV replication and the emergence of drug resistance. Rifampicin causes up to a 75% reduction in the serum levels of PIs, thus necessitating dosage adjustment. NNRTIs and PIs can also boost or inhibit CYP and lead to altered blood levels of rifampicin (Tiberi et al.,

2017)(Marzinke, 2016). These adverse reactions plus the length and pill load involved might hinder treatment adherence.

# CHAPTER THREE: METHODOLOGY

## 3.0.Introduction

This chapter deals with the study design, study area, population characteristics, data collection and operation procedures used. It mainly involved data collection, processing and interpretation.

## 3.1. Study Design

A review of records retrospective study design was employed that made use of both qualitative and quantitative approaches.

## 3.2. Study Area

The study was conducted at Fort Portal Regional Referral Hospital (FPRRH) TB and HIV clinics.

## 3.3. Study Population

HIV or TB infected adults attended to at the HIV and TB clinics.

## 3.4. Selection Criteria

### 3.4.1. Inclusion Criteria

All files/records of adult HIV and/or TB patients attended to at the HIV and TB clinics within the study period.

### 3.4.2. Exclusion Criteria

All files/records of adult HIV and/or TB patients attended to at the HIV and TB clinics outside the study period.

## 3.5. Sample Size Determination

The sample size was determined using Fishers et al., 2006 formula i.e. $N=Z^2PQ/D^2$:

Where;

N is the desired sample size

Z is the standard normal deviation taken as 1.96 at a confidence interval of 95%.

P is the prevalence of HIV-TB coinfection in Uganda taken as 50% (Stop TB Partnership, 2015)

D is the degree of accuracy= 0.05.

Q= (1-P)

Therefore, $N= 1.96^2 \text{ X } 0.5\ (0.5) / (0.05)^2 = 384$

Three hundred and eighty-four was the representative sample for the study but being a prevalence study, all files whose owners met the inclusion criteria were included for the study.

### 3.6. Sampling Procedures

Consecutive sampling technique was used whereby patient files/records were used as their owners met the inclusion criteria. From the total number obtained, it was divided by the required sample size of 384 in order to obtain the sampling interval.

### 3.7. Data Collection Methods and Management

Being a study that employed review of records as its main data collection technique, a special checklist was used that facilitated achievement of the study objectives. Information to be collected included, age, gender, TB diagnosis, HIV diagnosis, duration since diagnosis, anti-TB and ART regimen currently on, duration since commencement of treatment, latest CD 4 count and viral load measurement if available, any other comorbidities or opportunistic infections present.

### 3.8. Data Analysis

Quantitative statistical data was entered into EpiInfo software application and univariate analysis done using SPSS version 17.0. Results were presented in tables, charts, graphs and narratives.

### 3.9. Quality Control

Data obtained was scrutinized for consistency and where any uncertainties arose clarifications sought. Only patient records that would have been fully and properly filled were used for the study. In case of any gaps, clarifications were sought where possible failure to which those records were excluded from the study.

### 3.10. Ethical Considerations

Approval to conduct this study was obtained from KIU-IREC. Participants signed written consent to participate in this study.

### 3.11. Limitations/De-Limitations of the Study

In anticipation of financial constraints to be faced in the study, the researcher planned to outsource for extra funding from family and close relatives and budgeting the funds diligently with allocation of a 15% contingency on the total proposed budget. With proper time management and period given for the study, the researcher did not anticipate any problems with achieving the objectives of the study within the timeframe allocated.

# CHAPTER FOUR: STUDY FINDINGS

## 4.0.Introduction

This chapter presents the findings of the study by objective and in the form of narratives, tables, graphs and charts. Patient records spanning a period of 6 months, from July 2018 to December 2018 were reviewed. According to the HIV/TB registry, there were 754 records of TB patients falling within the study period and whose owners were eligible to be enrolled for the study. By dividing by the sample size of 384, a sampling interval of 2 was obtained and every fifth file was picked and recruited for the study. The records were then reviewed specifically for following the items in the checklist and tabulated. Entries were then tallied and clustered for ease of analysis.

## 4.1. Basic Information of TB Patients (N=384)

### 4.1.1. Age

| AGE | NUMBER (n) | PERCENTAGE (%) |
|---|---|---|
| 18 – 22 | 38 | 9.90 |
| 23 – 27 | 57 | 14.84 |
| 28 – 32 | 105 | 27.34 |
| 33 – 37 | 69 | 17.97 |
| 38 – 42 | 42 | 10.94 |
| 43 – 47 | 36 | 9.38 |
| 48 – 52 | 24 | 6.25 |
| 53 – 57 | 13 | 3.39 |
| **TOTALS** | **384** | **100** |

*Table 1: Age of TB patients (N=384)*

The age distribution of the TB patients was ranging from 18 years to 57 years with a mean age of 33.76 years. The 28 – 32-year age group made the largest proportion of the TB patients while the 53 – 57 years' age group the least with only 3.39%.

### 4.1.2. Sex

Most of the TB patients were male. 230 (59.90%) of them were males while the remaining 154 (40.10%) were females. The male: female ratio was 1.49: 1. This is shown in figure 2 below.

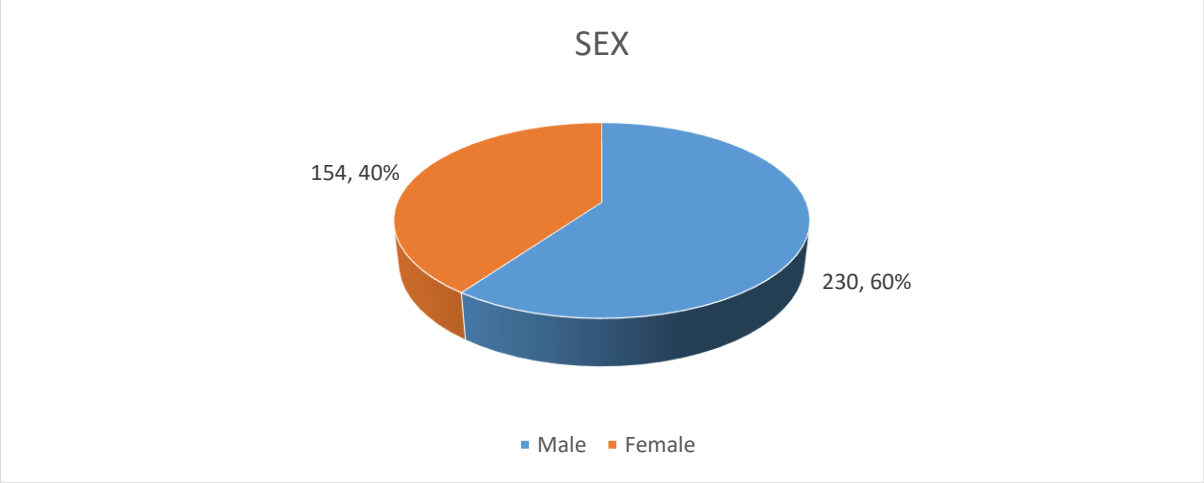



*Figure 2: Sex Distribution of TB Patients (N=384)*

### 4.1.3. Duration since TB Diagnosis was Made (N=384)

For purposes of classification, the TB patients were grouped into two depending on the duration since the TB diagnosis was made. The grouping was into those who were diagnosed 2 months or less (meaning they were still in the initiation phase of treatment) and those that were above 2 months (implying that they were in the maintenance phase of therapy).

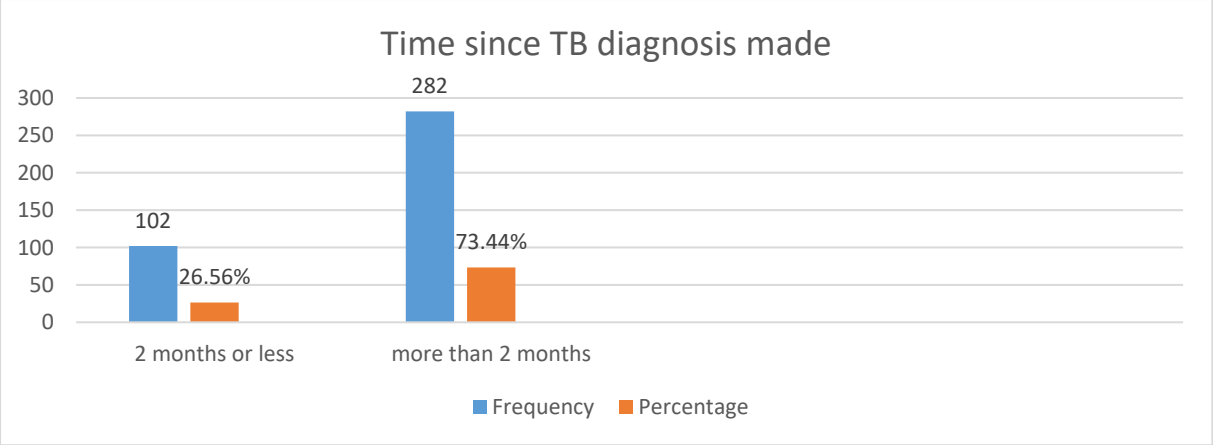



*Figure 3: Duration of Time Since TB Diagnosis was Made (N=384)*

From Figure 3 above, most of the TB patients had been diagnosed more than 2 months meaning that they would be in the maintenance phase of therapy. 282 (73.44%) were in the maintenance phase and thus on a combination of Isoniazid and Rifampicin while 102 (26.56%) were still on the initiation phase with a 3-drug combination of Pyrazinamide, Rifampicin and Isoniazid. There was no report of any patient on second line anti-tuberculous agents.

### 4.2. Prevalence of TB/HIV Coinfection (N=384)

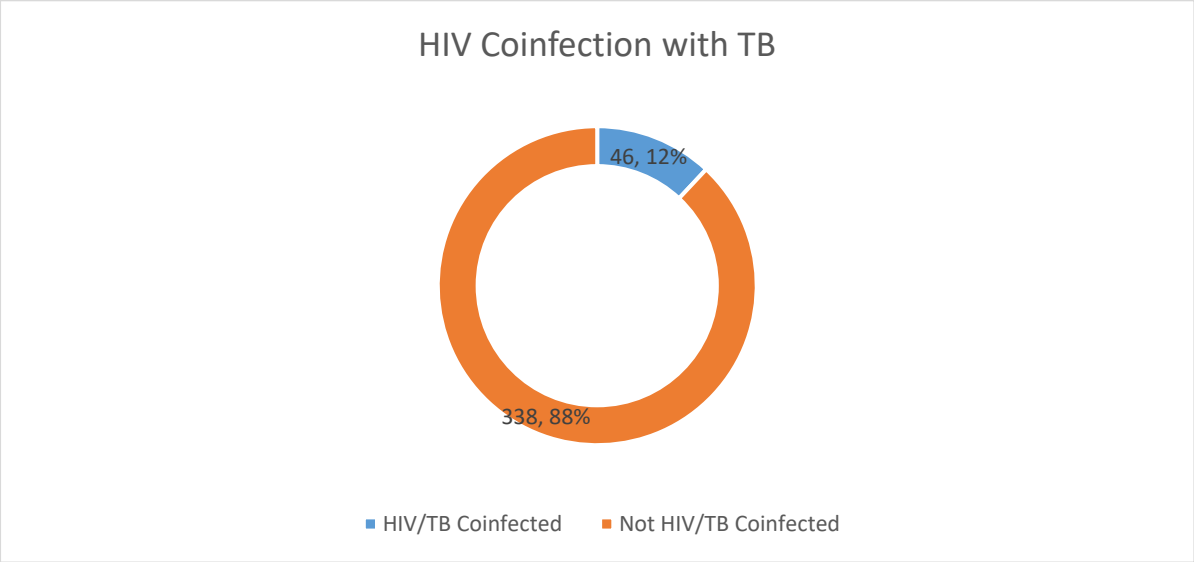



*Figure 4: Prevalence of TB/HIV Coinfection in TB Patients (N=384)*

Figure 4 above shows that the prevalence of TB/HIV coinfection was 12%. 46 of the TB patient also were HIV positive while 338 (88%) were HIV negative.

#### 4.2.1. Duration since HIV Diagnosis & whether on treatment at the time (N=46)

Again the patients were grouped into two; those whose HIV diagnosis was only 2 months or less and those who were diagnosed more than 2 months prior.

| **Duration (months)** | **Frequency (n)** | **Percentage (%)** |
|---|---|---|
| 2 and below | 28 | 60.87 |
| More than 2 | 18 | 39.13 |
| **TOTAL** | **46** | **100** |

*Table 2: Duration Since HIV Diagnosis (N=46)*

Most (60.87%) of the patients' HIV diagnosis was made about 2-months or less prior while in 39.13% the diagnosis had been made more than 2 months prior. All of the 46 (100%) of those found HIV positive were on HAART, most (60.87%) being into there second month of treatment or less.

### 4.3. Prevalence of Extrapulmonary TB

Records were reviewed for any physician-reported cases of EPTB documented among the 384 TB patients. 38 cases of EPTB were reported while the remaining 346 were categorized into PTB. The prevalence of EPTB was thus 9.90% and that of PTB 90.10%. The different presentations of EPTB recorded were as shown in Figure 5 below.

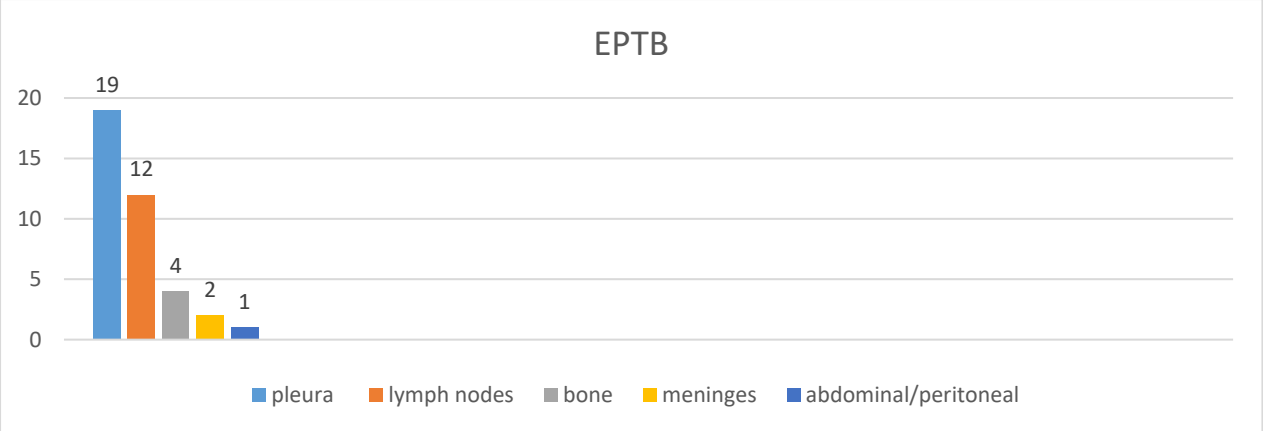



*Figure 5: Various Forms of EPTB Reported (N=38)*

The most common form of EPTB reported was that involving pleura (19, 50%), followed by TB adenitis (12, 31.58%), bone (4, 10.53%), meninges (2, 5.26%) and lastly abdominal/peritoneal (1, 2.63%). 32 (84.21%) of the EPTB cases were reported among the HIV positive while only 6 (15.79%) of the HIV negative developed extra-pulmonary TB.

**4.4. TB/HIV Coinfection, Treatment Adherence & Overall Outcome**

As reported earlier, at the time of the study, all the TB cases and all the HIV cases were on treatment. No defaulting was on record and no switch of medications for any reason whatsoever was reported. At the time of conclusion of the study, only 2 (0.52%) cases (those who had a diagnosis) of TBM were on record as to have died and 3 (0.78%) had gotten lost to follow-up. The rest had completed their TB treatment with no treatment failures or cases of drug resistance reported. Overall, no other major opportunistic infections were reported save for oral thrush and dermatosis.

# CHAPTER FIVE: DISCUSSIONS, CONCLUSIONS AND RECOMMENDATIONS

## 5.0.Introduction

This chapter discusses the study findings, presents the conclusions derived from these findings and the recommendations made.

## 5.1. Discussions

### 5.1.1. Prevalence of TB/HIV coinfection

A total of 384 TB cases were assessed in the study made up of largely males (59.90%) aged between 28 – 32 years. Among them, a diagnosis of HIV was assessed and the prevalence of TB/HIV coinfection was found at 12%.

This value is way higher than the global value estimated at 8% by (WHO, 2017) and this could be because the global estimate was just an average arrived at after including 92 countries with low and high TB and HIV prevalence. The population in this study represents a country and a region with high prevalence values for both HIV and TB reported (Avert, 2017), (Hermans, 2012). It is, however, within the ranges reported by (Pimpin et al., 2011) in the European Union in a study that compared, and found varied prevalence between eastern, western parts and central European Union countries. The central European countries had lower prevalence of TB/HIV infection than the former two, a fact that emphasizes the wide regional variation that exists.

India's TB/HIV coinfection prevalence was higher (18.1%) than this study's may be chiefly because of the high TB prevalence India, a country that has earned itself the title of being the world's TB capital contributing 24% of the global TB prevalence (Tripathi et al., 2015). India's larger value could be attributable to the fact that it is the second most populous country in the world with high rates of over-crowding that is known to be a major risk factor for TB transmission and spread (Oxlade & Murray, 2012). The high HIV rates could be because of the increased sex trade rampant in Indian slums which are also filthy, crowded and TB risks (Bandewar, Bharat, Kongelf, Pisal, & Collumbien, 2016).

This study's high prevalence value drive home the fact that TB/HIV coinfection is still one of the biggest public health challenge in sub-Saharan Africa, a fact reported by (Gao et al., 2013), and reiterated by (Glaziou et al., 2018) who reported a prevalence range of between 3.85 and 22.3% in SSA, within which our study findings fall. Similarly, higher values have been tabled by quite a number of studies conducted in Ethiopia! (Mitku et al., 2016) reported a prevalence of 27.7% in the Amhara region, (Tesfaye et al., 2018) reported 25.59% and (Belay et al., 2015) reported 28.6%. These high TB/HIV coinfection prevalence may be as a result of high HIV prevalence in Ethiopia as reported by (Wondimeneh, Muluye, & Belyhun, 2012). Also, delay

in diagnosis, especially amongst the pastoralist communities of Ethiopia increase transmission risk and spread as reported by (Gele, Bjune, & Abebe, 2009) and in whom HIV has been on the surge recently and unfortunately has been neglected (Serbessa, Mariam, Kassa, Alwan, & Kloos, 2016).

Though being a unit higher than the 11% reported in Tanzania by (Gunda et al., 2018), this study's value still contributes to the argument that TB/HIV coinfection, is really a problem in SSA. This slight variation between the two studies may be the result of the fact that the Tanzanian study was assessing for TB among HIV-positive patients while this study was assessing for HIV in TB patients. All in all, the fact still remains that TB and HIV are a problem within these two populations.

Of importance to note is the fact that this study's findings are way below the 42% reported by (Burnett et al., 2018) in health facilities in rural Uganda. This big difference could be as a result of a number of reasons among them being the difference in population and regional characteristics between the two studies, practice differences of the health facilities or more importantly, varying impact of the "test and treat policy" instituted in Uganda in the fight against TB and HIV. It could be implied that, FPRRH has made considerable progress in this fight compared to the rural facilities involved in that particular study back in 2018.

### 5.1.2. Prevalence of Extrapulmonary TB

The prevalence of EPTB was reported at 9.90% (with the most common extra-pulmonary site being the pleura and the least common being the abdomen/peritoneum), a value that, though higher than the 5.8% and much lower than the 44.4% reported in the EU study by (Sandgren et al., 2013), it again spotlights the wide variation talked about earlier. This variation was replicated in several other studies conducted prior. Throughout studies reviewed, the one fact that clearly stand out is the fact that this study's findings are way lower than values previously recorded – values in studies like those by (Singh et al., 2011), (Sanches, Carvalho, & Duarte, 2015) and (Mohammed et al., 2018) to mention but a few.

Two reasons could explain this huge difference; problems with diagnosis and sampling shortfalls. Much more EPTB cases could have been present but many could have gone undiagnosed and/or unrecorded as (Solovic et al., 2013) found out in their study. Also, during sampling, a majority of the EPTB cases could have been excluded from the study. On the flipside, it could mean effective immunological and laboratory control through treatment adherence and thus the bacilli was prevented from growing and spreading locally (Schutz et al., 2010).

### 5.1.3. Effect of TB/HIV Coinfection & Adherence to Treatment

No adverse effects, development of treatment resistance and treatment failures nor worsening of either conditions through major opportunistic infections and worsening of prognosis was reported. This could be attributable to the fact that no default cases were reported either. This is indicative of effective and uninterrupted treatment within the study population being beneficial as reported by (Kompala et al., 2013). There were also less EPTB cases reported compared to previous studies, which may be an indicator of effective viral load control and prevention of $CD^{+}4$ decline, which maintains the immune system's ability to prevent the growth and local spread of the mycobacterium (Schutz et al., 2010). No major opportunistic infection such as Pneumocystis Jiroveci Pneumonia was reported, again indicating effective viral load control with good immunological status with high $CD^{+}4$ counts (Ismail & Bulgiba, 2013). The impressive treatment adherence to could be attributable to supervised drug intake and support from loved in reminding to take drugs and to go for refills.

## 5.2. Conclusions

The prevalence of TB/HIV coinfection was high at 12% though not as high as estimates from previous studies elsewhere. This notwithstanding, urgent interventions are needed to reverse this.

The prevalence of EPTB was low at 9.9%, values far lower than estimates of previous studies. Treatment adherence was not adversely affected by TB/HIV coinfection and for this reason no unfavourable outcomes were reported. 2 case-fatality rates were reported in the patients with a diagnosis of TBM.

## 5.3. Recommendations

### 5.3.1. To patients diagnosed with TB

Keep up the good record of treatment adherence but at the same time protect themselves from contracting HIV/AIDS because it increases the chances of developing EPTTB which has a worse prognosis compared to PTB. It would also minimize the risk of drug interactions that may result with the concurrent use of ant-TB drugs and ARVs.

### 5.3.2. To administration and staff of FPRRH

Revamp the fight against HIV and TB through awareness-creation and education on the significant burden of the infections both as separate entities and as coinfections. Also, education on the fact that TB is a curable condition and suspicious cases should seek medical advice as soon as possible. Stringent diagnostic approach with high index of suspicion for EPTB among HIV positive patients.

### 5.3.3. To fellow researchers

This study utilized a retrospective, record-review approach that was not without its limitations and shortfalls. A prospective study approach could get rid of these limitations especially in the aspect of diagnosis, recording and reporting of opportunistic infections, EPTB cases among others. A prospective study would also facilitate regular monitoring and recording of viral loads, $CD^{+}4$ counts, adverse reactions, sputum analysis among others.

**REFERENCES**


Avert. (2017). Global HIV and AIDS statistics | AVERT. *Avert*. https://doi.org/10.1596/1813-9450-6869

Bandewar, S. V. S., Bharat, S., Kongelf, A., Pisal, H., & Collumbien, M. (2016). Considering risk contexts in explaining the paradoxical HIV increase among female sex workers in Mumbai and Thane, India. *BMC Public Health*. https://doi.org/10.1186/s12889-016-2737-2

Bekker, L., & Wood, R. (2010). The Changing Natural History of Tuberculosis and HIV Coinfection in an Urban Area of Hyperendemicity. *Clinical Infectious Diseases*, *50*(s3), S208–S214. https://doi.org/10.1086/651493

Belay, M., Bjune, G., & Abebe, F. (2015). Prevalence of tuberculosis, HIV, and TB-HIV co-infection among pulmonary tuberculosis suspects in a predominantly pastoralist area, northeast Ethiopia. *Global Health Action*, *8*(5), 1–7. https://doi.org/10.3402/gha.v8.27949

Burnett, S. M., Zawedde-Muyanja, S., Hermans, S. M., Weaver, M. R., Colebunders, R., & Manabe, Y. C. (2018). Effect of TB/HIV Integration on TB and HIV Indicators in Rural Ugandan Health Facilities. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *79*(5), 605–611. https://doi.org/10.1097/QAI.0000000000001862

Davies, P. D. O., Gordon, S. B., & Davies, G. (2014). Clinical tuberculosis. In *Clinical Tuberculosis, Fifth Edition*. https://doi.org/10.1201/b16604

Didilescu, C., & Tanasescu, M. (2012). [Proportion and site distribution of extrarespiratory tuberculosis in 2007-2010 in Romania]. *Pneumologia (Bucharest, Romania)*.

Diedrich, C. R., & Flynn, J. A. L. (2011). HIV-1/Mycobacterium tuberculosis coinfection immunology: How does HIV-1 exacerbate tuberculosis? *Infection and Immunity*. https://doi.org/10.1128/IAI.01126-10

Drummond, I., Pinto, J. A., Mesquita, J. D., Schall, V. T., Mutahar, R., Masoudnia, E., … Norr, K. F. (2015). Global HIV & AIDS statistics — 2018 fact sheet. *Indian Journal of Sexually Transmitted Diseases and AIDS*. https://doi.org/27367846293461

Gaifer, Z. (2017). Epidemiology of extrapulmonary and disseminated tuberculosis in a tertiary care center in Oman. *International Journal of Mycobacteriology*, *6*(2), 162. https://doi.org/10.4103/ijmy.ijmy_31_17

Gao, J., Zheng, P., & Fu, H. (2013). Prevalence of TB/HIV Co-Infection in Countries Except China: A Systematic Review and Meta-Analysis. *PLoS ONE*, *8*(5). https://doi.org/10.1371/journal.pone.0064915

Geldmacher, C., Zumla, A., & Hoelscher, M. (2012). Interaction between HIV and

Mycobacterium tuberculosis: HIV-1-induced CD4 T-cell depletion and the development of active tuberculosis. *Current Opinion in HIV and AIDS*. https://doi.org/10.1097/COH.0b013e3283524e32

Gele, A. A., Bjune, G., & Abebe, F. (2009). Pastoralism and delay in diagnosis of TB in Ethiopia. *BMC Public Health*, *9*, 5. https://doi.org/10.1186/1471-2458-9-5

Glaziou, P., Floyd, K., & Raviglione, M. C. (2018). Global Epidemiology of Tuberculosis. *Seminars in Respiratory and Critical Care Medicine*. https://doi.org/10.1055/s-0038-1651492

Gray, J. M., & Cohn, D. L. (2013). Tuberculosis and HIV coinfection. *Seminars in Respiratory and Critical Care Medicine*. https://doi.org/10.1055/s-0032-1333469

Gunal, S., Yang, Z., Agarwal, M., Koroglu, M., Arc, Z. K., & Durmaz, R. (2011). Demographic and microbial characteristics of extrapulmonary tuberculosis cases diagnosed in Malatya, Turkey, 2001-2007. *BMC Public Health*. https://doi.org/10.1186/1471-2458-11-154

Gunda, D. W., Maganga, S. C., Nkandala, I., Kilonzo, S. B., Mpondo, B. C., Shao, E. R., & Kalluvya, S. E. (2018). Prevalence and risk factors of active TB among Adult HIV Patients Receiving ART in Northwestern Tanzania: A Retrospective Cohort Study. *Canadian Journal of Infectious Diseases and Medical Microbiology*, *2018*. https://doi.org/10.1155/2018/1346104

Hermans, S. (2012). *HIV and tuberculosis co-infection in Uganda Clinical management , immune reconstitution and health service delivery*.

Ismail, I., & Bulgiba, A. (2013). Predictors of Death during Tuberculosis Treatment in TB/HIV Co-Infected Patients in Malaysia. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0073250

Karakousis, P. C., & Piggott, D. A. (2011). Timing of antiretroviral therapy for HIV in the setting of TB treatment. *Clinical and Developmental Immunology*. https://doi.org/10.1155/2011/103917

Kompala, T., Shenoi, S. V., & Friedland, G. (2013). Transmission of tuberculosis in resource-limited settings. *Current HIV/AIDS Reports*. https://doi.org/10.1007/s11904-013-0164-x

Kulchavenya, E., Zhukova, I., & Kholtobin, D. (2013). Spectrum of urogenital tuberculosis. *Journal of Infection and Chemotherapy*. https://doi.org/10.1007/s10156-013-0586-9

Lin, J. N., Lai, C. H., Chen, Y. H., Lee, S. S. J., Tsai, S. S., Huang, C. K., … Lin, H. H. (2009). Risk factors for extra-pulmonary tuberculosis compared to pulmonary tuberculosis. *International Journal of Tuberculosis and Lung Disease*.

Marzinke, M. A. (2016). Therapeutic Drug Monitoring of Antiretrovirals. In *Clinical Challenges in Therapeutic Drug Monitoring: Special Populations, Physiological Conditions, and Pharmacogenomics*. https://doi.org/10.1016/B978-0-12-802025-8.00006-4

Mazza-Stalder, J., Nicod, L., & Janssens, J. P. (2012). La tuberculose extrapulmonaire. *Revue Des Maladies Respiratoires*. https://doi.org/10.1016/j.rmr.2011.05.021

Mitku, A. A., Dessie, Z. G., Muluneh, E. K., & Workie, D. L. (2016). Prevalence and associated factors of TB/HIV co-infection among HIV infected patients in Amhara region, Ethiopia. *African Health Sciences*, *16*(2), 588–595. https://doi.org/10.4314/ahs.v16i2.29

Mohammed, H., Assefa, N., & Mengistie, B. (2018). Prevalence of extrapulmonary tuberculosis among people living with HIV/AIDS in sub-Saharan Africa: a systemic review and meta-analysis. *HIV/AIDS - Research and Palliative Care*, *Volume 10*, 225–237. https://doi.org/10.2147/HIV.S176587

Namme, L., Achu, J., Christopher, K., Elvis, T., Hugo Bertrand, M., & Marie-Solange, D. (2013). Extrapulmonary tuberculosis and HIV coinfection in patients treated for tuberculosis at the Douala General Hospital in Cameroon. *Annals of Tropical Medicine and Public Health*. https://doi.org/10.4103/1755-6783.115207

National Institute of Health. (2018). Guidelines for the prevention and treatment of oppoutunistic infections in HIV-infected adults and adolescents. https://doi.org/10.1021/ja305252t

Ollé-Goig, J. E. (2010). Tuberculosis in rural Uganda. *African Health Sciences*, *10*(3), 226–229. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21327132

Oxlade, O., & Murray, M. (2012). Tuberculosis and Poverty: Why Are the Poor at Greater Risk in India? *PLoS ONE*. https://doi.org/10.1371/journal.pone.0047533

Ozer, E. K., Goktas, M. T., Toker, A., Pehlivan, S., Bariskaner, H., Ugurluoglu, C., & Iskit, A. B. (2017). Thymoquinone protects against the sepsis induced mortality, mesenteric hypoperfusion, aortic dysfunction and multiple organ damage in rats. In *Pharmacological Reports* (Vol. 69). https://doi.org/10.1016/j.pharep.2017.02.021

Peto, H. M., Pratt, R. H., Harrington, T. A., LoBue, P. A., & Armstrong, L. R. (2009). Epidemiology of Extrapulmonary Tuberculosis in the United States, 1993–2006. *Clinical Infectious Diseases*. https://doi.org/10.1086/605559

Pimpin, L., Drumright, L. N., Kruijshaar, M. E., Abubakar, I., Rice, B., Delpech, V., … Ködmön, C. (2011). Tuberculosis and HIV co-infection in European Union and European Economic Area countries. *European Respiratory Journal*, *38*(6), 1382–1392.

https://doi.org/10.1183/09031936.00198410

Raghavan, S., Alagarasu, K., & Selvaraj, P. (2012). Immunogenetics of HIV and HIV associated tuberculosis. *Tuberculosis*. https://doi.org/10.1016/j.tube.2011.08.004

Ramappa, V., & Aithal, G. P. (2013). Hepatotoxicity Related to Anti-tuberculosis Drugs: Mechanisms and Management. *Journal of Clinical and Experimental Hepatology*, *3*(1), 37–49. https://doi.org/10.1016/j.jceh.2012.12.001

Sanches, I., Carvalho, A., & Duarte, R. (2015a). Who are the patients with extrapulmonary tuberculosis? *Revista Portuguesa de Pneumologia (English Edition)*, *21*(2), 90–93. https://doi.org/10.1016/j.rppnen.2014.06.010

Sanches, I., Carvalho, A., & Duarte, R. (2015b). Who are the patients with extrapulmonary tuberculosis? *Revista Portuguesa de Pneumologia*. https://doi.org/10.1016/j.rppnen.2014.06.010

Sandgren, A., Hollo, V., & van der Werf, M. J. (2013). Extrapulmonary tuberculosis in the European union and European economic area, 2002 to 2011. *Eurosurveillance*. https://doi.org/10.1103/PhysRevB.89.155426

Schutz, C., Meintjes, G., Almajid, F., Wilkinson, R. J., & Pozniak, A. (2010). Clinical management of tuberculosis and HIV-1 co-infection. *European Respiratory Journal*. https://doi.org/10.1183/09031936.00110210

Scott, L., Da Silva, P., Boehme, C. C., Stevens, W., & Gilpin, C. M. (2017). Diagnosis of opportunistic infections: HIV co-infections-tuberculosis. *Current Opinion in HIV and AIDS*. https://doi.org/10.1097/COH.0000000000000345

Serbessa, M. K., Mariam, D. H., Kassa, A., Alwan, F., & Kloos, H. (2016). HIV/AIDS among pastoralists and refugees in north-east Africa: a neglected problem. *African Journal of AIDS Research*, *15*(1), 45–54. https://doi.org/10.2989/16085906.2016.1148060

Sevgi, D. Y., Derin, O., Alpay, A. S., Gündüz, A., Konuklar, A. S., Bayraktar, B., … Sonmez, E. (2013). Extrapulmonary tuberculosis: 7 year-experience of a tertiary center in Istanbul. *European Journal of Internal Medicine*. https://doi.org/10.1016/j.ejim.2013.08.704

Shankar, E. M., Vignesh, R., Ellegård, R., Barathan, M., Chong, Y. K., Bador, M. K., … Larsson, M. (2014). HIV-Mycobacterium tuberculosis co-infection: A “danger-couple model” of disease pathogenesis. *Pathogens and Disease*. https://doi.org/10.1111/2049-632X.12108

Sharma, S. K., & Mohan, A. (2013). Tuberculosis: From an incurable scourge to a curable disease - Journey over a millennium. *Indian Journal of Medical Research*.

https://doi.org/IndianJMedRes_2013_137_3_455_110999 [pii]

Sharma, S. K., & Soneja, M. (2011). HIV & immune reconstitution inflammatory syndrome (IRIS). *Indian Journal of Medical Research*. https://doi.org/10.4103/0971-5916.92632

Singh, D., Vogel, M., Müller-Stöver, I., el Scheich, T., Winzer, M., Göbels, S., … Richter, J. (2011). TB or not TB? Difficulties in the diagnosis op tuberculosis in HIV-negative immigrants to Germany. *European Journal of Medical Research*. https://doi.org/10.1186/2047-783X-16-9-381

Solovic, I., Jonsson, J., Korzeniewska-Kosela, M., Chiotan, D. I., Pace-Asciak, A., Slump, E., … van der Werf, M. J. (2013). Challenges in diagnosing extrapulmonary tuberculosis in the European Union, 2011. *Eurosurveillance*. https://doi.org/10.2807/ese.18.12.20432-en

Stop TB Partnership. (2015). Stop TB Partnership Annual Report. *Stop TB Partnership*, 54.

Tesfaye, B., Alebel, A., Gebrie, A., Zegeye, A., Tesema, C., & Kassie, B. (2018). The twin epidemics: Prevalence of TB/HIV coinfection and its associated factors in Ethiopia; A systematic review and meta-analysis. *PLoS ONE*, *13*(10), 1–18. https://doi.org/10.1371/journal.pone.0203986

Tiberi, S., Carvalho, A. C. C., Sulis, G., Vaghela, D., Rendon, A., Mello, F. C. d. Q., … Pontali, E. (2017). The cursed duet today: Tuberculosis and HIV-coinfection. *Presse Medicale*. https://doi.org/10.1016/j.lpm.2017.01.017

Tripathi, K., Tripathi, A. C., & Tripathi, R. (2015). Prevalence of HIV-TB Co-Infection Among Patients Attending Antiretroviral Clinic in Northern Semi-Urban India. *Open Forum Infectious Diseases*, *2*(suppl_1). https://doi.org/10.1093/ofid/ofv133.1234

Uganda AIDS Comission. (2017). *Uganda Hiv / Aids Country Progress Report July 2016-June 2017*. Kampala, Uganda.

WHO, UNAID, G. (2016). *UGANDA POPULATION-BASED HIV IMPACT ASSESSMENT UPHIA 2016–2017*. https://doi.org/10.1038/jcbfm.1983.1

WHO. (2015). Global Tuberculosis Report 2015. In *Global Tuberculosis Report 2015*. https://doi.org/978 92 4 156450 2

WHO. (2017a). *HIV-Associated TB*. https://doi.org/10.1016/j.tsf.2010.10.004

WHO. (2017b). *Uganda Tuberculosis Profile 2015*. Retrieved from www.who.int/tb/dat

Wiler, J. L., Shalev, R., & Filippone, L. (2010). Case report and review: Potts disease and epididymal tuberculosis presenting as back pain and scrotal mass. *American Journal of Emergency Medicine*. https://doi.org/10.1016/j.ajem.2009.06.015

Wondimeneh, Y., Muluye, D., & Belyhun, Y. (2012). Prevalence of Pulmonary tuberculosis and immunological profile of HIV co-infected patients in Northwest Ethiopia. *BMC*

*Research Notes*. https://doi.org/10.1186/1756-0500-5-331

World Health Organization. (2014). Global tuberculosis report 2014 (WHO). In *WHO Library*

**APPENDICES**

**Appendix 1: Authorization Later from IREC**

**Appendix 2: Research Instrument**

**CHECKLIST**

**SERIAL NO: …….**

**INTRODUCTION**

**STUDY TITLE:** HUMAN IMMUNODEFICIENCY VIRUS AND TUBERCULOSIS COINFECTION AT FORT PORTAL REGIONAL REFERRAL HOSPITAL.

**CONFIDENTIALITY:** I am **Aminu Sulaiman Yusuf.,** a final year medical student at Kampala International University – Western Campus carrying out the above research.

IP No. …….

Age …….

Sex ……...

1. TB Diagnosis negative ☐ positive ☐
   a. When was the diagnosis made? …….
   b. On treatment for TB? Yes ☐ no ☐
   c. Anti-TB regimen the patient has been on ……
   d. For how long has the patient been on this regimen? ……
   e. Any issues with TB treatment defaulting? yes ☐ no ☐
2. HIV Diagnosis negative ☐ positive ☐
   a. When was the diagnosis made? …….
   b. On HAART? Yes ☐ no ☐
   c. ART regimen the patient has been on ……
   d. For how long the patient has been on this regimen? ……..
   e. Any issues with ART defaulting recorded? Yes ☐ no ☐
3. Any opportunistic infections suffered since time of diagnosis? Yes ☐ No ☐

   Which ones? ……

**Appendix 3: Map of Uganda Showing the Location of Kabarole District (Red Arrow)**