# FACTORS ASSOCIATED WITH TB-HIV CO-INFECTION IN CHILDREN RECEIVING ANTI-RETROVIRAL THERAPY IN IMO STATE, NIGERIA

**BY**

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## CERTIFICATION

This is to certify that this work "**FACTORS ASSOCIATED WITH TB-HIV COINFECTION IN CHILDREN RECEIVING ANTIRETROVIRAL THERAPY (ART) IN IMO STATE**" was carried out by **OGINI IKENNA OLUEBUBE (20184141428)** in partial fulfillment for the award of the degree of Master of Public Health (MPH in Epidemiology and Biostatistics) in the Department of Public Health, Federal University of Technology, Owerri.

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## DEDICATION

This is project work is dedicated to all lovers of education in the field of Public Health.

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## Abstract

Nearly 90% of children living with HIV and Tuberculosis are domiciled in Sub-Saharan Africa. While HIV and TB care has improved over the years, low and middle-income countries still fall behind. Given the paucity of data on TB-HIV co-infection in children, understanding the risk factors for co-infection in this age group has been difficult. In this study, we used a matched case-control study design to understand the risk factors of TB-HIV in children receiving antiretroviral treatment (ART) in Imo, State, Nigeria. 30 TB-HIV incident cases and 90 control children living with HIV receiving ART were recruited from selected HIV treatment sites in Imo State. A structured questionnaire was used to collect information on family size, socioeconomic status, passive smoking, household food security, and household TB exposure. Our analysis included cases matched by age and gender in a ratio of 1:3 to controls. The study showed a prevalence of 6.2 in children receiving ART in Imo state. The largest proportion of study participants was among children aged 15-17 (39.2%). The risk of co-infection increased as the number of people living with the child increased. Having at least three people living with a child in a room was found significant in TB-HIV coinfection (p = 0.006, 95%CI for odds =1.76 – 28.78). Almost all items assessed for household food security were significant factors in TB-HIV co-infection. Reduced food intake for children was found to be a significant factor in TB-HIV coinfection (p=0.004, $x^2$ = 8.50). Having a family member living with HIV (p=0.016, $x^2$ = 5.75) or having symptoms of TB (p=0.0001, $x^2$ = 50.39). The significant factors of passive smoking were the extent to which the respondents think they are exposed to tobacco smoke at home (p=0.0001, $x^2$ = 24.14), having some members of the family smoke inside the home (p=0.0001 $x^2$ = 17.57), and having some degree of exposure to tobacco smoke in socialization areas outside the household (p=0.0001, $x^2$ = 22.80). None of the social-economic status factors assessed in this study was found significant for co-infection except those who earn income to support the family (p=0.023, $x^2$ = 11.36) and the hours of work they do each week (p=0.038, $x^2$ =6.54). This study showed that household food security, passive smoking, family size, and household TB exposure are associated with TB-HIV co-infection in children. Our data is consistent with other studies of TB-HIV co-infection that family size, exposure to tobacco smoke and socioeconomic status are associated with HIV-TB Co-infection. The study recommended the improvement of socio-economic status and sensitization of families with HIV positive children to reduce tobacco exposure.



**Keywords: Coinfection, HIV, TB, Children, Antiretroviral Therapy**

# CHAPTER ONE

# INTRODUCTION

## 1.1. Background Information

Over 150,000 children aged 0–9 were newly infected with HIV in 2019, according to the United Nations Children's Fund (UNICEF), bringing the total number of children living with HIV to 1.1 million [780,000–1.3 million] (UNICEF, 2020). It is concerning that about 90% of these children reside in sub-Saharan Africa (UNICEF, 2020). Less than 60% of pregnant women living with HIV in western and central Africa have access to methods to prevent vertical HIV transmission, according to the Joint United Nations Programme on HIV/AIDS (UNAIDS) (UNAIDS, 2020). In both resource-rich and resource-limited settings, children's survival has significantly increased since the advent of antiretroviral therapy (ART). Although ART coverage is increasing, only around 53% [36–64%] of children under the age of 15 who require treatment are believed to be receiving it in low- and middle-income countries, compared to 68% [54–80%] among adults (UNAIDS, 2020).

The most prevalent coinfection, which still has a high mortality and morbidity rate worldwide, is TB/HIV. 4.4% of the world's cases of tuberculosis are found in Nigeria. Globally, there were 10.2 million new cases of TB in 2020, with 8.2% being co-infected with HIV. There were also 1.2 million deaths worldwide, 208,000 of which were HIV-positive people (WHO, 2020). For more than 50% of HIV-positive patients, tuberculosis is the initial sign of AIDS (WHO, 2004). Especially in sub-Saharan Africa, where this percentage is claimed to be higher than 50% in some countries, deaths that are attributable to TB are alarmingly high (Lange et al., 2014). Yet,

because smear-positive TB is uncommon in children and is difficult to diagnose in children, TB in HIV-infected children continues to go unreported (Moyo et al., 2010; Martinson et al., 2009).

There are few statistics on the prevalence of HIV among children with TB diagnoses and the incidence of TB among children who are HIV-positive. The difficulty in interpreting the information is related to issues with diagnosis, under-ascertainment, and study population selection (i.e., most are recruited from hospitals or referral hospitals rather than the community). According to estimates from the World Health Organization (WHO), the prevalence of HIV in children with TB in nations with moderate to high prevalence ranges from 10 to 60%, with the prevalence varied according to the background rates of HIV infection (WHO, 2011). Estimated rates of tuberculosis among children with HIV also vary greatly, in part depending on whether the study is being conducted in a region with a high TB prevalence or not. The availability of highly active antiretroviral therapy (HAART) in that region, as well as the challenges associated with making a conclusive diagnosis of tuberculosis in children living with HIV, are additional factors.

After contracting *Mycobacterium tuberculosis*, children are at a significant risk of developing the disease, especially those under the age of two who frequently get non-pulmonary forms of TB (Marais et al., 2004). Confirming a TB diagnosis in children can be difficult due to the disease's paucibacillary nature, variety of symptoms, and difficulties getting samples for laboratory testing. Understanding the disease's natural history and epidemiology is made more challenging by this. Current indirect burden estimation methods forecast paediatric TB incidence by using mathematical modeling of exposure and disease progression risks (Dodd et al., 2014). Children develop HIV illness more quickly than adults do, rendering them more prone to opportunistic

infections (Tobin & Aldrovandi, 2013). In children with HIV infection, antiretroviral therapy (ART) can boost immunity and lower morbidity and mortality rates.

There is a chance that Covid-19 will have a medium-term effect on the annual number of TB cases. Regarding the probable effect of the COVID-19 pandemic on worldwide TB fatalities, there have been two modeling assessments with comparable findings (Glaziou, 2021; Rachael Hore, 2020). According to these analyses, the annual number could reach the heights of 2015 or even 2012. In a separate analysis, the WHO estimated the additional number of TB fatalities that could occur worldwide in 2020 for various combinations of a decline in case detection (compared with levels before the pandemic) and the amount of months for which this decline occurred. According to this analysis, there could be between 200,000 and 400,000 extra TB deaths in 2020, bringing the total to approximately 1.6-1.8 million if the number of people with TB detected and treated were to fall by 25-50% over three months – a range considered plausible based on data from several high TB burden countries. The world will return to 2015 levels with an increase of 200,000, and 2012 levels with an increase of 400,000. By 2020 and 2025, Covid-19 may contribute to an additional 6.3 million TB cases worldwide (Rachael Hore, 2020).

Considering all of these, the goal of this study is to identify the factors associated with TB-HIV co-infection in children receiving antiretroviral therapy in Imo State**.** The following research questions were formulated to guide the study:

1. What is the prevalence of TB-HIV co-infection in children receiving ART in Imo State, Nigeria?
2. What is the association of family size with TB-HIV co-infection in children receiving ART in Imo State?

3. What is the association of family socioeconomic status with TB-HIV co-infection in children receiving ART in Imo State?
4. What is the association of passive smoking with TB-HIV co-infection in children receiving ART in Imo State?
5. What is the association of household food insecurity with TB-HIV co-infection in children receiving ART in Imo State?
6. What is the association of household TB exposure with TB-HIV co-infection in children receiving ART in Imo State?

### 1.2. Problem Statement

Children develop HIV illness more quickly than adults do, rendering them more prone to opportunistic infections (Tobin & Aldrovandi, 2013). Yet, it can be difficult to diagnose TB in children, which makes it more difficult to comprehend the epidemiology and natural history of the illness. Newer indirect methods of burden estimating have predicted paediatric TB incidence by mathematical modelling of exposure and disease progression risks (Dodd et al., 2014). In children with HIV infection, antiretroviral therapy (ART) can boost immunity and lower morbidity and mortality rates. No matter the clinical disease stage or level of immunosuppression, according to updated WHO recommendations issued in 2015, all HIV-positive children should start antiretroviral therapy (ART) (Hsiao et al., 2016a). Whereas just 53% of children who are eligible for ART receive it, compared to 68% of adults, children's ART coverage lags behind that of adults (WHO, 2020).

Research on the risk factors for HIV/TB coinfection in children is scarce. Adults are the primary subject of many prevalence studies on the co-infection of HIV and TB. In order to pinpoint the

risk factors for this twin epidemic in children, certain cohort studies have been carried out. Sadly, there are not many case-control studies of HIV/TB coinfection in Nigeria, and those that do tend to are older. Cui et al. (2017) conducted the most recent matched case-control study in an adult population in China to investigate risk factors for TB/HIV coinfection.

### 1.3. Objectives of the Study

This study aims to determine the factors associated with TB-HIV co-infection in children receiving Antiretroviral Therapy in Imo State. Specifically, the following objectives were formulated to guide the study:

1. To determine the prevalence of TB-HIV co-infection in children receiving ART in Imo State, Nigeria.
2. To determine the association of family size with TB-HIV co-infection in children receiving ART in Imo State, Nigeria .
3. To determine the association of family socioeconomic status with TB-HIV co-infection in children receiving ART in Imo State, Nigeria.
4. To determine the association of passive smoking with TB-HIV co-infection in children receiving ART in Imo State, Nigeria.
5. To determine the association of household food insecurity with TB-HIV co-infection in children receiving ART in Imo State, Nigeria.
6. To determine the association of household TB exposure with TB-HIV co-infection in children receiving ART in Imo State, Nigeria.

### 1.4. Hypotheses of the Study

The following null hypotheses were formulated to guide the study:

1. There is no statistically significant association between TB-HIV co-infection in children receiving ART in Imo State , Nigeria and family size.
2. There is no statistically significant association between TB-HIV co-infection in children receiving ART in Imo State, Nigeria and family socioeconomic status.
3. There is no statistically significant effect of passive smoking on TB-HIV co-infection in children receiving ART in Imo State, Nigeria.
4. There is no statistically significant association between TB-HIV co-infection in children receiving ART in Imo State, Nigeria and household food insecurity.
5. There is no statistically significant association between TB-HIV co-infection in children receiving ART in Imo State, Nigeria and household TB exposure.

### 1.5. Justification of Study

There is little information on other factors associated with TB-HIV co-infection in children, which this study believes to be associated with TB-HIV co-infection in children. Many studies point to viral load and ART as the main factors associated with TB-HIV co-infection, primarily in adults, and little knowledge on children.

With a focus on Imo State, the findings of this study have the potential to advance our understanding of the factors that contribute to TB-HIV co-infection in children on ART. At the conclusion of this investigation, it will be known how factors such as family size, socioeconomic

status, TB exposure in the house, food insecurity, and indoor air pollution relate to HIV/TB coinfection.

Policymakers, caregivers, and health professionals will gain from this study's new perspective on the risk factors related to childhood TB-HIV co-infection. By changing these determinants, particularly those outside of the facilities, and avoiding the double epidemicity of these diseases, will contribute to better care.

### 1.6. Scope of Study

The study was delimited to factors associated with TB-HIV co-infection in children receiving ART in Imo State, Nigeria.

# CHAPTER TWO

# LITERATURE REVIEW

## 2.1. CONCEPTUAL FRAMEWORK

### 2.1.1. Concept of HIV:

**Definition of HIV:**

Human immunodeficiency virus (HIV) is a virus that attacks the body's immune system, explicitly the white blood cells known as the CD4 cells. HIV destroys these CD4 cells, debilitating an individual's immunity against infections such as tuberculosis and some cancers., sexually transmissible virus (WHO, 2018b).

HIV infection results in HIV illness, which has symptoms that are remarkably similar to those of HIV-1 or HIV-2. The risks of progression and transmission vary.

**Types of HIV:**

Two particular species of HIV (HIV-1 and HIV-2) have been recognised, and each is made of numerous subtypes or clades. All clades of HIV-1 tend to cause similar disease; however, the global distribution of the clades varies. This may have implications for any future vaccine, as the B clade is predominant in the developed world (where the large pharmaceutical companies are located). This is rarely found in developing countries such as Nigeria, which are more severely affected by the disease.

The origin of HIV-1 probably is from one or more cross-species transfers from chimpanzees in central Africa (Gao et al. 1999). HIV-2, on the other hand, shares characteristics with viruses that

infect sooty mangabeys in western Africa (Hirsch et al. 1989). HIV-1 and HIV-2 are superficially similar genetically, but each contains unique genes and distinct replication processes.

**Mode of Transmission:**

Heterosexual transmission remains the predominant method of transmission, and 85% of all HIV-1 infections can be attributed to this. "The most significant factor that increases the risk of sexual transmission of HIV is the number of copies per mL of plasma HIV-1 RNA (viral load), with 2·4 times increased risk of sexual transmission for every 1 log10 increase" (Quinn et al. 2000). Acute HIV infection, which causes highly increased plasma viral loads in the first few months, is an essential driver of HIV epidemics (Cohen et al. 2011). A reduction in plasma viral load of 0·7 log10 is estimated to reduce HIV-1 transmission by 50% (Lingappa et al. 2010). Seminal and endocervical viral load are independently associated with HIV-1 sexual transmission after adjusting for plasma viral load (Baeten et al. 2011). Other factors associated with a higher risk of sexual transmission of HIV are sexually transmitted infections (especially herpes simplex type-2 infection (Glynn, Biraro, and Weiss 2009), genital ulcers of any cause (R??TTINGEN, WILLIAM CAMERON, and GARNETT 2001), pregnancy (Mugo et al. 2011), bacterial vaginosis (Atashili et al. 2008), and receptive anal intercourse (Baggaley, White, and Boily 2010). There is, however, an association between male circumcision and reduced risk of sexual transmission of HIV (Gandhi et al. 2012).

Some observational studies have shown an association between the use of long-acting injectable progesterones for contraception with an increased risk of HIV-1 infection in women but not oral contraceptives are combined (Polis and Curtis 2013).

Behavioural factors which have been identified to increase HIV-1 sexual transmission include concurrent partnerships (Epstein and Morris 2011) and having many sexual partners (Tanser et al. 2011), and study of African heterosexual serodiscordant couples showed that self-reported condom use reduced the per-coital act risk of HIV-1 transmission by 78% (Hughes et al. 2012). It is noteworthy that sex inequality is a significant driver of the HIV epidemic, notably in subSaharan Africa, where 57% of people living with HIV are women (UNAIDS, 2013). There is an association between injection and non-injection drug use, including increased sexual risk behaviour and alcohol. Injection drug use causes HIV transmission by shared needles (Crawford and Vlahov 2010). Another study in South Africa also found that women who reported violence by intimate partners had an increased incidence of HIV infection (Jewkes et al. 2010). UNAIDS has identified stigma against HIV, and discrimination and punitive laws against high-risk groups (e.g., men who have sex with men, people who inject drugs, and commercial sex workers) as barriers for people to undergo HIV testing, access care, and access prevention measures (Meyer-Rath et al. 2012).

**Epidemiology of HIV:**

In 2018, 37.9 million [32.7 million–44.0 million] people were estimated to be living with HIV (UNAIDS 2019). The highest burden of HIV globally occurs in the East and southern, with 20.6 million people living with the virus and 5.0 million in central and western Africa, which puts Africa under a high burden of HIV (UNAIDS. 2018). However, remarkable changes have occurred in the global epidemiology of HIV infection due to the expansion of antiretroviral therapy access, with 24.5 million [21.6 million–25.5 million] people accessing antiretroviral therapy at the end of June 2019 (UNAIDS 2019). The prevalence of HIV has increased globally from 31·0 million in 2002 to 37.9 million in 2018, which can be attributed to longer lives

witnessed among individuals on antiretroviral treatment (Frank et al. 2019). Also, a decrease in the global incidence from 3·3 million in 2002 to 1.7 million [1.4 million–2.3 million] was recorded in 2018 (UNAIDS 2019). Some areas need more progress. At the end of 2019, 8.1 million people did not know their HIV status, and only 62% of all people with HIV were on ART (WHO 2018a) (a shortfall from the 90 targets of the UNAID).

Gay men, men who have sex with men, sex workers, transgender people, people who inject drugs, prisoners, and other incarcerated people as the five main key population groups. This group is particularly vulnerable to HIV and frequently lacks adequate access to services (UNAID 2016). Outside of sub-Saharan Africa, key populations and their sexual partners accounted for 80% of new HIV infections in 2016 (Hsiao et al. 2016a). Even in sub-Saharan Africa, key populations accounted for 25% of new HIV infections in 2016. The drivers of the HIV epidemic in men who have sex with men are complicated. They include increased risk behaviour since the introduction of effective antiretroviral therapy (a phenomenon termed therapeutic optimism) (Mayer and Mimiaga 2011) and high transmission risk of receptive anal intercourse, sexual networks, and stigma restricting access to care (Beyrer et al. 2013).

Since 2009, there has been a 48% decline in new HIV infections among children in the 21 Global Plan priority countries, a reduction from 330 000 [300 000–370 000] in 2009 to 170 000 [150 000–200 000] in 2014. The number of new HIV infections among children declined by 13% between 2000 and 2008 and 48% between 2009 and 2014 (Hsiao et al. 2016b). In 2018, 770,000 people died from HIV/AIDS (WHO 2018b). However, access to antiretroviral therapy is much lower in children than in adults. HIV is a significant contributor to the global burden of disease.

Findings of a study (Sonnenberg et al. 2005) done in South Africa in the pre-antiretroviral therapy era showed that tuberculosis doubled within a year after HIV infection, thereafter incidence increased as immunity decreased, and reached a very high incidence of 25·7 per 100 person-years in patients with CD4 T-cell counts lower than 50 cells per μL.17 Worldwide, HIV-related tuberculosis mortality is decreasing,15 but many people with HIV in Africa die of undiagnosed tuberculosis (Cohen et al., 2010).

**Screening and Diagnosis of HIV:**

Screening for human immunodeficiency virus (HIV) infection is paramount since infected individuals may remain asymptomatic for years while the infection progresses. Serologic tests are the most important studies in the evaluation of HIV infection. Secondary testing that may be performed to assist with diagnosis or staging includes the following:

1. Viral culture
2. Proviral DNA polymerase chain reaction (PCR)
3. Lymph node biopsy
4. Genotyping of viral DNA/RNA

In June 2014, the Centers for Disease Control and Prevention (CDC) issued new recommendations for HIV testing in laboratories (Bernard M. et al. 2014) to reduce the time needed to diagnose HIV infection by 3-4 weeks over previous testing approaches. The new testing procedure is as follows :

Diagnosis starts with a fourth-generation test that detects HIV in the blood earlier than antibody tests can; it identifies the viral protein HIV-1 p24 antigen, which appears in the blood before antibodies do.

If this test is positive, an immunoassay that differentiates HIV-1 from HIV-2 antibodies should be performed; results from such assays can be obtained faster than they can from the Western blot test.

In patients with positive results on the initial antigen test but with negative or indeterminate results on the antibody differentiation assay, HIV-1 nucleic acid testing should be performed to determine whether the infection is present.

In August 2013, the FDA approved the Alere Determine HIV-1/2 Ag/Ab Combo test (Orgenics, Ltd), the first rapid HIV test for the simultaneous detection of HIV-1 p24 antigen as well as antibodies to both HIV-1 and HIV-2 in human serum, plasma, and venous or fingerstick whole blood specimens (US FDA 2013). Detection of HIV-1 antigen permits earlier detection of HIV-1 infection than is possible by testing for HIV-1 antibodies alone.

This rapid test can be used in outreach settings to identify HIV-infected individuals who might not be able to be tested in traditional healthcare settings. The test does not distinguish between antibodies to HIV-1 and HIV-2 and is not intended to screen blood donors.

The staging of HIV disease is based partially on clinical presentation, but other laboratory tests can help decide whether to initiate or modify treatment.

Baseline laboratory studies for other infections (e.g., tuberculosis) are essential in the initial workup of a patient with a newly diagnosed HIV infection (Kwong and Gabler 2015). In addition, baseline levels of factors that may be affected by antiretroviral therapy (eg, lipids) should be measured.

**Screening for HIV Infection:**

The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians screen for HIV in all adolescents and adults at increased risk for HIV infection and pregnant women (Moyer 2013).

The American College of Obstetricians and Gynecologists (ACOG) recommends that all females aged 13-64 years be tested for HIV at least once during their lifetime. Retesting annually or more often is recommended for those at high risk because of injection drug use, sex with an injection drug user, sex for money or drugs, sex since their most recent HIV test with men who have sex with men, or sex since their most recent HIV test with more than one person (ACOG, 2014).

The Centers for Disease Control and Prevention (CDC) recommends HIV screening for patients in all healthcare settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening); the CDC recommends that persons at high risk for HIV infection be screened for HIV at least annually (CDC, 2006).

Citing the benefits of early diagnosis and treatment and the failure of risk-based screening to identify a substantial proportion of HIV-infected patients early in the disease, the American College of Physicians recommends that clinicians adopt routine screening for HIV and encourage all patients to be tested (Qaseem 2009).

**Staging of HIV:**

The CDC classifies HIV infection into three categories according to the presence of certain infections or diseases. These conditions may be exacerbated by HIV infection or represent true opportunistic infections.

**Category A:** is an asymptomatic HIV infection without a history of symptoms or AIDS-defining conditions.

**Category B:** is HIV infection with symptoms directly attributable to HIV infection (or a defect in T-cell–mediated immunity) or that are complicated by HIV infection. These include, but are not limited to, the following:

1. Bacillary angiomatosis
2. Oropharyngeal candidiasis (thrush)
3. Vulvovaginal candidiasis, persistent or resistant
4. Pelvic inflammatory disease (PID)
5. Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
6. Oral hairy leukoplakia
7. Idiopathic thrombocytopenic purpura
8. Constitutional symptoms, such as fever (>38.5°C) or diarrhea lasting more than one month
9. Peripheral neuropathy
10. Herpes zoster (shingles) involving two or more episodes or one or more dermatomes

**Category C:** is HIV infection with AIDS-defining opportunistic infections, as outlined in Pathophysiology.

These three categories are further subdivided based on the CD4+ T-cell count. Categories A1, B1, and C1 are characterized by CD4+ T-cell counts higher than 500/µL. Categories A2, B2, and C2 are characterized by CD4+ T-cell counts between 200/µL and 400/µL. HIV infections in a patient with CD4+ T-cell counts under 200/µL are designated as A3, B3, or C3.

Importantly, once an HIV infection has been staged into a higher clinical category, it remains in that category permanently. In addition, the disease is classified based on the lowest CD4+ T-cell count in that patient (CDC, 2013).

**WHO Clinical Staging of HIV in Children**

According to WHO (2014)**,** the following are the clinical stages of HIV in children:

**Clinical Stage 1**

- Asymptomatic
- Persistent generalized lymphadenopathy

**Clinical Stage 2**

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Fungal nail infection
- Angular cheilitis
- Lineal gingival erythema
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections (otitis media, otorrhea, sinusitis, or tonsillitis)

**Clinical Stage 3**

- Unexplained moderate malnutrition or wasting, not adequately responding to standard therapy
- Unexplained persistent diarrhea (14 days or more)
- Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month)
- Persistent oral candidiasis (after first 6–8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis or periodontitis
- Lymph node tuberculosis
- Pulmonary tuberculosis
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease, including bronchiectasis
- Unexplained anemia (<8 g/dl), neutropenia (<0.5 × 109 per litre), and or chronic thrombocytopenia (<50 × 109 per litre)

**Clinical Stage 4**

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe presumed bacterial infections (e.g., empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)

- Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration or visceral at any site)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Esophageal candidiasis (or candida of the trachea, bronchi, or lungs)
- central nervous system toxoplasmosis (outside the neonatal period)
- HIV encephalopathy
- Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age over one month
- Extrapulmonary cryptosporidiosis, including meningitis
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
- Chronic Cryptosporidiosis
- Chronic Isosporiasis
- Disseminated non-tuberculous mycobacteria infection
- Acquired HIV-associated rectal fistula
- Cerebral or B cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

**Treatment of HIV:**

The treatment of human immunodeficiency virus (HIV) disease depends on the stage of the disease and any concurrent opportunistic infections. In general, the goal of treatment is to

prevent the immune system from deteriorating to the point that opportunistic infections become more likely. Immune reconstitution syndrome is also less likely in patients whose immune systems are weakened to this point.

Highly active antiretroviral therapy (HAART) is the principal method for preventing immune deterioration. In addition, prophylaxis for specific opportunistic infections is indicated in particular cases.

Successful long-term HAART results in a gradual recovery of CD4 T-cell numbers and improved immune responses and T-cell repertoire (previously lost antigen responses may be restored). The peripheral T-cell counts initially surge after therapy is initiated, but this represents a redistribution of activated T cells from the viral replication centers in the lymph nodes rather than a true increase in total-body CD4 T-cell counts.

In addition to virologic response and reduced risk of opportunistic infection, there is evidence suggesting that non-AIDS-defining illnesses, particularly psychiatric and renal disease, may also be reduced when on HAART. Although multifactorial (transmission mode and patient educational level are independent risk factors for these events), there may also be a direct role of HIV in these events or an indirect role mediated through the subsequent immune dysfunction. Some non-AIDS-defining illnesses, such as liver and cardiovascular disease, are not improved by HAART.

## Prevention of HIV:

### Mother-To-Child Transmission

Prevention of mother-to-child transmission has seen advances in both industrialised and resource-constrained settings (Gueye et al. 2019; McIntyre 2006; Thorne and Newell 2004). Intrapartum transmission has been reduced by increasing access to interventions such as one dose of nevirapine to the mother and newborn baby (Ekouevi, Tonwe-Gold, and Dabis 2005). Concerns about drug-resistant viral strains have led to several trials with combination treatments to reduce transmission during intrapartum (Chaix et al. 2006; Cressey et al. 2005; McIntyre 2006). In some settings, elective delivery by caesarean section can further reduce HIV-1 transmission during the intrapartum period. Still, the benefits of the intervention could be countered by post-partum sepsis and increasing maternal mortality (Read and Newell 2005).

### Other Prevention Routes

The reduction of heterosexual transmission is crucial for controlling the epidemic in many parts of the world (Chan, 2005; UNAIDS, 2013). Prevention is achieved by reducing the number of discordant sexual acts or modifying the probability of HIV-1 transmission in discordant sexual acts. The first can be achieved through abstinence and sex between concordantly seronegative individuals. Abstinence and lifelong monogamous relationships might not be adequate solutions for many people. Therefore, several interventions aimed at lowering the risk of transmission per discordant sexual act are in the process of clinical testing. Male and female condoms provide a proven and affordable prevention option (Bharadwaj 2015). In combination, these options are also more commonly referred to as the ABC (abstinence, be faithful, condom use) approach.

Other biomedical prevention interventions include male circumcision, antiretrovirals for prevention (e.g., pre-exposure or post-exposure), chemoprophylactic treatment of herpes simplex virus-2 (HSV-2), microbicides, and vaccines. Post-exposure prophylaxis is recommended after occupational (e.g., needle stick) (Ministry of Health Singapore 2017) and non-occupational (e.g., rape, sexual abuse) (Fitzpatrick et al. 2014) exposure, although data for efficacy and optimum drug combinations are few (Siegel, Kan, and Benator 2008).

### 2.1.2. CONCEPT OF TUBERCULOSIS (TB)

#### Definition of TB

Tuberculosis (TB) is an infectious disease that is a significant cause of ill health, one of the top 10 causes of death worldwide, and the leading cause of death from a single infectious agent (ranking above HIV/AIDS) (WHO 2020). TB is caused by members of the *Mycobacterium tuberculosis* complex, including the tubercle bacillus (*M. tuberculosis*), *M. bovis, M. africanum, M. microti, and M. canetti* (Phelan, El-Gammal, and O'Connor 2011).

#### Classification of TB:

Tuberculosis (TB) may be classified into active disease or latent infection. The most common form of active TB is lung disease, but it may invade other organs, so-called "extrapulmonary TB."

#### Active TB Disease

Active TB is an illness in which the TB bacteria rapidly multiply and invade different organs of the body. The typical symptoms of active TB variably include cough, phlegm, chest pain,

weakness, weight loss, fever, chills, and sweating at night. A person with active pulmonary TB disease may spread TB to others by airborne transmission of infectious particles coughed into the air. Active disease can occur as primary tuberculosis, developing shortly after an infection, or postprimary tuberculosis, emerging after a long latent infection period. Primary tuberculosis occurs most commonly in children and immunocompromised patients who present with lymphadenopathy, pulmonary consolidation, and pleural effusion (Nachiappan et al. 2017).

**Miliary TB**

This type of tuberculosis is a severe and rare form of TB. It is often due to a haematogenous spread of the bacillus of Koch and represents less than 2 % of TB (Zaghba et al. 2018). Miliary TB occurs when TB bacteria find their way into the bloodstream. In this form, the bacteria quickly spread all over the body in tiny nodules and affect multiple organs at once.

**Latent TB Infection**

Latent tuberculosis infection refers to an asymptomatic, nontransmissible infection with *Mycobacterium tuberculosis*, carrying a 5% to 10% lifetime risk of progressing to active disease (Hartman-Adams et al., 2014). Latent tuberculosis infection (LTBI) affects one-third to one-fourth of the human population. It is the reservoir for a significant proportion of emerging active tuberculosis (TB) cases, especially in low-incidence countries (Matteelli et al. 2017). Many of those who are infected with TB do not develop the overt disease. They have no symptoms, and their chest x-ray may be normal. The only manifestation of this encounter may be a reaction to the tuberculin skin test (TST) or interferon-gamma release assay (IGRA). However, there is an ongoing risk that the latent infection may escalate to active disease. The risk is increased by other illnesses, such as HIV or medications which compromise the immune system.

**Mode of Transmission:**

Tuberculosis is caused by the bacillus *Mycobacterium tuberculosis*, which spreads when people sick with TB expel bacteria into the air, for example, by coughing. It typically affects the lungs (pulmonary TB) but also affects other sites (extrapulmonary TB). About a quarter of the world's population is infected with M. tuberculosis and thus at risk of developing TB disease (WHO, 2014).

**Epidemiology of TB:**

In recent years, the number of people who fell ill globally due to TB has been relatively stable, with 10.0 million (range, 9.0–11.1 million) infected in 2018 (WHO 2020). The burden is not the same among countries, from fewer than five to more than 500 new cases per 100,000 population per year, with the global average being around 130. In 2018, there were an estimated 1.2 million (range, 1.1–1.3 million) TB deaths among HIV-negative people (a 27% reduction from 1.7 million in 2000), and an additional 251 000 deaths (range, 223 000–281 000) among HIV-positive people (a 60% reduction from 620 000 in 2000) (WHO 2020). People of both sexes in all age groups are affected by TB but have the highest occurrence in men (aged ≥15 years), making up 57% of all TB cases in 2018, while women accounted for 32% and children (aged <15 years) for 11%. Among all TB cases, 8.6% were people living with HIV (PLHIV)(WHO, 2020).

Around the world, South-East Asia (44%), Africa (24%), and the Western Pacific (18%) had the highest burden. In comparison, Eastern Mediterranean (8%), the Americas (3%), and Europe (3%) had lower burdens. India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%), and South Africa (3%) has the highest-burden by

country. The eight countries and 22 other countries in WHO's list of 30 high TB burden countries accounted for 87% of the world's cases (Hamada et al., 2018). However, drug-resistant TB continues to threaten public health. In 2018, 500,000 new cases of rifampicin-resistant TB (of which 78% had multidrug-resistant TB) were recorded (United Nations 2018). India (27%), China (14%), and the Russian Federation (9%) are the three countries with the highest burden of rifampicin-resistant TB. Globally, 3.4% of new TB cases and 18% of previously treated cases had multidrug-resistant TB or rifampicin-resistant TB (MDR/RR-TB); countries of the former Soviet Union had the highest proportions (>50% in previously treated cases) (WHO 2018a).

**Diagnosis of TB:**

All individuals, regardless of whether a positive test result or symptoms, must be assessed for TB disease. The majority of people with TB have the symptoms of the disease. However, if an individual tests negative for TB test after showing symptoms, it is recommended that the person be still evaluated for TB disease (CDC, 2012).

When a person tests positive for TB but a medical assessment does not show TB disease, latent TB is diagnosed. When risk factors for the development of TB are considered and the probability of the individual developing TB disease, then a decision on initiation of treatment for latent TB can be made.

To make a definitive diagnosis of TB, a combination of several different investigations, such as imaging, staining, and culture, needs to be made (Phelan et al. 2011). Before an individual can be classified as a suspect case of TB, the following should be used:

1. Loss of appetite

2. Night sweats
3. Unexplained weight loss
4. Fatigue
5. Fever

Symptoms of extrapulmonary TB (TB in other parts of the body are dependent on the area of the body affected. Pulmonary TB (TB in the lungs) manifests through the following:

1. Coughing for longer than three weeks
2. Hemoptysis (coughing up blood)
3. Chest pain

**Treatment of TB:**

The treatment of TB is frequently carried out using a combination of several antibiotics. When an early diagnosis and initiation of treatment for TB is made, the prognosis is favourable (Diel 2019).

For TB disease to be treated, three basic principles defined by the WHO and the International Union Against Tuberculosis and Lung Disease (IUATLD) can be used. First is the use of potent bactericidal drugs in combination to prevent disease transmission by the patient and prevent the transfer to other people. The second principle ensures that prolonged treatment eradicates even the dormant bacteria and prevents relapse. Thirdly, regular treatment with correct doses is given to avoid the development of drug resistance. A proper combination can still cure most tuberculosis cases of isoniazid, rifampicin, pyrazinamide, and ethambutol administered for two months, followed by isoniazid and rifampicin for four months (WHO, 2017).

It is, however, imperative that people who have TB disease are treated, finish the medicine, and exactly as prescribed. If they stop taking the drugs too soon, the disease can relapse; if they do not take the drugs correctly, the TB bacteria still alive may form resistance to those drugs. Drug-resistant TB is more challenging and more expensive to treat.

**Prevention of TB:**

The BCG (Bacille Calmette-Guérin) is a live vaccine against tuberculosis. The vaccine is prepared from the attenuated bovine tuberculosis bacillus strain, *Mycobacterium bovis.* The BCG is currently the only licensed vaccine against TB and has been in use since 1921. It is one of the most widely used vaccines worldwide though there is evidence that the existing BCG vaccines provide incomplete and variable protection against pulmonary TB (Dockrell and Smith 2017). Early diagnosis and treatment is the most effective way to prevent the spread of tuberculosis. A person with infectious TB could infect up to 10–15 other people yearly. But once diagnosed with TB and started on treatment, most patients are no longer infectious after about two weeks on medication.

### 2.1.3. Concept of HIV/TB Co-Infection:

Co-infection occurs when a person acquires two different viral strains simultaneously or when a chronically HIV-infected individual is reinfected with HIV-1, a phenomenon also known as superinfection (International Encyclopedia of Public Health, 2017).

Co-infections in PLHIV usually do matter, and most have adverse consequences. HIV co-infection is a particular case because of lifelong infection and acquired immunodeficiency. The burden of co-infection in PLHIV is hard to quantify. Some insights come from intervention

studies, such as the recent randomised controlled trial of combined antifungal, antituberculous, antihelminthic, and antibacterial prophylaxis started at the time of ART initiation in African children and adults with profound immunosuppression. This regime prevented one death for every 30 patients treated compared to standard prophylaxis with cotrimoxazole alone over 24 weeks (Hakim et al. 2017).

Tuberculosis is the leading cause of opportunistic infection and death among PLHIV. HIV is a potent risk factor for TB and complicates every aspect of tuberculosis care, from prevention to diagnosis and treatment. In contrast, TB increases the progression of HIV and contributes to slower CD4 recovery and faster virological failure on ART (Scriba, Coussens, and Fletcher 2017). Recent work has shown that TB incidence after ART initiation is significantly lower in PLHIV with CD4 more than 500 cells/ml than their counterparts with lower CD4 counts (Bock et al. 2018). Ongoing HIV replication is a significant risk factor for tuberculosis, regardless of CD4 cell counts (Fenner et al. 2017). However, when appropriately controlled for laboratory values and ART exposure, tuberculosis risk does not differ before and after ART initiation (Pettit et al. 2016). Timely tuberculosis diagnosis is challenging in PLHIV because of high smear-negative and extrapulmonary tuberculosis rates. Clinical screening performs poorly in PLHIV and may miss up to 25% of all laboratory-confirmed tuberculosis cases and up to 70% among HIV-infected pregnant women (Modi et al. 2016). Molecular and lateral flow diagnostics with greater sensitivity promise to improve the situation (Carlucci et al. 2017; Huerga et al. 2017; Kendall et al. 2017; Lawn et al. 2017; Suwanpimolkul et al. 2017).

Treatment of tuberculosis in PLHIV is challenging because of drug-drug interactions and overlapping toxicities with ART. Despite this, early ART initiation within the first eight weeks of antituberculous therapy was associated with favourable outcomes in children's large

multinational cohort study (Carlucci et al. 2017). Preventing tuberculosis in PLHIV is also complicated – although isoniazid preventive therapy (IPT) has been shown to be effective, there are concerns that widespread use will drive the spread of isoniazid resistance. New estimates suggest that in the context of a declining/controlled tuberculosis epidemic, tuberculosis incidence and mortality benefits of continuous IPT for PLHIV outweigh the potential resistance risks (Kunkel et al. 2016). A systematic review of universal IPT in children with no known tuberculosis exposure showed a reduction among children not receiving ART but, perhaps surprisingly, no clear benefit for children on ART (Zunza et al. 2017).

## 2.2. THEORETICAL STUDIES/FRAMEWORK

### 2.2.1 Bradford Hill Criteria for Causality

Sir Austin Bradford-Hill made a practical approach to causation, which he systematically described in 1965 (Hill 2015). Hill outlined nine criteria by which population-based cause and effect determinations could be made when substantial epidemiologic evidence links a disease or injury with an exposure (Morabia 2013). The Hill Criteria have served as the seminal basis from which virtually all subsequent systematic approaches to general (population) and specific (individual) causation have been derived. This will guide the identification of causality in this study.

The nine criteria, as stated by (Hill 1965), include the following:

**Strength of association:** A strong association is more likely to indicate a causal relationship than a modest or weak association. The strength of association is generally considered the most

important determinant of causation. Most simply stated, a strong association is more likely to indicate a causal relationship than a modest or weak association.

**Consistency:** In general causation, the repetitive observation of a causal relationship in different circumstances strengthens the causal inference. This means the credibility of findings increases with repetition, including consistency of study findings across different populations and geographical locations.

**Specificity:** In general causation, specificity refers to how a factor is associated with a particular outcome or population. This means causality is more likely if the exposure causes only one specific disease or syndrome or if a specific location or population are being affected.

**Temporality:** For this criterion to be satisfied, the potential causal factor must precede the outcome it is assumed to affect. The outcome cannot occur before it is physiologically feasible or after too great of a latency period. In simple terms, this criterion requires that the exposure must occur before the disease and not after a latency period that is too long. This criterion must always be fulfilled for causality to be concluded.

**Biological gradient:** The injury outcome increases proportionately with an increasing dose of exposure. This means the argument for causality is stronger in the presence of a dose-response relationship, where higher or longer exposure leads to an increased risk of disease.

**Plausibility:** For both general and specific causation, plausibility refers to the degree to which known scientific principles can explain the observed association. This means a conceivable mechanism for causation between disease and exposure should exist for there to be a causal relationship.

**Coherence:** A causal conclusion should not fundamentally contradict present substantive knowledge – it should "make sense" given current knowledge. This means the current association should not contradict any previous knowledge available about the disease and/or exposure.

**Experiment:** This criterion can involve scientific experiments and addresses the association of exposure with the disease. However, 'experiment' relates to the decrease in disease risk when the exposure is removed and often involves animal models. In some cases, there may be evidence from randomized experiments on animals or humans, although in most cases of injury, there will not.

**Analogy:** An analogous exposure and outcome may be translatable to the circumstances of a previously unexplored causal investigation. This criterion uses previous evidence of an association between a similar exposure and disease outcome to strengthen the current argument for causation.

### 2.2.2 Epidemiological Model

The interplay between the variables that determine the course of infection and disease within an individual and the variables that control the pattern of infection and disease within communities is the basis of the epidemiological model (Abanobi 2010). This model is very effective for communicable and infectious diseases. This study will utilize this epidemiological model to understand risk factors of TB-HIV co-infection among children receiving ART in Imo state, Nigeria.

Diseases in humans occur due to interaction between agent, host, and environment. These three components make up what is known as the epidemiological triad. It is the traditional model for disease causation. The Epidemiological triad theory states that "an external agent can cause diseases on a susceptible host when there is a conducive environment" (Agu, Agbaje, and Anyoha 2015; Park 2011).

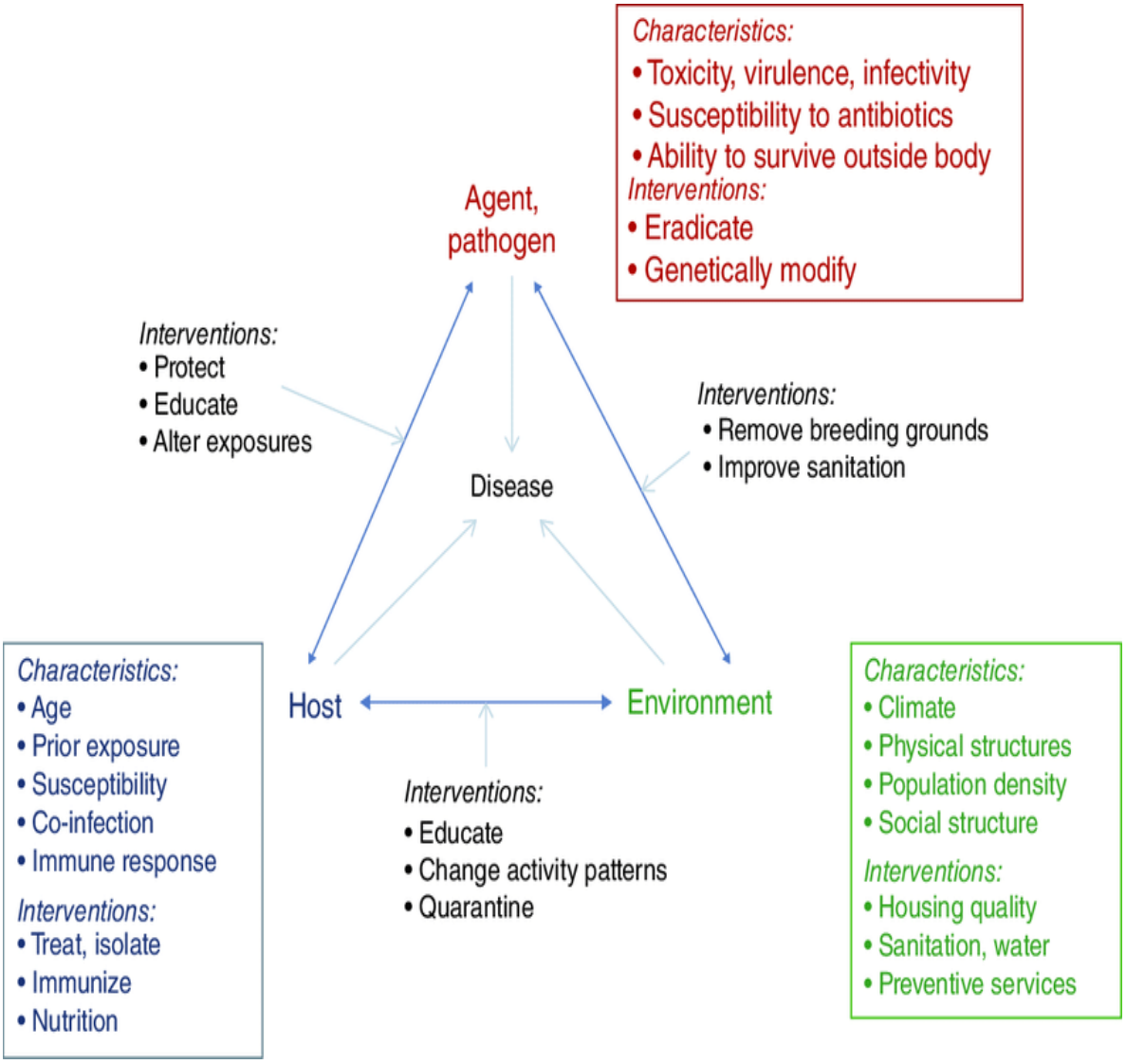



Figure 1: Epidemiological Triad (Souce: Johnson-Walker & Kaneene, 2018)

## 2.3. EMPIRICAL STUDIES

In a study, López-Medina et al. (2020) sought to describe the changing epidemiology and clinical presentation of TB-HIV coinfection in a cohort of HIV-infected children in Spain. Children diagnosed with TB between 1995 and 2016 in the paediatric HIV cohort were identified. The incidence and clinical presentation were compared in three periods: 1995-1999 (P1, before initiation of combined antiretroviral therapy, cART), 2000-2009 (P2, increase in immigration), and 2010-2016 (P3, decrease in immigration). The study included 29 TB cases among 1183 children aged <18 years (2.4%, 243/100 000 person-years). The proportion was stable in P1 and P2 (1.3%) but decreased in P3 (0.8%). The median age at TB diagnosis was 6.4 years (IQR 4-10.6); most children in P3 were aged >10 years (20% vs. 23.1% vs. 83.3%, P =14 0.01). TB was diagnosed at HIV presentation in 11/29 children (37.9%). Foreign-born children accounted for respectively 0%, 8%, and 67% of the total number of children in each period ($P \leq 0.0001$). One-third had extrapulmonary TB; four children died (13.8%). The study also found that the incidence of TB-HIV co-infection decreased with a decline in immigration in the cohort.

Okonko et al. (2020), in a study, evaluated the HIV/TB co-infection rate among HIV-1 infected individuals in old Cross River State, Nigeria. 417 HIV-infected individuals participated in this study, 241 (57.8%) from Calabar, Cross River State, Nigeria, and 176 (42.2%) from Uyo, Akwa-Ibom State, Nigeria. The age range of the 417 HIV-1-positive individuals who participated in the study was 4–72 years, with an average age of 39.1 years. Plasma samples were analyzed for HIV and TB using a fourth-generation Enzyme-Linked immunosorbent Assay. The CD4 count was enumerated using the Partec CyFlow® Counter. Plasma viral loads (PVL) were determined using the Abbott Real-Time HIV-1 assay. Results showed that 230 (55.2%) of the participants were in the 31–45 years age range. The majority (67.4%) of the HIV-1 infected individuals were

females, and 32.6% were males. The overall prevalence of HIV/TB coinfection in Old Cross River State, Nigeria was 1.4%, with Akwa Ibom State (0.6%) and Cross River State (1.2%). A higher prevalence of HIV/TB coinfection was observed among females (1.8%) than males (0.7%). Higher prevalences of HIV/TB coinfections was observed in patients above 45 years of age (2.2%), married (2.3%), tertiary education (1.8%), followed by those with secondary education (1.4%), traders and civil servants (3.1%), patients with CD4 counts 200–349 and ≥500 cells/μl (1.9%), and those with viral load <40 copies/mL (2.7%). This study confirmed the presence of HIV/TB co-infection in old Cross River State, Nigeria. This study also found that, although the prevalence rate of HIV/TB coinfection was low, its presence alone among HIV-1 infected individuals makes it a major source of concern.

In a retrospective cohort study, (Osei, Oppong, and Der 2020) explored the trends of TB case detection, mortality, and HIV co-infection and examined the predictors of TB deaths in ten districts of the Volta region of Ghana. This study included all TB cases registered from 2013 to 2017 in 10 districts of the Volta Region of Ghana. Case detection rate (CDR) was computed as the ratio of the number of new and relapse TB cases notified to NTP to the number of estimated incident TB cases in a given year. Case fatality rates were estimated using data from the 2012–2016 cohort of TB patients. Simple and multiple logistic regression was used to identify predictors of TB deaths with odds ratios and 95% confidence intervals estimated. The study found that 3,735 new and relapse TB patients commenced anti-TB treatment during the period, representing a case detection rate of 40.1% with district variations. The CDR remained stable during the five years. Of the total cases, HIV status was documented for 3,144 (84.2%), among whom 712 (22.6%) were HIV positive. The TB/HIV co-infection was more prevalent among children under 15 years of age (30.1%), males (30.6%), treatment after loss to follow-up patients

(33.3%), and smear-negative pulmonary TB patients (29.1%). TB/HIV co-infection prevalence did not significantly change over the years. The overall case-fatality rate was 13% (n = 486), with considerable variation among HIV-positives and HIV-negative TB patients (21.8% and 11% respectively) (p<0.001) and among districts. TB/HIV co-infection, sputum smear-negative pulmonary TB, and district of anti-TB treatment predicted TB mortality.

(Turaka et al. 2019) used the case-control study design to recognise the risk factors related to the development of active TB in HIV-infected individuals. This study was done at a large tertiary care hospital in South India. The cases in the investigation were HIV-infected individuals aged more than 18 years with confirmed TB. For every case, two controls (people diagnosed to be HIV positive but negative to active TB with no history of TB). Odds ratios (ORs) and logistic regression analysis were used to measure risk factors. A sum of 150 patients, 50 cases (mean age: 39.3 ± 7.2 years), and 100 controls (mean age: 40.2 ± 7.1 years) took part in the study. On univariate analysis, smoking (OR 8.14, 95% confidence interval [CI]: 3.13–21.21; P < 0.001), chronic obstructive pulmonary disease (P = 0.013), ethanol consumption (OR 8.61, 95% CI: 3.57–20.81; P < 0.001), low body mass index (OR 6.31, 95% CI: 2.75–14.48; P < 0.001), CD4 cell count < 200 cells/μL (OR 13.12, 95% CI: 5.64–30.50; P < 0.001), and not on antiretroviral treatment (ART) (13.34, 95% CI: 5.85–30.41; P < 0.001) were associated with active TB. CD4 counts < 200 cells/μL (OR 5.75, 95% CI: 1.81–18.20; P = 0003), smoking (OR 7.40, 95% CI: 1.47–37.15; P = 0.015), and not being on ART (OR 13.94, 95% CI: 3.84–50.61; P < 0.001) were found to be independently associated. Early ART initiation and patient education on modifiable risk factors, such as discontinuing smoking among HIV-positive people, were recommended at the end of the study.

Ama et al. (2019) in a study, aimed to determine the prevalence of TB among older adults with HIV, their HIV/AIDS knowledge, and vulnerability to hypertension, diabetes, and asthma using the 2013 BAIS IV data. The BAIS IV study, from which the data for this article is derived, used a stratified two-stage probability sampling design. The first stage was the selection of 297 Enumeration Areas (EAs) as Primary Sampling Units, and the second stage was the selection of households (5,415) in the EAs. The study targeted all usual members of the selected households aged six weeks and above for the Biomarker or testing for HIV and those aged 10 - 64 years old for the behavioral questionnaire. The study showed that the older adults (50 - 64 years) with TB have a low level of education, and HIV prevalence is very high (44% for age 50 - 54, 40.6% for age 55 - 59, and 68.4% for age 60 - 64 years). The rate of HIV/TB coinfection, 21.9%, is high, and the prevalence of TB among the older adults is 8.6% (13%, males and 5.3%, females), while only 0.8% are currently on treatment. Only 67.2% know that if a pregnant mother is infected with HIV, there is a way of preventing transmission of the virus to the child. Age, level of education, marital status, and employment status significantly ($p < 0.01$) predict TB diagnosis and treatment. The study concluded that lower education seems to be an obstacle to accessing TB treatment.

In a cross-sectional study, Sivabalan & Rajkumar, (2019) aimed to find out the prevalence of HIV infection among children with TB and the correlation of CD4 cell count level with different types of TB. This study was carried out in children below 12 years diagnosed as having TB, using the modified Kenneth Jones criteria (742 TB-infected children) between 2008 and 2010. Descriptive statistics were used to calculate the frequency, mean, median, and standard deviation. The linear trend of proportions and chi-square trend was used to find out the association test. The HIV prevalence rate among children with Tuberculosis was 9.7%. In

TB/HIV coinfection, Pulmonary TB was 44 (61.1%), lymph node TB was 22 (30.6%), Central Nervous System TB was 4 (5.6%), abdominal TB was 1 (1.4%), and spine TB was (1.4%). Pulmonary TB was the most common type is the not significant, mild, and advanced grade of immune suppression. CNS tuberculosis was the most common type in the severe grade of immune suppression. CNS TB occurred more commonly in children more than 60 months of age. Lymph node TB is the commonest type of tuberculosis in children with HIV coinfection less than 35 months of age. The study also found the prevalence of HIV among tuberculosis children to be 9.7%.

Oloyode et al. (2019), in a retrospective cross-sectional study, assessed the sociodemographic features and the diagnostic methods of childhood tuberculosis in Nigerian children. In this study, data were extracted from the case notes of children managed for tuberculosis in the Pediatric ward and the DOTs clinic of UUTH from January 2013 to December 2017. Information extracted from the case records included the patients' epidemiological data, duration of illness, signs and symptoms, TB score, chest radiograph findings, and microbiological diagnosis. The study defined pulmonary tuberculosis as a symptomatic child with: (1) bacteriologically-confirmed tuberculosis, (2) radiologically-confirmed tuberculosis, or (3) probable tuberculosis (as defined). Probable TB was defined as a TB score > 7 and a good clinical response to antituberculosis treatment in the absence of bacteriological confirmation or radiological certainty. Radiologically-certain TB was defined as agreement between two independent radiologists that the chest X-ray indicated certain tuberculosis and a TB score 1 to 6 in the absence of bacteriological confirmation and a good clinical response to antituberculosis treatment. Result(s): Thirty-three patients met the criteria for TB as defined in this study. The total inpatients from January 2013 to December 2017 were 3276, while the total number of

respiratory cases for this period was 1307. The study found the prevalence of TB was 1% and 2.5% of the total ward admissions and respiratory admissions, respectively for the period studied. Most patients (56%) were in the 0 to 5-year age group, predominately males (72%). Ten patients (31%) had a positive history of contact with an adult with chronic cough, and 30 patients (94%) had BCG vaccination. Cough (72%) was the commonest symptom recorded, with a mean duration of 13 weeks, followed by weight loss (63%) and fever (63%). Pallor (47%) was the commonest clinical sign, followed by lymphadenopathy (44%). Nine patients (28%) had abnormal chest signs. Two patients (7%) had a positive sputum AAFB result, geneXpert was positive in the gastric aspirate sample of one patient and negative for all the sputum and lymph node aspirate results. The chest radiograph was suggestive of TB in 21 (84%) patients, while TB-HIV coinfection was present in nine (29%) patients. Tuberculin skin test (Mantoux) measurement ranged from 0-23mm with a mean +/- SD of 10+/-7.8. Nine (53%) patients had a Mantoux result of 10mm and above. The TB score ranged from 6 to 17, with 96% of the patients having a seven and above TB score.

In a study to sum up the prevalence of TB/HIV co-infection in Ethiopia, Tesfaye et al. (2018) utilised meta-analysis dependent on a systematic review of published articles & grey literature. They looked through Pub Med, Google Scholar, CINAHL, Africa Journals Online, and Google, systematically utilising search terms following the PRISMA guideline. Cochran's Q test and 1 2 statistics were done using STATA version 11 to determine heterogeneity across the studies. Prevalence was utilised to conduct the pooled effect size, while associations were measured utilising odds ratio. Moreover, the univariate meta-regression was performed by considering the sample size to determine potential sources of heterogeneity. Egger's weighted regression and Begg's rank correlation tests were used to account for potential publication bias. Twenty-one

studies with 12,980 participants were used in the study which found the pooled prevalence of TB/HIV Co-infection to be 25.59% (95% CI (20.89%±30.29%). A significant association was found between advanced WHO stage (OR: 6.81; 95% CI: 3.91, 11.88), low CD4 counts (OR: 3.53; 95% CI: 1.55, 8.06), and TB/HIV/AIDS Co-infection. The authors recommended conducting surveillance to determine the HIV burden among TB patients and TB burden among HIV patients. They additionally recommended heightening the three I's (Intensive case finding, INH Preventive Therapy, and Infection control) should be routine work of clinicians. Also, early screening & treatment of patients with low CD4 count and advanced WHO stage was similarly recommended.

A study was undertaken by Caleb et al. (2018) to decide the prevalent associated risk factors of childhood pulmonary TB in a high diseased burdened setting. This cross-sectional study was conducted among children aged 18 months to 15 years in six selected health facilities in Nasarawa State, Nigeria. Study participants were screened for pulmonary TB using chest X-ray, sputum or gastric aspirate acid-fast bacilli microscopy and mycobacterium culture. They were additionally screened for HIV infection. Detailed information on the risk factors: a history of contact with adult TB source case, household contact, duration of contact, household size, number of people sleeping in a room, cross ventilation, BCG immunisation, socioeconomic, educational, and HIV status of parents, and ingestion of unpasteurised milk and chronic illness other than TB. The study participants had a physical examination for BCG scar and nutritional status. One hundred fifty children in the study had a mean age of 9.12 ± 4.66 years and a median age of 10.0 years. The study found a prevalence rate of 32% for definite TB cases (5.5 times higher than the reported national average). The risk factors associated with pulmonary TB include lower socioeconomic status (79.2%), history of contact with an adult TB case source

(72.9%), overcrowding (72.9%), absence of cross ventilation (68.8%), ingestion of unpasteurised milk (45.8%) and severe malnutrition among children under five using MUAC parameter (12.5%). The most significant independent predictors of TB in children were the absence of cross ventilation (OR = 3.27), contact with adult source case (OR = 2.91), and overcrowding (OR = 2.30).

Fernandez et al. (2018) in a study, examined the association between TB, HIV, and HIV-TB coinfection among pregnant mothers and obstetric complications, alcohol use, drug abuse, and depression. Inpatient hospital discharges in the United States from January 1, 2002, through December 31, 2014 were examined. Multivariable survey logistic regression was used to generate adjusted estimates for the association between infection status and study outcomes—approximately 57 million records of pregnant women and their delivery information. HIV-TB coinfection was associated with the highest risks for several obstetric complications, alcohol use, and drug abuse. The risk for alcohol abuse was more than twice as high among HIV-monoinfected as compared to TB-monoinfected mothers. That risk gap more than doubled with HIV-TB coinfection. Both HIV-monoinfected and HIV-TB coinfected mothers experienced similarly increased risks for depression. The study also found that mothers with HIV-TB coinfection experienced relatively heightened risks for obstetric complications, alcohol use, and drug abuse.

In another study, Susilowati et al. (2018) used a case-control study design to investigate the factors associated with TB-HIV/AIDS co-infection at a general hospital in Kedu, Central Java. A sample of 152 patients with HIV was recruited into the study consisting of those with and without TB-HIV co-infection. The dependent variable was TB-HIV/ AIDS co-infection. In contrast, independent variables were education level, history of TB contact, BCG immunisation

status, opportunistic infection, adherence to treatment, drug-taking supervisor support, and community health worker support. Medical records and questionnaires were used to collect data and analysed using multiple logistic regression. The study found that TB-HIV/AIDS coinfection was associated with low education (OR=4.70; CI= 95%; 2.11 to 10.47 p= 0,001), history of TB contact (OR= 3.75; CI= 95%; 1.26 to 5.72; p= 0.01), absence of BCG immunization (OR= 3.59; CI= 95%; 1.07 to 6.23; p= 0.033), opportunistic infection (OR= 3.42; CI= 95%; 1.23 to 5.89; p=0.010), non-adherence to treatment (OR= 5.15; CI= 95%; 1.50 to 7.16; p= 0.001), lack of drug-taking supervisor support (OR= 4.61; CI= 95%; 1.94 to 10.50; p= 0.001), and lack of community health worker support (OR= 4.51; CI= 95%; 1.94 to 10.50; p= 0.001). They concluded that TB-HIV/AIDS co-infection is associated with low education, history of TB contact, absence of BCG immunisation, opportunistic infection, nonadherence to treatment, lack of drug-taking supervisor support, and lack of community health worker.

A study by Bock et al. (2018) evaluated TB incidence in a cohort of HIV-positive individuals starting ART regardless of CD4 count in a programmatic setting at three clinics included in the HPTN 071 (PopART) trial in South Africa. The cohort involved HIV-positive individuals aged ≥18 years starting ART between January 2014 and November 2015. Follow-up was continued until 30 May 2016 or censored on the date of incident TB, loss to follow-up from HIV care or death, or elective transfer-out; whichever occurred first. Two thousand four hundred twenty-three individuals with a median baseline CD4 count of 328 cells/μL (interquartile range 195-468) participated in the study. TB incidence rate of 4.41/100 person-years (95% confidence interval [CI]: 3.62 to 5.39) was recorded. The adjusted hazard ratio of incident TB was 0.27 (95% CI: 0.12 to 0.62) when comparing individuals with baseline CD4 >500 and ≤500 cells/μL. Among individuals with baseline CD4 count >500 cells/μL, there were no incident TB cases in the first 3

months of follow-up. The adjusted hazard of incident TB was also higher among men (adjusted hazard ratio 2.16; 95% CI: 1.41 to 3.30). The researchers concluded by stating that incidence after ART initiation was significantly lower among individuals starting ART at CD4 counts above 500 cells/μL. They recommended a scale-up of ART, irrespective of CD4 count, can significantly reduce TB incidence among HIV-positive individuals. This should be combined with strengthening other TB prevention strategies that target both HIV-positive and HIV-negative individuals.

In a pair-matched case-control study, (Cui et al. 2017) investigated the risk factors associated with TB among people living with HIV/AIDS in Guangxi, China. A surveillance survey was conducted of 1019 HIV-infected patients receiving care at three AIDS prevention and control departments from 2013 to 2015. Cases for this study were newly reported active TB/HIV coinfected patients. At the same time, controls were patients with HIV without active TB, latent TB infection, or other lung diseases. They were matched with the case group based on sex and age (± 3 years). One hundred sixty study participants (15.70%) were diagnosed with active TB, including 85 clinically diagnosed cases and 75 confirmed cases. Smoking (OR = 2.996, 0.992±9.053), lower CD 4+ T-cell count (OR = 3.288, 1.161±9.311), long duration of HIV-infection (OR = 5.946, 2.221±15.915) and non-use of ART (OR = 7.775, 2.618±23.094) were independent risk factors for TB in people living with HIV/AIDS after a multivariate analysis. The researchers, after the study recommended that medical and public health workers should strengthen health education for TB/HIV prevention and treatment and promote smoking cessation.

In another study, Pathmanathan et al. (2017) estimated the incidence and characterised factors associated with TB after ART initiation in Nigeria. Retrospective cohort data from a nationally

representative sample of adult patients on ART. Data were abstracted from 3,496 patient records, and analyses were weighted and controlled for sophisticated survey design. The researcher performed a domain analysis on patients without documented TB disease and used a Cox proportional hazard model to assess factors associated with TB incidence after ART. The study found that at the initiation of ART, 3,350 patients (95.8%) were not receiving TB treatment. The incidence of TB after ART initiation was 0.57 per 100 person-years, which was significantly higher in patients with CD4<50/μL (adjusted hazard ratio [AHR]: 4.2, 95% [CI]: 1.4-12.7) compared with CD4≥200/μL. Patients suspected with but untreated TB at the initiation of ART and those having a history of prior TB were at higher risk of developing incident TB (AHR: 12.2, 95% CI: 4.5-33.5, and AHR: 17.6, 95% CI: 3.5-87.9, respectively). After the study, the incidence of TB among PLHIV after initiation of ART was low and affected by the advancement of HIV, suspected but untreated TB, or previous TB. The researchers recommended improved TB screening and diagnosis for high-risk PLHIV initiating ART and reinforcing early ART and other TB prevention efforts.

Carlucci et al. (2017), in a retrospective cohort study among HIV/TB coinfected children, investigated treatment outcomes in TB by diagnostic modality, ART status, and IP regimen. The study participants were children enrolled at the International Epidemiology Database to Evaluate AIDS treatment sites from 2012 to 2014. They used multivariable logistic regression to model TB outcome, IP regimen, ART status, and diagnostic modality. The study found that out of the 386 HIV-infected children diagnosed with TB, 20% had confirmed TB, and 20% with unfavourable TB outcomes. 78% received treatment with a 4-drug regimen during IP, and 31% were receiving ART at the time of TB diagnosis. Thirty-two percent initiated ART within eight weeks of TB after diagnosis. Initiation of ART within 8 weeks after TB diagnosis was higher for

those with favourable TB outcomes (64%) compared with those with unfavourable outcomes (40%) (P = 0.04). Finally, there was no association between either diagnostic modality (odds ratio 1.77; 95% confidence interval: 0.86 to 3.65) or IP regimen (odds ratio 0.88; 95% confidence interval: 0.43 to 1.80) TB outcome. They recommended early ART for children with HIV/TB co-infection, and reinforced implementation research for improved paediatric TB management (Carlucci et al. 2017).

In another study, Olowe et al. (2017) aimed to determine the prevalence of TB–HIV co-infection and the pattern of infection in TB patients. Treatment outcome among coinfected patients with those not coinfected. A six-year retrospective review of records of patients managed at the Tuberculosis Treatment Center of the LAUTECH Teaching Hospital, South-Western Nigeria, from January 2009 to December 2014 was carried out. One hundred and five (26.3%) of the 399 TB patients seen in the study period were coinfected with HIV. About 10% of the subjects had extrapulmonary TB. Treatment failure was significantly worse among patients with both HIV and TB than those who had TB only (49.5% vs. 32%, p = 0.001). The death rate was also higher in the coinfected individuals implying a more unsatisfactory clinical outcome. High prevalence of TB–HIV co-infection and poor treatment outcome in this group of individuals, though predictable, calls for a more concerted effort in managing TB–HIV co-infection.

In another study, Adler et al. (2017) sought to describe the incidence and diagnostic challenges of TB in human immunodeficiency virus (HIV) infected children with Severe Acute Malnutrition (SAM) in the Academic Tertiary Referral Hospital in Durban, South Africa. They used a posthoc analysis of a randomised controlled trial that enrolled antiretroviral therapy-naive, HIV-infected children with SAM. Trial records and hospital laboratory results were explored for clinical diagnoses, and bacteriologically confirmed cases of TB. In analysing data, they used a negative

binomial regression to measure associations among the confirmed TB cases. Those whose microbiological confirmation did not back their clinical diagnosis were excluded from the study. Of 82 children recruited into the study, 21 (25.6%) had TB, with bacteriological confirmation in 8 cases. The study found that there was an association between sputum sampling (as opposed to gastric washings) increased risk of a subsequent diagnosis of TB (adjusted relative risk [aRR] 1.134, 95%CI 1.02-1.26). There was also an association between culture-proven bacterial infection and reduced risk of TB (aRR 0.856, 95%CI 0.748-0.979), suggesting a false-negative microbiological test secondary to empiric broad-spectrum antibiotics. The study found TB to be common among HIV-infected children with SAM, and microbiological confirmation of the diagnosis is feasible. Empiric treatment remains common, which may be due to suboptimal testing and false negativity in TB diagnosis. At the end of the study, the researchers recommended a rigorous integration of microbiological TB investigation into the programmatic management of HIV and SAM.

Zhu et al. (2017) in a study, investigated the extent of and risk factors for TB and HIV coinfection in Scotland from 2001 to 2010. Patients in the national TB database were linked to those in the national HIV database using probabilistic data linkage. Patient records were anonymised to maintain confidentiality. From 2001 to 2010, 106/4, 097 (2.6%, 95% CI: 2.1 to 3.1) TB patients matched with HIV patients, equating to a 10-year incidence of 2.1 cases per million population. Patients with TB and HIV were more often born outside the United Kingdom, were of black African ethnicity, had refugee status, and had extra-thoracic lymph node involvement or cryptic/disseminated TB disease. Individuals with TB and HIV coinfection were younger and symptomatic for a shorter time before their diagnosis of TB, compared with TB

patients without HIV. The study found TB and HIV coinfection to be relatively uncommon in Scotland in the study period.

Megersa & Phaladze, (2017) in a case-control and quantitative study, assessed the risk factors associated with TB co-infection in 367 randomly selected HIV/AIDS patients taking antiretroviral therapy (ART) in one of the public hospitals in Ethiopia. Ninety-two of the patients were co-infected with TB, and a self-structured questionnaire was used for data collection. The study showed that educational status (OR = 2.61; 95% CI: 1.13, 5.22), waste disposal system (OR = 2.75; 95% CI: 1.61, 4.69), monthly income (OR = 2.09; 95% CI: 1.20, 3.64), contact history with a patient of active tuberculosis or presence of a family member with active tuberculosis (OR = 15.31; 95% CI: 5.28, 44.37), ART drug adherence (OR = 24.84; 95% CI: 7.32, 84.22), knowledge on tuberculosis prevention (OR = 6.07; 95% CI: 1.04, 35.37) and history of exposure to substance (OR = 36.80; 95% CI: 12.88, 105.13) were independently associated with active TB occurrence among HIV/AIDS patients on ART. At the end of the study, the researchers recommended ongoing educational, informational, and other interventions to address the identified risk factors.

In another study, Suresh et al. (2016) tried to understand the impact of TB-HIV co-infection on pregnancy outcomes. They also sought to determine the incidence, treatment, and delivery outcomes of TB-HIV coinfected pregnant women in programmatic settings in Karnataka State in southern India. The study participants were all HIV-infected pregnant women screened for TB under the NACP from 2008 to 2012. Out of 3,165,729 pregnant women, 17 were identified to have TB-HIV co-infection (for an incidence of 5.4 per million pregnancies) and a median age of 24 years. The coinfected women were majorly primiparous with WHO HIV stage III disease and were on a stavudine-based ART regimen. Before delivery, the maternal mortality rates were 18%

and 24% after delivery. An abortion and neonatal mortality rates of 24% and 10% were recorded, respectively. Also, the anti-tuberculosis treatment was 30%, and the antiretroviral treatment outcome mortality rate was 53%. At the end of the study, the incidence of TB among HIV-infected pregnant women was marginally less than among non-HIV-infected women, and the delivery outcomes were relatively poorer. The researchers recommended an urgent review of the current strategy for managing TB among HIV-positive pregnant women.

Ebonyi et al. (2016) in a study, investigated the prevalence of and risk factors for pulmonary TB (PTB) in newly diagnosed (treatment-naïve) HIV-1 infected children at the paediatric HIV clinic of the Jos University Teaching Hospital (JUTH) in Nigeria. This study was a retrospective analysis of 876 children who were aged 2 months – 13 years diagnosed with HIV-1 infection between July 2005 and December 2012. 286 of the children were diagnosed with PTB at the presentation after TB screening. The AIDS Prevention Initiative in Nigeria (APIN)-supported Paediatric HIV clinic at JUTH, Jos was the study site. A multivariate forward logistic regression modelling was used to identify risk factors for PTB-HIV co-infection. The study found a prevalence of 32% for PTB-HIV co-infection. Severe immunosuppression (SI) and the World Health Organization (WHO) HIV clinical stage 3/4 were found to be the independent risk factors for PTB-HIV co-infection in HIV-infected children. The odds of PTB-HIV co-infection was increased two-fold in HIV-infected children with WHO clinical stage 3/4 compared to those with stage 1/2 (adjusted odds ratio (AOR) 1.76 [1.31-2.37], $p<0.001$) and 1.5-fold in children with SI compared to those without SI (AOR 1.52 [1.12-2.06], $p=0.007$). The researchers recommended improved strategies for early diagnosis of both HIV and PTB to optimise clinical outcomes.

In a cross-sectional descriptive study, Isaac et al. (2016) investigated the occurrence of TB and HIV/AIDS co-infection among ninety samples positive for sputum acid-fast bacilli (AFB)

attending DOTS point centre in Sokoto. They used HIV 1/2 Determine®, Unigold®, and Stat-Pak® rapid test kits in a serial algorithm to test for HIV antibodies after receiving patient consent. The prevalence of HIV co-infection among TB patients obtained from this study was 5.6% (2.2% female and 3.3% male), the female-to-male ratio of TB patients was 1:2.9, while the ratio of co-infection of HIV among TB patients for a female to male was 1:1.5. All the coinfected patients were married and 80.4% of coinfected patients were illiterates while 58.9% of them were businessmen and the remaining 19.6% were farmers and unemployed. Co-infection was not found among civil servants patients, and the sociodemographic factors indicate a no statistically significant difference (p-value > 0.05). The result also revealed that co-infection occurred in the age range of 21-40 years only, with the age group 31 – 40 years having the highest prevalence of co-infection.

In another study, Brennan et al. (2016) used a prospective cohort study design to evaluate the association between age and incident tuberculosis (TB) among human immunodeficiency virus (HIV) infected patients receiving antiretroviral treatment (ART) in South Africa between April 2004 and April 2012. They analysed data using Generalised Estimating Equations (GEE) together with modified Poisson regression clustered by treatment site as a function of sex, age, nucleoside reverse transcriptase inhibitor, CD4 count, haemoglobin levels, and year of ART initiation. They geographically displayed incidents using cumulative incidence functions, stratified by age, and controlled for death as a competing risk. At the end of the study, GEE models showed that patients aged <1 year had a 40% increase in the risk of TB compared to those aged 30-39.9 years. Male patients, those with low CD4, those with low haemoglobin, and those who initiated ART before 2010 were at a higher risk of developing TB. The researchers

suggested that reducing TB incidence in HIV-positive adults could substantially impact the risk of TB in young children.

In a study to assess the association between novel, modifiable risk factors and TB in Indian children, Faisal et al. (2016) used a case-control study design. Children aged ≤5 years with confirmed/probable TB based on World Health Organization definitions (definition 1) were put in the case group, while healthy children aged ≤5 years were in the control group. They used logistic regression to estimate the adjusted odds ratio (AOR) of being a TB case given exposure, including indoor air pollution (IAP; exposure to tobacco smoke and/or biomass fuels) and vitamin D deficiency. They re-analysed according to a new consensus research definition of paediatric TB (definition 2). Sixty cases and 118 controls were enrolled in the study. Vitamin D deficiency was high n the two groups (55% vs. 50%, P = 0.53). In the multivariable analysis, an association was found between TB and household TB exposure (aOR 25.41, 95% CI 7.03-91.81), household food insecurity (aOR 11.55, 95% CI 3.33-40.15) and IAP exposure (aOR 2.67, 95% CI 1.02-6.97), but no association was found with vitamin D deficiency (aOR 1.00, 95% CI 0.38-2.66).

In another study, Amoakwa et al. (2015) investigated the risk factors for developing active TB after treating latent TB in adults infected with HIV. The study consisted of 908 individuals from the Soweto/Johns Hopkins Novel Tuberculosis Prevention Regimens Trial. Out of these, they found self-reported alcohol consumption, low baseline CD4 count, high baseline viral load, and tuberculin skin test size >15mmas independent risk factors for incident tuberculosis. The 908 participants in the three included arms were observed for a total of 3032.7 person-years (median follow-up time, 3.73 years). There were 59 cases of incident tuberculosis during follow-up (1.95 cases per 100 person-years; 95% confidence interval [CI], 1.51–2.50). The study participants had

a median age of 30 years (interquartile range [IQR], 26–34), 83% were female, and all were black. Their median CD4 was 489 cells/mm3 (IQR, 348–677) and 4.2 log10 copies/mL (IQR, 3.5–4.7) for viral load at entry. The median baseline BMI was 25 kg/m2 (IQR, 22–29). Participants initiated on ART were 167, and ART use made up 10% of the total follow-up time. Multivariate analysis was used to identify independent risk factors for incident tuberculosis which were as follows: TST induration size of >15mm vs. 5–9 mm (hazard ratio [HR], 2.74; CI, 1.06–7.06; P = .037); self-reported alcohol consumption (HR, 2.08; CI, 1.21–3.50; P = .007) and alcohol consumption >10 units per week (HR, 2.87 CI, 1.14–7.23; P = .025); baseline viral load greater than the median, ie, 14 600 (4.2 log10) copies/mL (HR, 3.13; CI, 1.64–5.97; P = .001); and baseline CD4 cell count <500 cell/mm3 (HR, 1.94; CI, 1.07–3.49; P = .028). In univariate or multivariate analysis, other factors did not have a statistically significant association with incident tuberculosis. Smoking (past or present) was associated with an increased hazard of incident tuberculosis in univariate analysis (HR, 1.60; CI, 0.95–2.72), but the association was mitigated in multivariate analysis (HR, 0.98; CI, 0.49–1.98). A second multivariate analysis that included only variables with a P < .2 from the first multivariate analysis showed almost identical results.

In a study to obtain estimates of the incidence of TB among patients receiving HIV Treatment and the relationship between incident TB and change in CD4 count over a follow-up period, Musa et al. (2015) analysed the incidence of TB over 10 years from the initiation of HIV treatment among 345 HIV treatment-naive persons, who were enrolled in a cohort in Kano, Nigeria. To identify the determinants of TB incidence and model the relationship between the occurrences of TB with a change in CD4 count over the follow-up period General Estimation Equation (GEE) was used. The study found that during the ten years, 47(13.62%) had TB

[incidence was 7.43 per (1,000) person-year)]. This was associated with decreasing age (OR = 0.98), female gender (OR = 0.83), being on first-line ART other than AZT (OR = 0.87), poor adherence (OR = 1.25), change in ART regimen (OR = 2.3) and ART treatment failure (OR = 1.51). There was an association between the odds of TB occurrence and CD4 increment at 10 years (OR = 0.99). They also found those coinfected with TB/HIV have a statistically significant shorter time to failing first-line ART regimen compared to those with HIV infection alone. At the end of the study, the researchers recommended early TB screening and re-screening among all HIV patients.

In another study, Shobowale et al. (2015) evaluated the demographic characteristics of patients with TB and rates of HIV co-infection. The researchers retrospectively analysed 100 patient records over a 3-month period. Sputum smears using the Ziehl Neelsen method were used to determine patient response to therapy. HIV co-infection rates in persons with suspected Tuberculosis was 20.2% (n = 20), 23% (n = 23) had sputum smear results definitively showing Acid-fast bacilli. The researchers recommended improved systems for the accurate diagnosis of TB and improved treatment.

A retrospective study was done by Daniel et al. (2015) to determine the access to HIV services by HIV-TB coinfected children in Lagos, Nigeria, from 1 January 2012 to 31 December 2013. One thousand one hundred ninety-nine children aged between 0 and 14 years who were diagnosed with TB participated in the study, and 1095 (91.3%) who underwent testing for HIV, 320 (29.2%) were HIV seropositive. 57 (17.8%) were aged <1 year, 86 (26.9%) 1-4 years and 186 (58.1%) 5-14 years; 186/320 (58.1%) began cotrimoxazole preventive therapy (CPT), and 151 (47.2%) were put on antiretroviral treatment (ART). The male-to-female ratio of HIV-TB positive outcomes was 1:0.9. It was found that uptake of ART was not significantly higher in

facilities where HIV-TB services were co-located (P > 0.05), and the uptake of CPT and ART was low. They recommended an intensified effort to improve access to HIV services in Lagos State, Nigeria.

However, (Ojiezeh, Ogundipe, and Adefosoye 2015) conducted a five-year retrospective study from January 2008 to December 2012. This study was done using profiles of new cases of PTB individuals that attended the National Tuberculosis and Leprosy Control Programme (NTBLCP), Owo centre. The researchers used pre-designed case record forms to identify 342 new cases. Vital demographic data and social and medical history were retrieved, including laboratory results, treatment access, and mortality reports. The study found the prevalence of HIV seropositive individuals with PTB among the 342 new cases retrieved to be 14.0%. However, the incidence of infection was higher among 35 to 44 years age group, 53.8% are males and 46.2% are females. 28.1% were classified as cured, 9.1% died, and 10.5 % defaulted or transferred out.

Dainguy et al. (2015) in a study, aimed to identify the characteristics of HIV and tuberculosis (TB) coinfection in children. This was a retrospective, descriptive, analytical cohort study performed in HIV-infected children followed at the paediatric department of the University Hospital of Cocody, Abidjan, Cote d'Ivoire, from November 2005 to September 2013. Sixty-eight children with HIV were coinfected with TB. The prevalence of coinfection was 10.5%. The sex ratio was 0.88. Patients had a mean age of 6.95 years. Most of the children had moderate (35.3%) or severe (47.1%) immunodeficiency. Malnutrition was associated in 69.1% of children, and 42.6% of them had severe forms. More than half of the children (55.9%) had been vaccinated against TB. Contact with a TB patient was found in 14 children (20.6%). TB revealed HIV infection in 61 patients (89.7%). Pulmonary localization was the most frequent (76.4%). Extrapulmonary TB was noted in 7.3% and multifocal TB in 16.1%. Parenchymal lesions were

bilateral in 96%. Tuberculin test was positive in 6 patients. Sputum was positive in 32.3% of children. The mortality rate was 39.7%. Deaths were significantly related to localization of TB infection (P=0.04), and antiretroviral therapy was not associated with TB treatment (OR=0.02, CI=0.00-0.17, P=0.000). At the end of the study, the development of new TB screening techniques in children and early initiation of antiretroviral therapy was recommended to reduce morbidity and mortality associated with TB/HIV coinfection.

In another study, Chang et al. (2015) in a multicentre long-term survey, sought to determine the incidence rate and predictors of TB in adults in the Harvard/AIDS Prevention Initiative in Nigeria (APIN) and President's Emergency Plan for AIDS Relief (PEPFAR) Nigeria ART program. Methods. The researchers used data collected from 2004 to 2012 through the Harvard/APIN PEPFAR program. They used multivariate Cox proportional hazards regression with time-dependent covariates to determine risk factors. The study found that out of the 50,320 adults enrolled from 2005 to 2010, 11,092 (22%) had laboratory-confirmed active TB disease at ART initiation, and 2021 (4%) developed active TB after commencing ART. The TB incidence rate was 25.8 cases per 1000 PY (95% confidence interval [CI], 24.7-27.0) during 78 228 total person-years (PY) of follow-up overall, and it decreased significantly both with the duration on ART and calendar year. Earlier ART enrolment year, tenofovir-containing initial ART regimen, and World Health Organization clinical stage above one were identified as risk factors for incident TB at ART initiation. Low body mass index, low CD4+ cell count, unsuppressed viral load, anemia, and ART adherence below 80% were identified as time-updated risk factors. Conclusions. The rate of incident TB decreased with a longer duration on ART and over the program years. The researchers recommended reinforcing the importance of consistent clinical

and laboratory monitoring of ART patients in prompt diagnosis and treatment of TB and other co-infections.

In another study, Karo et al. (2014) evaluated the long-term incidence density rate (IDR) of TB and risk factors among PLWHA based on a combination antiretroviral therapy (cART)-status. They enrolled PLWHA from 2001 to 2011 in the German ClinSurv, and survival analysis and Cox regression were used to investigate the cohort. The study found that TB was diagnosed in 233/11,693 PLWHA either at enrolment (N = 62) or during follow-up (N = 171). The TB IDR during follow-up was 0.37 cases per 100 person-years (PY) overall [95% CI, 0.32-0.43], and was higher among patients who never started cART and among patients originating from Sub-Saharan Africa (1.23 and 1.20 per 100PY, respectively). In two multivariable analyses, both patients (I) who never started cART and (II) those on cART shared the same risk factors for TB, namely: originating from Sub-Saharan Africa compared to Germany (I, hazard ratio (HR); [95% CI]) 4.05; [1.87-8.78] and II, HR 5.15 [2.76-9.60], CD4+ cell count <200 cells/μl (I, HR 8.22 [4.36-15.51] and II, HR 1.90 [1.14-3.15]) and viral load >5 log10 copies/ml (I, HR 2.51 [1.33-4.75] and II, HR 1.77 [1.11-2.82]). There was no independent association between gender, age, or HIV-transmission risk group and TB. At the end of the study, they recommended early screening for latent TB infection and implementing isoniazid preventive therapy.

Appunni et al. (2014) examined TB and HIV risk factors among residents of South Africa in a study. Data was collected from the General Household Survey of South Africa in 2006 and analysed. The age group studied ranged from 15–49 years (25,859 males and 29,525 females). Five thousand nine hundred thirty-five people had illness/injury, including 2469 (41.6%) males and 3466 (58.4%) females. Weighted multivariate logistic regression was used to assess TB and/or HIV association with the province, background characteristics of the target population,

and selected socioeconomic and demographic variables included in the survey. The study showed that TB is the second most prevalent cause of illness in the provinces of KwaZulu-Natal (KN) (9.1%), North West (5.4%), and Limpopo (4.2%). Married people had a 50% lower risk than those not married in falling ill to TB and/or HIV. Individuals living with spouses had a 5% lower risk of TB and/or HIV diseases than those with dead partners. The researchers recommended follow-up care and special preventative measures in the provinces with higher incidence and prevalence of TB and/or HIV.

In another case-control study, Jubulis et al. (2014) measured the association of novel modifiable risk factors and TB in Indian children. The WHO definition (definition 1) was used to select 60 cases (children aged ≤5 years with a confirmed/probable TB, while 118 controls were healthy children aged ≤5 years. They used logistic regression to estimate the adjusted odds ratio (AOR) of being a TB case given exposure, including indoor air pollution (IAP; exposure to tobacco smoke and/or biomass fuels) and vitamin D deficiency. A new consensus research definition of paediatric TB (definition 2) was used for re-analysis. The two groups had high levels of vitamin D deficiency (55% vs. 50%, P = 0.53). ITB was associated with household TB exposure (aOR 25.41, 95%CI 7.03-91.81), household food insecurity (aOR 11.55, 95%CI 3.33-40.15), and IAP exposure (aOR 2.67, 95%CI 1.02-6.97), but not vitamin D deficiency (aOR 1.00, 95%CI 0.38-2.66) after multivariate analysis. The use of definition 2 reduced the number of cases to 25, which showed TB exposure, household food insecurity, and IAP remained associated with TB after multivariate analysis.

Akinboro et al. (2014) in a study, assessed the predictors of pulmonary tuberculosis co-infection among Nigerians with human immunodeficiency virus infection and acquired immunodeficiency syndromes. They used a cross-sectional design for probability sampling to select 140 HIV-

positive individuals for the study. Physical examination, radiological and microbiological screening for TB were performed. Serum selenium was assessed using an atomic absorption spectrophotometer to assess serum selenium and CD4 count estimated. Bivariate and multivariate analysis was done using SPSS version 17.0. The mean ages of the study participants with and without PTB were not significantly different: 34.76±6.79 vs 35.17±9.43 years (P=0.847), while HIV patients were significantly females (85.4%), P=0.008. Chronic cough was significantly and equally present in both groups 50.0% (P<0.001). Weight loss 60.8% (P<0.001), skin rash 61.8% (P=0.004), parlor 63.2% (P=0.004), xerosis 56.5% (P=0.003), fluffy hair 56.2% (P=0.002), blue nail 55.6% (P=0.008), and oral candidiasis 57.1% (P=0.001) were significantly associated with HIV mono-infection. The mean ±SD of serum selenium (0.32±0.31 vs. 0.65±0.43 μmol/L; P=0.002), CD4 count (137.72±110.95 vs. 324.30±229.29 cells/mm3; P<0.001), and body mass index (19.96±3.31 vs. 22.03±3.43; P=0.005) were significantly low among patients with HIV-PTB co-infection compared with those with HIV mono-infection. Low serum selenium 5.7 times (95% CI 1.3 to 25.7, P=0.021), the chronic cough was 5.1 times (95% CI 1.8 to 14.1; P=0.002) predicts PTB co-infection among HIV patients after multivariate analysis.

In another case-control study, Molaeipoor et al. (2014) investigated the predictors of TB-HIV co-infection in Tehran, Iran. 2,388 PLHIV were recruited for the study. Individuals with TB co-infection were in the case group (241), while those without co-infection were put in the control group (2,147). Association between TB-HIV co-infection and several predictors was assessed using multiple logistic regression. Odds ratios (ORs) and their 95% confidence intervals (CIs) were also calculated. The study found that sex, age, marital status, educational level, imprisonment, smoking, narcotic use, route of HIV transmission, previous TB infection,

isoniazid preventive therapy (IPT), antiretroviral therapy (ART), and low CD4 count (<350 cells/mm(3)) were independently associated with M. tuberculosis/HIV co-infection (p<0.001). However, only the association between TB-HIV co-infection and the following predictors remained statistically significant after adjusting for all other variables in the model: imprisonment (odds ratio [OR], 3.82; 95% confidence interval [CI], 2.11-6.90), previous TB infection (OR, 5.54; 95% CI, 1.99-15.39), IPT (OR, 0.13; 95% CI, 0.06-0.31), ART (OR, 1.81; 95% CI, 1.26-2.61), and CD4 count <350 cells/mm(3) (OR, 2.34; 95% CI, 1.36-4.02).

Oladeinde et al. (2014) in a laboratory-based cross-sectional study, sought to determine the prevalence and associated risk factors of HIV infection among patients with PTB from 2006-2011 at a rural tertiary hospital in Edo State, Nigeria. HIV antibodies were tested for using venous blood from 250 patients newly diagnosed with PTB using standard technique. The instrument for data collection was a structured questionnaire which was used to obtain demographic information. The study found the prevalence of HIV infection among the study subjects to be 32.8%. Although there was an observed prevalence drop of HIV from 36.5% in 2006 to 29. 2% in 2011, the difference was not statistically significant (P = 0.98). Gender was not a risk factor for HIV-PTB co-infection [female vs. male: 37.3% (53/142) compared to 26.8% (29/108); P = 0.10, OR = 1.622; 95% CI = 0.941, 2.797]. Age was identified as a risk factor for HIV-PTB co-infection (P < 0.0001), with participants within the age group of 21-30 years having the highest risk. The prevalence of HIV-TB co-infection was not significantly affected by educational status (P = 0.48), occupation (P = 0.19), and marital status (P = 0.23) of study participants.

In an observational prospective cohort study, Batista et al. (2013) investigated the incidence and risk factors for TB in PLHIV in referral health centres in Recife, Brazil. The study enrolled 2069

HIV-infected patients into the research, and these study participants were observed between July 2007 and December 2010. The Kaplan-Meier method was used to estimate the probability of survival free of tuberculosis and Cox regression analysis to identify risk factors associated with TB development. The study found survival free of tuberculosis (TB) was 91%. 2.8 per 100 persons/years the incidence rate of TB was recorded. Incidence of TB was higher when subjects had CD4 cell count <200 cells/mm3; were not on antiretroviral therapy; in those who had, a body mass index <18.5 kg/m2, anaemia (or were not tested for it), were illiterate or referred previous tuberculosis treatment at entry into the cohort. There was a much higher risk (HR = 7.9) of TB in those not treated for latent TB compared to those with a negative tuberculin skin test (TST). Having a TST ≥5 mm but not being treated for latent TB infection increased the risk of incident tuberculosis even in those with a history of previous TB. After the study, the researchers recommended preventive actions to reduce the risk of TB in PHIV and inclusion appropriate HAART and treatment for latent TB infection in those with TST≥5 mm.

In another case-control study, Nibardo et al. (2013) investigated clinical and sociodemographic factors associated with the risk in individuals with TB-HIV co-infection. Individuals coinfected with HIV and pulmonary or extrapulmonary tuberculosis were put in the case group (47 cases) while the controls (94 individuals) for the study were individuals with no clinical tuberculosis and PPD negative matched for age and sex. Primary data were obtained from medical records and personal interviews. The study found underweight (malnutrition) (BMI ≤ 18.49), absence of antiretroviral therapy, CD4 + cells count ≤ 199 cells/mm3, RNA HIV-1 viral load ≥ 100,000 copies/mL as the main risk factors. There was an association between multiple risk factors and TB in HIV-infected patients. Clinical factors were more important than sociodemographic ones.

CD4+ cells count < 200 cells/μL, malnutrition IMC < 18.9 and RNA HIV-1 viral load > 100,000 copies/mL were, however, associated with tuberculosis in HIV-infected patients.

In a case-control study, (Ku et al. 2013) investigated the incidence of and risk factors for active TB in HIV-infected persons retrospectively analysed data of 1265 HIV-1 infected patients who visited four hospitals in South Korea between 1985 and 2012. Cases were HIV-infected individuals newly diagnosed with active TB, controls were those without active TB who had similar CD4+ T-cell counts and dates of the first visit, and a 1:2 matching was done for the two groups. The study found 185 (14.6%) subjects were diagnosed with active TB; the incidence was 4.2 cases/100py. In a multivariate analysis, low body mass index (P = 0.033) and current smoking (P = 0.003) were independent risk factors for TB in HIV-infected patients. When the study ended, the researchers recommended implementing further strategies to prevent and treat active TB, encourage smoking cessation, and support good nutrition among HIV-infected patients in South Korea.

In another cohort study, Li et al. (2013) assessed incident tuberculosis and risk factors among HIV-infected children in Tanzania. A longitudinal analysis of a cohort of HIV-infected children was done. Predictors of incident TB among HIV-infected children under age 15 years after enrolling in the HIV program were explored using Cox proportional hazard regression. Results: 5040 children [median age: 5 years, interquartile range (IQR) 1-9 years] participated in the study. During a median follow-up of 0.8 (IQR 0.1-2.5) years, 376 out of 5040 children met the case definition for TB. The overall incidence of TB was 5.2/100 person-years. Older age at enrolment [relative risk (RR) 1.7, 95%, confidence interval (CI) 1.5-1.8], severe wasting (RR 1.8, 95% CI 1.3-2.5), severe immune suppression (RR 2.6, 95% CI1.8-3.8), anaemia (RR 1.4, 95% CI 1.0-1.9) and WHO stage IV (RR 4.5, 95% CI 2.4-8.5) were all independently associated with a

higher risk of TB after multivariate analysis. Also, the use of antiretroviral drugs for more than 180 days reduced the risk of TB by 70% (RR 0.3, 95% CI 0.2-0.4).

Crofts et al. (2012) in a study, linked national tuberculosis (TB) and HIV surveillance data to investigate recent trends and factors associated with HIV co-infection (TB-HIV) in healthcare workers (HCWs) with TB in England and Wales. A 2-trend test and logistic regression were used in the analysis. The study found co-infection of TB-HIV in 14% (231/1627) of the HCWs, increasing from 8% in 1999 to 14% in 2005 (P<0 001). The majority (78%) of HCWs were non-UK born, and 74% of these developed TB 2 years post-entry. Being born in Sub-Saharan Africa was an independent predictor for TB-HIV, especially for female HCWs (odds ratio 66 5, 95% confidence interval 16 3-271 1), who also had a lower median CD4 count than other coinfected women (106/mm 3, interquartile range 40-200, P<0 01). When the study ended, the researchers recommended voluntary HIV testing of new HCWs.

### 2.3.1. Summary of Reviewed Related Literature

Majority of the reviewed literature were prevalence studies followed by cohort studies. Prevalence of HIV based on aged varied within each study. Some studies found HIV/TB coinfection to be more prevalent in children <15. A study found that the prevalence of HIV among children did not change significantly over the years. Most case-control studies used simple and multiple regression to analyse data. The risk factors for HIV/TB coinfection studies in these studies where; ethanol consumption, smoking, chronic obstructive pulmonary disease, low body mass index and not being on antiretroviral treatment. Others include BCG immunization, socioeconomic status, education, HIV status of parents, ingestion of unpasteurised milk, chronic illness other than TB, drug abuse, opportunistic infection, treatment adherence. Drug-taking supervisor support, community health worker support, long duration of HIV

infection, knowledge of tuberculosis prevention, Severe immunosuppression, baseline viral load, baseline CD4 cell count, anaemia, marital status, sex, and age were also identified as risk factors for HIV/TB coinfection.

# CHAPTER THREE

# MATERIALS AND METHODS

## 3.1. Study Design

A Case-Contol study design was adopted for this study. A case-control study design is applied in analytic epidemiology to establish a relationship between risk factors and exposure when two distinct population groups are compared. Analytic epidemiology is applied in this study to establish the relationship between a range of potential risk factors of TB-HIV co-morbidity in children receiving Anti-Retroviral Therapy (ART), to develop a prevention and health promotion programme with a focus on prevention of co-infection of TB and HIV amongst children receiving HIV care. This study design was used by Turaka et al. (2019) in a study of the risk factors for active tuberculosis in human immunodeficiency virus-infected individuals.

## 3.2. Area of Study

The study was conducted in Imo state in southeast Nigeria, which is the homeland of the Igbo. Imo state comprises three senatorial zones, namely Owerri, Okigwe, and Orlu, that constitute the bases of political representation in the central legislature. Together, these three senatorial zones are delineated into 27 local government areas (LGAs), where each LGA is an administrative entity created by Nigeria's political authorities.

The state has over 4.8 million people and the population density varies from 230 to 1,400 people per square kilometre. Christianity is the predominant religion. In addition to English being the official language, Imo state is a predominantly Igbo-speaking state, with Igbo people constituting 98%.

Imo State borders Abia state on the East, River Niger and Delta State to the West, Anambra State on the North, and Rivers State to the South. The state lies within latitudes 4°45'N and 7°15'N and longitude 6°50'E and 7°25'E with an area of around 5,100 sq km.

Like all States in the Federal Republic of Nigeria, Imo State is responsible for providing secondary health care services, while the local governments in the state are responsible for providing primary health ca re services. Experience has shown that the LGAs lack he capacity to carry out this function. According to the Imo state ministry of health, there are a total of 602 secondary health care facilities in Imo State; 536 private and 19 public health facilities spread across the 27 LGAs in the State While there are at least 3 private health care facilities in each LGA, 12 of the 27 LGAs have no secondary health care facility. In addition, there are a total of 563 primary health care facilities in the State, 414 public and 149 private respectively. There are at least 6 public primary health care facilities in all the LGAs. Most of the primary health care centres exits merely in name. In these communities, the bulk of health care services are delivered by voluntary/Mission hospitals. Their services account for about 55%. Cost of accessing health care is considered high by the people hence the people's preference for Patient Medicine Dealers resulting in low patronage of the public health facilities. Twenty health facilities provide HIV care services in 7 LGAs in Imo State at the time of study. The LGAs include: Ohaji/Egbema, Orlu, Ehime Mbano, Oru East, Okigwe, Owerri West, Owerri Municipal.

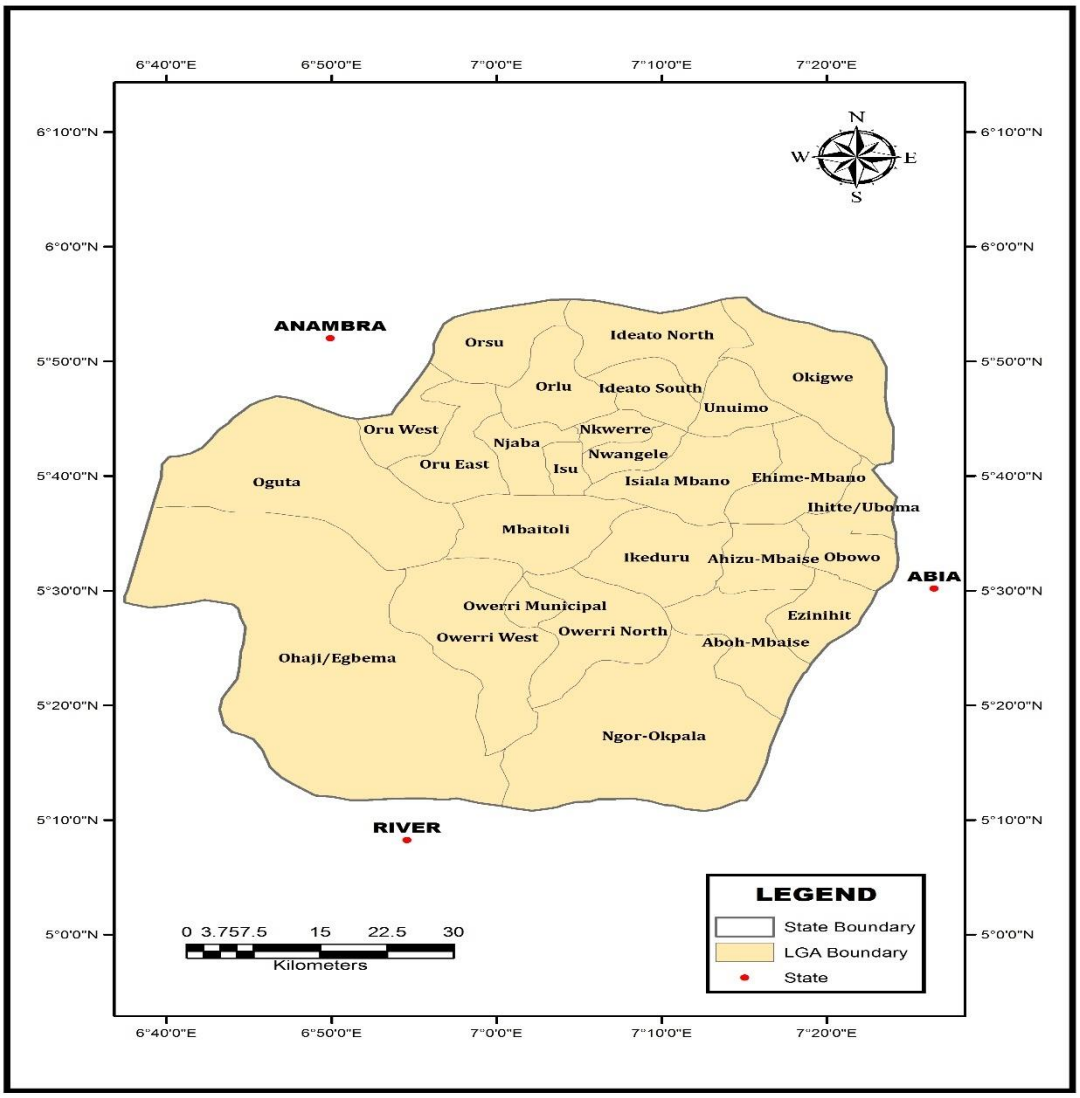



**Figure 2: Map of Imo State, Nigeria (Source: Gamers, 2018).**

### 3.3. Study Population

The study population consisted of all children confirmed HIV positive with or without TB and are receiving Anti-Retroviral Treatment in Imo State. The study population was defined as follows:

**Children:** This study adopted the UNICEF definition of children. UNICEF defines a child as person under the age of 18 (Detrick, 2001) .

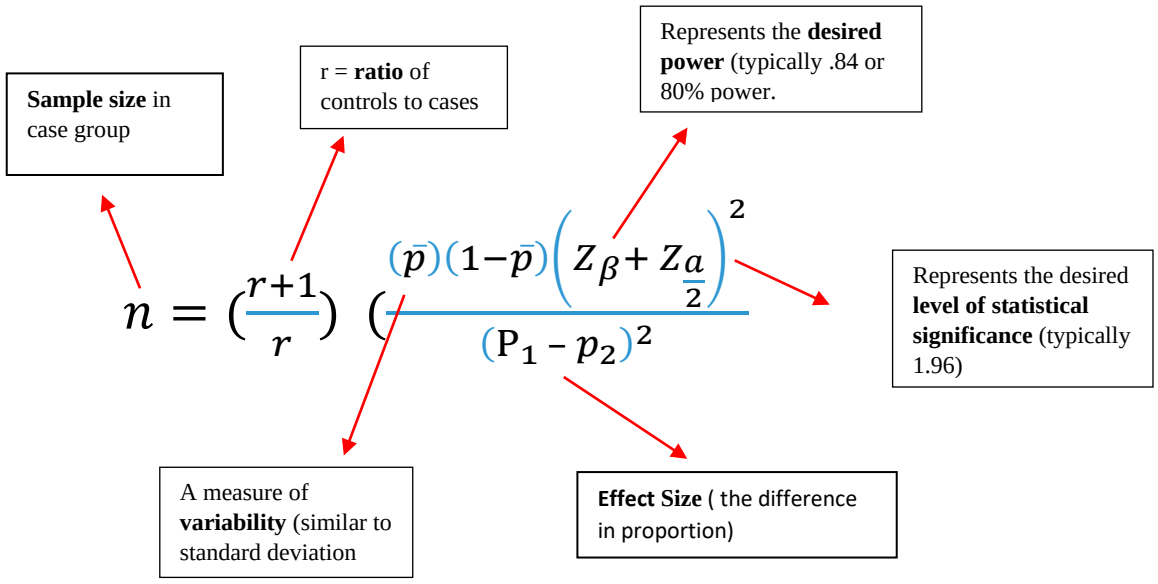
**Cases:** The cases were selected from HIV-positive children confirmed to be coinfected with TB aged less than 18 years, irrespective of sex and date of diagnosis, whether or not they had developed AIDS.

**Controls:** The controls were selected from HIV-positive children without TB. The controls were selected from a control group from the same database from which the cases were chosen to make the study base of the two groups the same.

### 3.4. Sample Size and Sampling Methods

#### 3.4.1. Sample Size Calculation

The sample size of 120 (30 cases, 90 controls) was gotten using the formula for calculating sample size in a case-control study. The formula (Charan et al. 2021) is given below:




Where: **r = 3, p = 0.175 , $Z_{\beta}$ = 0.84, $Z_{\frac{a}{2}}$ = 1.96, $P_1$ = 0.20, $p_2$ = 0.015**

### 3.4.2. Sampling Procedure

A total of 20 health facilities provide HIV care services in 7 Local Government Areas in Imo State at the time of study. These facilities were used as an entry point for the study. The study groups were defined as follows:

Study subjects whose guardians or treatment partners did not give informed consent and subjects with suspected but unconfirmed TB were excluded from the study. All TB–HIV coinfected children attending HIV care clinics and those receiving TB treatment were included. Matched controls were allotted based on the number of cases available in each facility, with a control-to-case ratio of 3:1, and sampled by systematic random sampling with a sampling interval of five.

### 3.4.3. Inclusion Criteria

For this study, the following criteria were used to include participants in the study:

- An HIV-positive child diagnosed with tuberculosis (clinical or laboratory criteria) (TB case) Diagnosed or treated for TB in Imo State.
- An HIV-positive person who is receiving ART and is aged below 18 years.
- HIV-positive persons receiving ART were exposed to a TB index case.
- Consent from the patient's guardian/caregiver to participate in the study.

### 3.4.4. Exclusion Criteria

For this study, the following criteria were used to exclude participants in the study:

- HIV-positive child's guardian does not provide consent for the child to participate.
- HIV-positive person aged >18 years old who do not provide assent.
- HIV-positive child who is not on ART.

### 3.4.5. Case Definition

For this study, the following was used to guide the selection of cases,

**Tuberculosis Suspect**

Any HIV positive child who presents with symptoms or signs suggestive of TB. The most common symptom of pulmonary TB is a productive cough of any duration, which may be accompanied by other respiratory symptoms (shortness of breath, chest pains, haemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).

**Case of Tuberculosis**.

A definite case of TB (defined below) or one in which a health worker (clinician or other medical practitioners) has diagnosed TB and has decided to treat the patient with a full course of TB treatment.

Note. Any given HIV-positive child on treatment for TB was considered as a case.

**A Definite Case of Tuberculosis:**

An HIV positive child with *Mycobacterium tuberculosis* complex identified from a clinical specimen, either by culture or by a newer method such as molecular line probe assay. In countries that lack the laboratory capacity to routinely identify *M. tuberculosis*, a pulmonary case

with one or more initial sputum smear examinations positive for acid-fast bacilli (AFB) is also considered to be a "definite" case.

### 3.5. The Instrument for Data Collection

A 30 item structured questionnaire (instrument) was used to collect data from respondents. It was prepared in an easy to understand English with the title "**FACTORS ASSOCIATED WITH TB-HIV CO-INFECTION IN CHILDREN RECEIVING ANTIRETROVIRAL THERAPY (ART) IN IMO STATE NIGERIA."** As shown in appendix A, the questionnaire contained questions to gather socio-demographic data in section A, questions to identify access to care profile of the guardians/treatment partners, section B contianed questions on the household food security of the participants which was adapted from the U.S. Household Food Security Survey Module (USDA 2012). Section C assessed the family size of the participants. Section D assessed the participant's exposure to a TB case; section E assessed the participants' socio-economic status, and section F asked questions on passive smoking. The instrument for data collection was administered after explaining the purpose of the study to the guardians/treatment partners/caregiver of the children.

### 3.6. Validity of Instrument

The instrument was validated for the relevance of its content and the appropriateness of language used. It was reviewed by three experts and two other researchers in the field of Public Health.

### 3.7. Reliability of Instrument

The questionnaire was administered to 40 respondents 40 guardians/treatment partners with similar characteristics to those in the target population. The instrument's reliability was tested using Cronbach Alpha Coefficient of Reliability test with a value of 0.70..

### 3.8. Method of Data Collection

The researcher contracted research assistants and trained them. They helped in the data collection process. The questionnaire was administered to the guardians of the children by the researcher or via a research assistant after informed consent was obtained. The literate respondents were allowed to fill out the questionnaire themselves. However, for those respondents that are non-literate, the questions were asked in their local language (or were translated to them through an interpreter) and their responses were filled by the researcher (or research assistant). Each questionnaire did not exceed 15 minutes to be completed.

### 3.9. Method of Data Analysis

Data were analysed using Statistical Package for Social Sciences computer software version 22. Frequency and percentage were used to analyse the child's demographics and socioeconomic characteristics of the guardians/treatment partners. Odds ratio was used to determine the risk (likelihood) of TB-HIV co-morbidity in children receiving ART in Imo State, while the chi-square test was be used to determine the relationship. A P-value less than or equal to 0.05 was considered to be statistically significant.

### 3.10. Ethical Consideration/Informed Consent

Ethical clearance was obtained from the ethical review committee of the Department of Public Health, School of Health Technology, Federal University of Technology, Owerri. An introductory letter was given for the benefits of conducting the study, and the method of questioning and confidentiality was attached to the cover page of the questionnaire. Also, Approval to carry out the research was obtained from The Imo State ministry of health, and all the study participants gave informed consent through a brief explanation about the purpose of the study.

# CHAPTER FOUR

# RESULTS AND DISCUSSION

## 4.1 Socio-Demographics Characteristics of the Respondents

The investigation included 120 HIV patients on ART, including 30 cases (with TB-HIV co-infection) and 90 controls (without TB-HIV co-infection). In both the case and control groups, the number of male and female children was equal. 39.2% of the subjects were between the ages of 15 and 17 (cases =40%, controls =38%). The respondents include sixty (50%) mothers (cases = 43.3%, control = 52.2%), twenty-five (20.8%) fathers (cases =16.7%, control = 22.2%), and twenty-six (21.7%) guardians (cases= 33.3%, control = 17.7%).

Currently, 82.5% of the children were enrolled in school (76.7% in the case group and 84.4% in the control group). 44 (42.2%) of the currently enrolled students were enrolled in secondary education, including 9 (39.1%) of the case group and 33 (43.4%) of the control group. There were 41 (41.1%) students enrolled in nursery and primary school (10 cases or 43.5%, 31 controls or 40.0%).

Over 37% of children have been diagnosed with HIV for two to three years, 29.2% for more than five years, and 9.2% for less than two years. 36.7% of co-infected cases were diagnosed with HIV for at least five years, compared to 26.7% of control cases. 40% of those diagnosed within two to three years were in the control group, compared to 30% in the coinfection (case) group. Over thirty-nine percent (case group =33.3%, control group = 41.1%) have been on ART for two to three years, while 21.73% (cases =30.0%, controls = 18.9%) and 28.3% (cases =26.7%, controls = 28.3%) have been on ART for four to five years and over five years, respectively.

**Table 4.1: Socio-Demographics Characteristics of the Respondents**

| | CASE | | CONTROL | | TOTAL | |
|---|---|---|---|---|---|---|
| | n=30 | | n=90 | | | |
| **SOCIO-DEMOGRAPHICS** | **Freq** | **%** | **Freq** | **%** | **Freq** | **%** |
| **Gender** | | | | | | |
| Male | 15 | 50.0 | 45 | 50.0 | 60 | 50.0 |
| Female | 15 | 50.0 | 45 | 50.0 | 60 | 50.0 |
| **Age** | | | | | | |
| 1 -5years | 4 | 13.4 | 12 | 13.4 | 16 | 13.4 |
| 6-10years | 4 | 13.3 | 24 | 26.7 | 28 | 23.3 |
| 11-14years | 10 | 33.3 | 19 | 21.1 | 29 | 24.2 |
| 15-17years | 12 | 40.0 | 35 | 38.9 | 47 | 39.2 |
| **Relationship with the child** | | | | | | |
| Father | 5 | 16.7 | 20 | 22.2 | 25 | 20.8 |
| Mother | 13 | 43.3 | 47 | 52.2 | 60 | 50.0 |
| Siblings | 2 | 6.7 | 7 | 7.8 | 9 | 7.5 |
| Guardian | 10 | 33.3 | 16 | 17.8 | 26 | 21.7 |
| **Child currently enrolled in a school** | | | | | | |
| Yes | 23 | 76.7 | 76 | 84.4 | 99 | 82.5 |
| No | 7 | 23.3 | 14 | 15.6 | 21 | 17.5 |
| **Class of the child (those in school only)** | | | | | | |
| Pre-Nursery | 1 | 4.3 | 4 | 5.3 | 5 | 5.0 |
| Nursery/Primary | 10 | 43.5 | 31 | 40.8 | 41 | 41.4 |
| Secondary | 9 | 39.1 | 33 | 43.4 | 42 | 42.4 |
| Post-Secondary | 3 | 13.0 | 8 | 10.5 | 11 | 11.1 |
| Total | 23 | 100 | 76 | 100 | 99 | 100 |
| **Duration since diagnosed with HIV** | | | | | | |
| Less than 2 years | 3 | 10.0 | 8 | 8.9 | 11 | 9.2 |
| 2-3 years | 9 | 30.0 | 36 | 40.0 | 45 | 37.5 |
| 4-5 years | 7 | 23.3 | 22 | 24.4 | 29 | 24.2 |
| Above 5 years | 11 | 36.7 | 24 | 26.7 | 35 | 29.2 |
| Total | 30 | 100 | 90 | 100 | 120 | 100 |
| **Duration since on ART** | | | | | | |
| 1 year or less | 3 | 10.0 | 10 | 11.1 | 13 | 10.8 |
| 2-3 years | 10 | 33.3 | 37 | 41.1 | 47 | 39.2 |
| 4-5 years | 9 | 30.0 | 17 | 18.9 | 26 | 21.7 |
| Above 5 years | 8 | 26.7 | 26 | 28.9 | 34 | 28.3 |
| Total | 30 | 100 | 90 | 100 | 120 | 100 |

### 4.2. Prevalence of HIV-TB Co-Infection in Imo State

The study found that 12,780 children were receiving antiretroviral therapy in Imo state. Out of this number, 792 children were co-infected with TB.

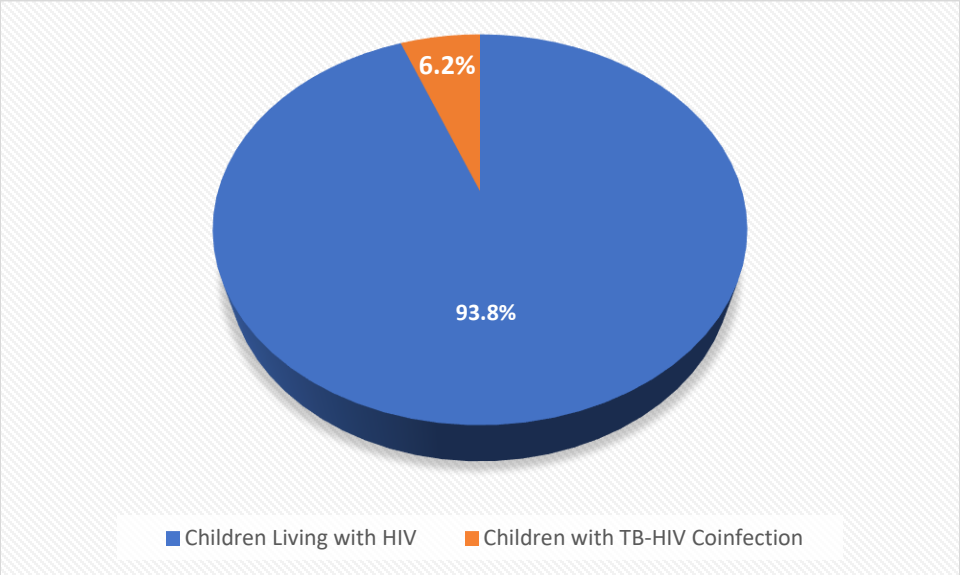



Figure 3: Prevalence of TB-HIV coinfection in children receiving antiretroviral therapy in Imo State, Nigeria

### 4.3: Family Size and HIV-TB Co-infection

None of the co-infection cases were recorded for those who responded that they were not living under the same roof with the child. On the other hand, cases were highest among those with 5 children (33.3%), followed by those with 4 children (27.3%), while significant association was found at 3 children only (p =0.019, 95% CI for AOR = 0.026 – 0.715). the odds were rather 86% (OR =0.14) lower in this group than in the group with one child.

Having at least three people living with a child in one room was found significant (p = 0.006, 95%CI for odds =1.76 – 28.78) with more cases= 33.3% compared to where 1-2 people live with the child in one room (cases= 17.5%). The odds were found to be about 7 times more in the 3 and above group.

**Table 4.3: Family Size and HIV-TB Co-infection**

| Family size | Case | Control | coef | s.e. | p | AOR | 95% C.I. for OR Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| Child living under the same roof | | | | | | | | |
| Yes (Reference) | 30 (27.5) | 79 (72.5) | | | | | | |
| No | 0 (0.0) | 11 (100) | -20.83 | 11284. | 0.999 | 0.00 | 0.000 | . |
| Number of children have | | | | | | | | |
| 1 (Reference) | 7 (43.8) | 9 (56.3) | | | | | | |
| 2 | 2 (11.8) | 15 (88.2) | -1.76 | 1.001 | 0.079 | 0.17 | 0.024 | 1.229 |
| 3 | 4(13.8) | 25 (86.2) | -2.00 | 0.849 | 0.019 | 0.14 | 0.026 | 0.715 |
| 4 | 9 (27.3) | 24 (72.7) | -0.99 | 0.793 | 0.209 | 0.37 | 0.078 | 1.747 |
| 5 | 8 (33.3) | 16 (66.7) | -0.58 | 0.832 | 0.484 | 0.56 | 0.110 | 2.851 |
| Number of people in the same household with the child | | | | | | | | |
| 1-2 (Reference) | 9 (26.5) | 25 (73.5) | | | | | | |
| 3-4 | 10 (22.2) | 35 (77.8) | -0.84 | 0.745 | 0.263 | 0.43 | 0.101 | 1.871 |
| 5-6 | 9 (31.0) | 20 (69.0) | -1.58 | 0.941 | 0.094 | 0.21 | 0.033 | 1.305 |
| 7+ | 2 (16.7) | 10 (83.3) | -2.54 | 1.200 | 0.034 | 0.08 | 0.008 | 0.829 |
| people are living with this child in one room | | | | | 0.023 | | | |
| 1-2 (Reference) | 11 (17.5) | 52 (82.5) | | | | | | |
| 3 and above | 19 (33.3) | 38 (66.7) | 1.96 | 0.713 | 0.006 | 7.11 | 1.757 | 28.78 |

AOR – Adjusted Odds Ratio, OR - Odds Ratio, C.I. – Confidence Interval

### 4.4. Household Food Security HIV-TB Co-infection

Almost all the items assessed for household food security were found to be significant factors of TB-HIV co-infection among HIV ART subjects studied (Table 4.3).

Been worried that household food budget or food supply may not meet basic needs at any time is a significant factor ($p=0.007$, $\chi^2 = 7.17$). Co-infection rate was found to be 31.1% for those who showed worries within the last 3 months against 6.7% for those who were less worries.

Also, thought of running out of food without having money to obtain more is also a significant factor ($p=0.013$, $\chi^2 = 6.14$), with 31% co-infection cases recorded among the groups that expressed their fear for such non-likelihood of having money to replace food shortage compared to 9.1% among those that showed opposite thoughts.

Believing that food consumed in the family is inadequate in quality and quantity was not significant, yet it showed 34% on coinfection cases for "yes" responses other than 18.6% against, Coinfection case on children was 32.6% for affirmative responses on having adjusted their regular food use, substituting cheaper and fewer food than usual in the last 3 months. This is significantly higher ($p=0.002$, $\chi^2 =9.25$) compared to 5.9% found in the opposite response group. Also, reduced food intake for children was found to be a significant factor of co-infection ($p=0.004$, $\chi^2 = 8.50$). Among the households that responded "yes" for reduced food intake of their child or children in the last 3 months, the cases were 34.2% compared to 10.6% obtained in the "no" response households,

**Table 4.4: Household Food Security HIV-TB Co-infection**

| Household Food Security | Total | Case | | Control | | Chi. sq | p |
|---|---|---|---|---|---|---|---|
| | | Freq | % | Freq | % | | |
| In the last 3 months, been worried at any time that household food budget or food supply may not meet basic needs | | | | | | | |
| Yes | 90 | 28 | 31.1 | 62 | 68.9 | | |
| No | 30 | 2 | 6.7 | 28 | 93.3 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 7.17 | 0.007 |
| In the last 3 months, having thought of running out of food without having money to obtain more | | | | | | | |
| Yes | 87 | 27 | 31.0 | 60 | 69.0 | | |
| No | 33 | 3 | 9.1 | 30 | 90.9 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 6.14 | 0.013 |
| Do you think that the food consumed in your family is inadequate in quality and quantity | | | | | | | |
| Yes | 50 | 17 | 34.0 | 33 | 66.0 | | |
| No | 70 | 13 | 18.6 | 57 | 81.4 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 3.70 | 0.054 |
| In the last 3 months, have you adjusted your normal food use, substituting cheaper and fewer food than usual | | | | | | | |
| Yes | 86 | 28 | 32.6 | 58 | 67.4 | | |
| No | 34 | 2 | 5.9 | 32 | 94.1 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 9.25 | 0.002 |
| In the last 3 months, have you reduced the food intake of your child or children | | | | | | | |
| Yes | 73 | 25 | 34.2 | 48 | 65.8 | | |
| No | 47 | 5 | 10.6 | 42 | 89.4 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 8.50 | 0.004 |

### 4.5. TB Exposure and HIV-TB Co-infection

Table 4.4 represents the influence of exposure to TB on having HIV-TB co-infection among the study group. Significant factors of HIV-TB co-infection found as a result of TB exposure include having any member of the household living with HIV ($p=0.016$, $\chi^2 = 5.75$), having any member of the household diagnosed of TB ($p=0.0001$) and having any household member with symptoms of TB such as weakness, sweating, weight loss and coughing ($p=0.0001$, $\chi^2 = 50.39$). Coinfection cases were higher in the children with a household member living with HIV (30.1%), than where no household member is living with HIV (7.4%). It was found to be very much higher in households where a member has been diagnosed with tuberculosis (82.4%) and where household members show apparent symptoms of TB (80%).

Awareness of the HIV status of people living in the household and the number of household members with HIV or TB was also not significant ($p>5\%$). The case for co-infection was higher among those who showed awareness of the HIV status of the household members. It could mean that having a member with HIV heightened their participation in HIV tests and increased awareness concerning the HIV status in the household.

**Table 4.5. TB Exposure and HIV-TB Co-infection**

| TB Exposure | Total | Case: n (%) | Control: n (%) | Chi. sq | p |
|---|---|---|---|---|---|
| aware of the HIV status of people living in your household | | | | | |
| Yes | 114 | 29 (25.4) | 85 (74.6) | | |
| No | 6 | 1 (16.7) | 5 (83.3) | | |
| Total | 120 | 30 (25.0) | 90 (75.0) | | 0.100† |
| Is anybody in your household living with HIV? | | | | | |
| Yes | 93 | 28 (30.1) | 65 (69.9) | | |
| No | 27 | 2 (7.4) | 25 (92.6) | | |
| Total | 120 | 30 (25.0) | 90 (75.0) | 5.751 | 0.016 |
| If yes, how many people? | | | | | |
| 1 | 38 | 9 (23.7) | 29 (76.3) | | |
| 2 | 39 | 11 (28.2) | 28 (71.8) | | |
| 3 | 13 | 7 (53.8) | 6 (46.2) | | |
| 4+ | 16 | 8 (50.0) | 8 (50.0) | | |
| Total | 93 | 28 (30.1) | 65 (69.9) | 3.821 | 0.148 |
| How many people are currently receiving care? | | | | | |
| 1-2 | 77 | 21 (27.3) | 56 (72.7) | | |
| 3-4 | 16 | 7 (43.8) | 9 (56.3) | | |
| Total | 93 | 28 (30.1) | 65 (69.9) | 1.709 | 0.191 |
| Has anybody in your household been diagnosed with Tuberculosis | | | | | |
| Yes | 17 | 14 (82.4) | 3 (17.6) | | |
| No | 103 | 16 (15.5) | 87 (84,5) | | |
| Total | 120 | 30 (25.0) | 90 (75.0) | | 0.0001† |
| If yes, how many people? | | | | | |
| 1 | 13 | 10 (76.9) | 3 (23,1) | | |
| 2 | 4 | 4 (100) | 0 (0.0) | | |
| Total | 17 | 14 (82.4) | 3 (17.6) | 1.129 | 0.290 |
| Has there been any person living within that has experienced weakness, sweating, weight loss, and coughing? | | | | | |
| Yes | 25 | 20 (80.0) | 5 (20.0) | | |
| No | 94 | 10 (10.6) | 84 (89.4) | | |
| Total | 119 | 30 (25.2) | 89 (74.8) | 50.39 | 0.0001 |
| If yes, how many people? | | | | | |
| 1 | 20 | 15 (75.0) | 5 (25.0) | | |
| 2 | 5 | 5 (100) | 0 (0.0) | | |
| Total | 25 | 20 (80.0) | 5 (20.0) | | 0.282† |

†. indicates that Fisher's exact test was used

### 4.6. Passive Smoking and HIV-TB Co-infection

The present study presents the relationship between passive smoking and HIV-TB coinfection in Table 4.5. The table shows that significant factors of passive smoking were the extent unto which the respondents think their child are exposed to tobacco smoke at home ($p=0.0001$, $\chi^2 = 24.14$), having some members of the family smoke inside in the home ($p=0.0001$, $\chi^2 = 17.57$), having some degree of exposure to tobacco smoke on socialization areas outside the household ($p=0.0001$, $\chi^2 = 22.80$).

Cases were higher at responses for those who think their child are exposed to tobacco smoke at high degree (100%) or to a small degree (47.8%) at home compared to 15.1% for the none exposure group. Those who do not have any member of the family smoke inside their homes recorded the lowest rate of co-infection (14.1%).

While cases were lower (13.3%) for those, who think there child are not exposed to tobacco smoke when they go outside the household to socialize compared to those who think their child is exposed to a small degree (48.3%) and to a high degree (71.4%). Among 8 children that visit bars where up to 5 people smoke, the coinfection case was 5 (62.5%).

## Table 4.6: Passive Smoking and HIV-TB Co-infection

| Passive Smoking | Total | Case Freq | % | Control Freq | % | $\chi^2$ | P |
|---|---|---|---|---|---|---|---|
| How much do you think your child is exposed to tobacco smoke at home | | | | | | | |
| Not at all | 86 | 13 | 15.1 | 73 | 84.9 | | |
| To a small degree | 23 | 11 | 47.8 | 12 | 52.2 | | |
| Neutral | 5 | 2 | 40.0 | 3 | 60.0 | | |
| To a high degree | 4 | 4 | 100 | 0 | 0.0 | | |
| To a very high degree | 2 | 0 | 0.0 | 2 | 100 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 24.14 | 0.0001†† |
| How many members of your family smoke inside your home | | | | | | | |
| One | 25 | 10 | 40.0 | 15 | 60.0 | | |
| Two | 12 | 8 | 66.7 | 4 | 33.3 | | |
| Three or more | 5 | 1 | 20.0 | 4 | 80.0 | | |
| None | 78 | 11 | 14.1 | 67 | 85.9 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 17.57 | 0.0001†† |
| On a 5-point scale, how much do you think your child is exposed to tobacco smoke when you go outside your household to socialize? | | | | | | | |
| Not at all | 75 | 10 | 13.3 | 65 | 86.7 | | |
| To a small degree | 29 | 14 | 48.3 | 15 | 51.7 | | |
| Neutral | 9 | 1 | 0.0 | 8 | 88.9 | | |
| To a high degree | 7 | 5 | 71.4 | 2 | 28.6 | | |
| To a very high degree | 0 | 0 | 0 | 0 | 0 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 22.80 | 0.0001†† |
| How many times per week do your child usually go out of your household to socialize | | | | | | | |
| Once | 44 | 8 | 18.2 | 36 | 81.8 | | |
| Twice | 12 | 2 | 16.7 | 10 | 83.3 | | |
| 3 times | 38 | 14 | 36.8 | 24 | 63.2 | | |
| 4 or more times | 26 | 6 | 23.1 | 20 | 76.9 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 4.43 | 0.219 |
| when your child go out to kiosks or bars, how long does he/she usually stay? | | | | | | | |
| Less than 1 hour | 91 | 21 | 23.1 | 70 | 76.9 | | |
| 1-2 hours | 19 | 7 | 36.8 | 12 | 63.2 | | |
| 3 hours or more | 10 | 2 | 20.0 | 8 | 80.0 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 1.63 | 0.443†† |
| How many times per week does your child usually go out to bars? | | | | | | | |
| Once | 42 | 8 | 19.0 | 34 | 81.0 | | |
| Twice | 19 | 3 | 15.8 | 16 | 84.2 | | |
| More than twice | 7 | 5 | 71.4 | 2 | 28.6 | | |
| None | 52 | 14 | 26.9 | 38 | 73.1 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 8.53 | 0.036†† |
| How many people smoke inside the bars your child usually go to? | | | | | | | |
| 1-2 people | 47 | 6 | 12.8 | 41 | 87.2 | | |
| 3-4 people | 11 | 3 | 27.3 | 8 | 72.7 | | |
| 5 people and above | 8 | 5 | 62.5 | 3 | 37.5 | | |
| None | 54 | 16 | 29.6 | 38 | 70.4 | | |
| Total | 120 | 29 | 24.4 | 90 | 75.6 | 9.95 | 0.019†† |

†† indicates that Likelihood ratio test was used

### 4.7. Socio-economic Status and HIV-TB Co-infection

HIV- TB co-infection among HIV children in relation to the socio-economic status of their parents, relatives or guardians is presented on Table 4.6. None of the social-economic status factors assessed in this study was found significant for co-infection except those who earn income to support the family ($p=0.023$, $\chi^2 = 11.36$), and the hours of work they do each week ($p=0.038$, $\chi^2 = 6.54$). TB-HIV coinfection was higher where no one earns income (53.3%) and where no relatives earn income (50%) compared to where the income is earned by relatives such as the mother (12.1%) or father (20%).

TB-HIV coinfection was lower at 20 hours work or less per week (20.4%) compared to working up to 21 – 40 hours in a week (34.6%), but on the other hand, it was found to be lower at working hours of more than 40 hours in a week.

**Table 4.7: Socioeconomic Status and HIV-TB Co-infection**

| Socioeconomic Status | Total | Case Freq | % | Control Freq | % | $\chi^2$ | p |
|---|---|---|---|---|---|---|---|
| Which of these will you consider as a place where your household lives? | | | | | | | |
| Rural | 72 | 18 | 25.0 | 54 | 75.0 | | |
| Semi-urban | 31 | 6 | 19.4 | 25 | 80.6 | | |
| Urban | 17 | 6 | 35.3 | 11 | 64.7 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 1.49 | 0.475 |
| Are you currently employed? | | | | | | | |
| Yes | 40 | 9 | 22.5 | 31 | 77.5 | | |
| No | 80 | 21 | 26.3 | 59 | 73.8 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 0.200 | 0.655 |
| Who earns income to support your family? | | | | | | | |
| None | 15 | 8 | 53.3 | 7 | 46.7 | | |
| Mother | 33 | 4 | 12.1 | 29 | 87.9 | | |
| Father | 50 | 10 | 20.0 | 40 | 80.0 | | |
| Other relatives | 18 | 6 | 33.3 | 12 | 66.7 | | |
| Non relatives | 4 | 2 | 50.0 | 2 | 50.0 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 11.36 | 0.023†† |
| How many hours each week do (es) the above person(s) work? | | | | | | | |
| 20hrs or less | 49 | 10 | 20.4 | 39 | 79.6 | | |
| 21-40hrs | 26 | 9 | 34.6 | 17 | 65.4 | | |
| More than 40hrs | 29 | 2 | 6.9 | 27 | 93.1 | | |
| Total | 104 | 21 | 20.2 | 83 | 79.8 | 6.54 | 0.038 |
| What best corresponds to the above person(s) current work situation? | | | | | | | |
| Working Full Time | 56 | 11 | 19.6 | 45 | 80.4 | | |
| Working Part Time | 16 | 4 | 25.0 | 12 | 75.0 | | |
| Not working and not looking for work | 3 | 1 | 33.3 | 2 | 66.7 | | |
| Unemployed and looking for work | 37 | 13 | 35.1 | 24 | 64.9 | | |
| Disabled or retired and not looking for work | 3 | 1 | 33.3 | 2 | 66.7 | | |
| Currently in school | 5 | 0 | 0.0 | 5 | 100 | | |
| Total | 120 | 30 | 25.0 | 90 | 75.0 | 5.87 | 0.319†† |

††: indicates that Likelihood ratio test was used

## 4.8. Discussion

The results of this study, which had a total population of 120 people, revealed that the age group of 15 to 17 years had the biggest population in the study region at 39.2% (cases =40.0%, control =38.9%). These were the significant findings of the study. The vast majority (99, or 82.5%) of the people who took part in the study were students at some point during the research. When compared to the case group's enrollment rate of 76.7%, the control group's enrollment rate of 84.4% was significantly higher. Children who had the disease for more than five years had a diagnosis rate of 29.2%, which was lower than the 9.2% of children who had the ailment for less than two years. This coincides with the results of a previous study that was conducted in Nigeria by Caleb Joseph Attah and his colleagues (2018). However, this was a cross-sectional study rather than a longitudinal one. According to our findings, the odds of becoming co-infected with tuberculosis increase by a factor of seven when three or more people live under the same roof as one another. This risk increases in direct proportion to the number of children living in the same household.

In a similar vein, our research discovered that the food security of a household is a key determinant in tuberculosis and HIV co-infection. In a study that looked at Indian children, researchers examined this component and discovered that the food security of the household was a significant factor in the incidence of tuberculosis in children (Faisal et al. 2016). Several studies (including Amoakwa et al. 2015, Cui et al. 2017, and Turaka et al. 2019), which examined smoking as a factor in TB-HIV co-infection, found that smoking was a factor. We considered this to be an indicator of children being exposed to passive smoking. We found that having any member of the household living with HIV, having any member of the household

diagnosed with TB, and having any member of the household with symptoms of TB such as weakness, sweating, weight loss, and coughing were significant in TB-HIV co-infection when household TB exposure was taken into consideration. Our findings have been replicated by researchers in Central Java (Susilowati et al. 2018), India (Faisal et al. 2016), Cote d'Ivoire (Sassan-Morokro et al. 1994), Nigeria (Attah et al. 2018), and Ethiopia (Megersa and Phaladze 2017). As a result of this, we have come to the conclusion that there is a compelling need to work toward an improvement in the socioeconomic standing of families in which children are living with HIV. This can be accomplished through the provision of opportunities such as scholarships and jobs that are tailored to the requirements of the target group. People who share their homes with HIV-positive children should also be educated about the importance of giving up smoking and limiting their children's exposure to secondhand smoke.

# CHAPTER FIVE

# CONCLUSION AND RECOMMENDATION

## 5.1 CONCLUSION

This chapter summarizes, concludes and recommends based on the findings the factors associated with TB-HIV co-infection in children receiving ART in Imo state.

As an underexplored topic in children, this study aimed to assess the factors associated with TB-HIV in children receiving ART in Imo State using a case-control study design. Significant findings in this study from a total population of 120 persons were that the age group of 15-17 years had the largest population, 39.2% (cases =40.0%, control =38.9%) in the study area. Most (99, 82.5%) of the study participants were enrolled in a school at the study time. School enrolment was higher in the control group (84.4%) compared to the case group (76.7%). Fewer children were diagnosed with HIV in less than two years (9.2%) compared to the disease for more than five years (29.2%). This is in line with what was found in a similar study in Nigeria by Caleb Joseph Attah et al. (2018). However, the study was a cross-sectional study. Our result showed that as the number of children living under the same roof increased, the risk of being coinfected with TB increased with odds seven times more when three or more people live under the same roof.

Similarly, our study found household food security as a significant factor in TB-HIV co-infection. This factor was measured in a study on Indian children, and household food security was found to be a significant factor in TB occurrence in children (Faisal et al. 2016). A number of studies measured and found smoking as a factor in TB-HIV co-infection (Amoakwa et al. 2015; Cui et al. 2017; Turaka et al. 2019). In children, we measured this as passive smoking.

When household TB exposure was considered, we found that having any member of the household living with HIV, having any member of the household diagnosed of TB and having any household member with symptoms of TB such as weakness, sweating, weight loss, and coughing were significant in TB-HIV co-infection. Similar studies in Central Java (Susilowati et al. 2018), India (Faisal et al. 2016), Cote d'Ivoire (Sassan-Morokro et al. 1994), Nigeria (Attah et al. 2018) and Ethiopia (Megersa and Phaladze 2017) is also consistent with our findings. After this study, we recommend that there is a need to improve the socioeconomic status of families of children living with HIV. This can be done through empowerment, scholarship opportunities, and job opportunities specific to this target population. Also, people living with children with HIV should be sensitised to the need to stop smoking and reduce children's exposure to passive smoking.

## 5.2 RECOMMENDATION

After the conclusion of this study, the researcher made the following recommendations:

1. There is need to improve the socioeconomic status of families of children living with HIV. This can be done through empowerment.
2. People living with children with HIV should be sensitized on the need to stop smoking and reduce children’s exposure to passive smoking.

## 5.3 CONTRIBUTION TO KNOWLEDGE

Most studies have pointed at viral load and ART as main factors associated with TB-HIV co-infection mainly in adults and little knowledge about children. This study however has broadened the understanding of other factors which are associated with TB-HIV co-infection in children. This will help guide further research and implementation of public health programs within this study group.

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**APPENDIX A**

# QUESTIONAIRE OF FACTORS ASSOCIATED WITH TB-HIV CO-INFECTION IN CHILDREN RECEIVING ART IN IMO STATE

## SECTION A: SOCIO-DEMOGRAPHIC DATA

1.Which of the following is the gender of your child?

Male ☐ Female ☐

2. Which of the following age ranges does your child fall into?

1 -5years ☐ 6-10years ☐ 14years ☐ 15-17years ☐

3. What is your relationship with the child?

Father Mother ☐ Sibling ☐ Guardian ☐ Other, spe ☐ ……..……

4. Is your child currently enrolled in a school?

Yes No ☐ ☐

5. What class is your child currently in?

Pre-Nursery ☐ Nursery ☐ Primary ☐ Secondary ☐ Post-Secondary ☐

6. How long has this child been diagnosed with HIV?

Less than 1 year ☐ 2-3 years ☐ 4-5 years ☐ Above 5 years ☐

7. How long has this child been on antiretroviral treatment?

Less than 1 year ☐ 2-3 years ☐ 4-5 years ☐ Above 5 ye ☐

## SECTION B: HOUSEHOLD FOOD SECURITY

8. In the last 3 months, have you at any time been worried that your household food budget or food supply may not meet your basic needs?

Yes ☐ No ☐

9. In the last 3 months, have you thought you might run out of food without having money to obtain more?

Yes ☐ No ☐

10. Do you think that the food consumed in your family is adequate in quality and quantity?

Yes ☐ No ☐

11. In the last 3 months, have you adjusted your everyday food use, substituting cheaper and fewer food than usual?

Yes ☐ No ☐

12. In the last 3 months, have you reduced the food intake of your child or children?

Yes ☐ No ☐

## SECTION C: FAMILY SIZE

13. Is this child living under the same roof with you?

Yes ☐ No ☐

14. How many children do you have?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 and above ☐

15. How many people are living in the same household with this child?

1-2 ☐ 3-4 ☐ 5-6 ☐ 7 and above ☐

16. If yes, how many people are living with this child in one room?

1-2 ☐ 3-4 ☐ 5-6 ☐ 7 and above ☐

## SECTION D: EXPOSURE TO TB CASE

17. Are you aware of the HIV status of people living in your household?

Yes No ☐ ☐

18. Is anybody in your household living with HIV?

Yes No ☐ ☐

19. If yes, how many people?

` 1 ☐ 2 ☐ 3 ☐ 3 and above ☐

20. How many people are currently receiving care?

1-2 ☐ 3-4 ☐ 5-6 ☐ 7 and above ☐

21. Has anybody in your household been diagnosed with Tuberculosis?

Yes No ☐ ☐

22. If yes, how many people?

1 ☐ 2 ☐ 3 ☐ 3 and above ☐

23. Has any person been living with this child that has experienced weakness, sweating, weight loss, and coughing?

Yes No ☐ ☐

24. If yes, how many people?

1 ☐ 2 ☐ 3 ☐ 3 and above ☐

## SECTION E: SOCIOECONMIC STATUS

25. Which of these will you consider as a place where your household lives?

Rural ☐ Semiurban ☐ Urban ☐

26. Are you currently employed?

Yes No ☐ ☐

27. Who earns income to support your family? ……..

28. How many hours each week do (es) the above person(s) work?.....

29. What best corresponds to the above person(s) current work situation?

Working Full Time ☐

Working Part-Time ☐

Not working and not looking for work ☐

Unemployed and looking for work ☐

Disabled or retired and not looking for work ☐

Currently in School ☐

## SECTION F: PASSIVE SMOKING

30. How much do you think you are exposed to tobacco smoke at home?

(1) Not at all (2) To a small degree (3) Neutral

(4) To a high degree (5) To a very high degree

31. How many members of your family smoke inside your home?

1 ☐ 2 ☐ 3 ☐ Above 3 ☐ None ☐

32. On a 5-point scale, how much do you think you are exposed to tobacco smoke when you go outside your household to socialise?

(1) Not at all (2) To a small degree (3) Neutral

(4) To a high degree (5) To a very high degree

33. How many times per week do you usually go out of your household to socialize?

Once ☐ Twice ☐ More than Twice ☐ None ☐

34. How long do you usually stay when you go to kiosks or bars?

Less than 1 hour ☐ 1-2 hours ☐ 2 hours and above ☐

35. How many times per week do you usually go out to bars?

Once ☐ Twice ☐ More than Twice ☐ None ☐

36. How many people smoke inside the bars you usually go to?

1-2 people ☐ 3-4 people ☐ 5 people and above ☐ None ☐

## APPENDIX B

## CONSENT FORM FOR VOLUNTARY STUDY PARTICIPATION

**FORM 1: Research Consent Form for Children**

Used for children (6months to 14 years) and adolescents (15-17 years old) living at home.

**FACTORS ASSOCIATED WITH TB-HIV CO-INFECTION IN CHILDREN RECEIVING ART IN IMO STATE, NIGERIA**

My name is ……. We want to learn more about the factors that are associated with TB-HIV co-infection in children. Among all children <18 years who are receiving ART in Imo State, Nigeria, you have been randomly chosen to participate in this study. We would like to ask you questions and the information you provide will help the government to plan health, Tuberculosis, and HIV program. This questionnaire usually takes about 30 minutes to complete.

**Benefit(s)**

You may or may not benefit from taking part in this study.

**Risk(s)**

Some of the questions may make you feel uncomfortable. You are free to skip a question and continue. The information you provide will be kept confidential and in a secure place.

**Costs to the participants, if any, of joining the research**

It will not cost you anything to take part in this study other than your time.

**Confidentiality**

Your information and your answers will be protected. A number will be used instead of your name to identify the answers you give. Any answers included in the final report will not have your name.

**Voluntariness**

You do not have to be in this study if you do not want to be. If you decide to stop after we begin, that's okay too. Your parents/guardians know about the study too.

**Consequences of participants' decision to withdraw from research and procedure for orderly termination of participation**

You can also choose to withdraw from the study interview or sample collection at any time. If you decide you want to be in this study, please sign your name.

**What happens to research participants and communities when the research is over:**

The researchers will inform you and your community members of the outcome of the study results through dissemination meetings that will be held at the zonal and community levels.

**Do you have any questions for me?**

**Consent Statement:**

I have read this form and/or someone has read it to me. I was encouraged to ask questions and given time to ask questions. Any questions that I had, have been answered satisfactorily. I agree to take part in this study. I know that after choosing to be in the study. I may withdraw at any time. Taking part is voluntary. I have been offered a copy of this consent form.

Do you agree to participate in this study? Yes ☐ No ☐

Respondent's signature …… Date…./…. / 2021

Name of the respondent (PRINTED) ……

Household ID number:

**[FOR NON-EDUCATED PARTICIPANTS]**

Signature of witness ……. Date: …. / …/2021

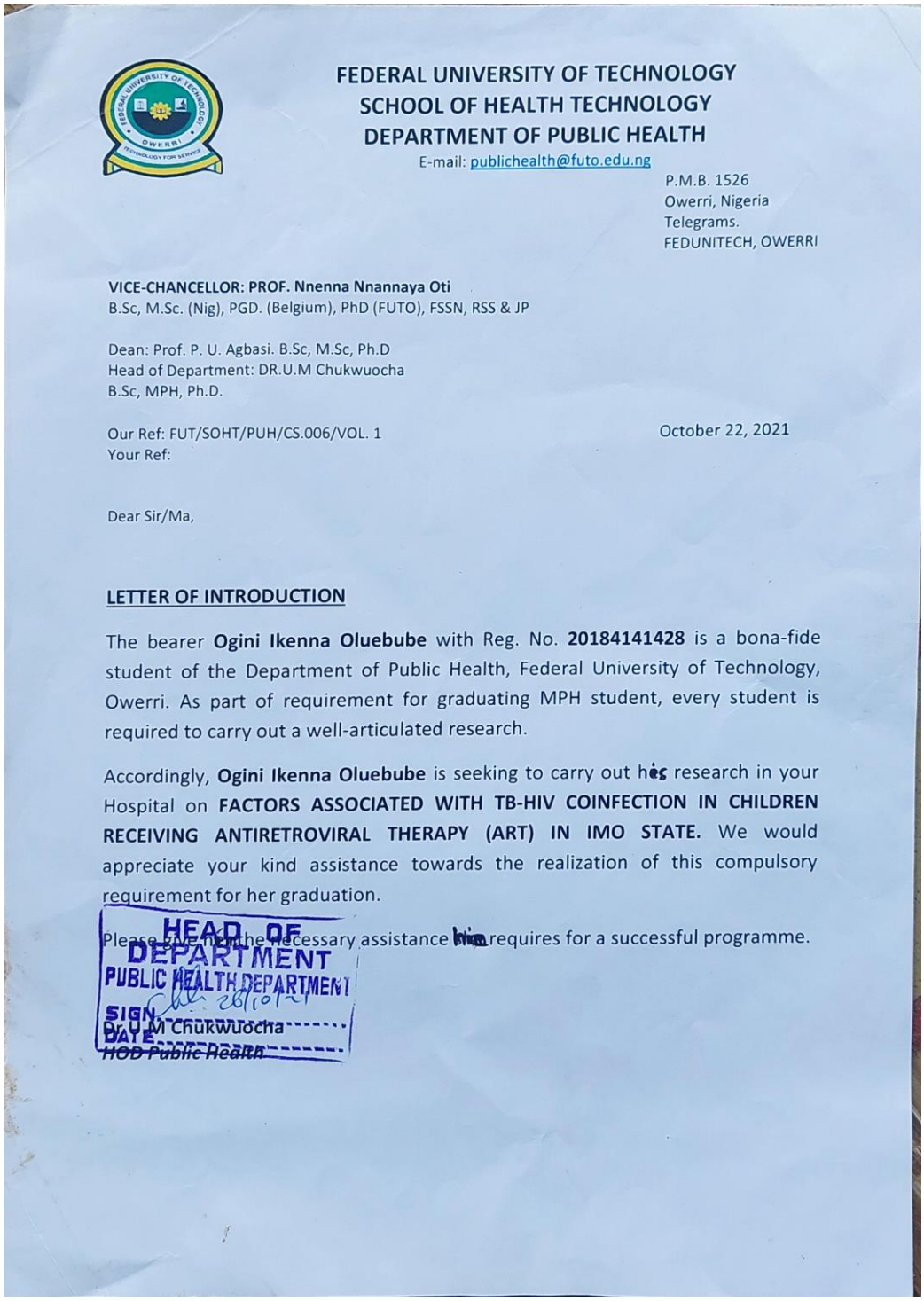
The printed name of the witness …….

**Signature of the person obtaining consent …….**

**Name of the person obtaining consent: (PRINTED) …….**

# APPENDIX C

# APPROVAL FOR THE STUDY



FEDERAL UNIVERSITY OF TECHNOLOGY
SCHOOL OF HEALTH TECHNOLOGY
DEPARTMENT OF PUBLIC HEALTH

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P.M.B. 1526
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FEDUNITECH, OWERRI

**VICE-CHANCELLOR: PROF. Nnenna Nnannaya Oti**
B.Sc, M.Sc. (Nig), PGD. (Belgium), PhD (FUTO), FSSN, RSS & JP

Dean: Prof. P. U. Agbasi. B.Sc, M.Sc, Ph.D
Head of Department: DR.U.M Chukwuocha
B.Sc, MPH, Ph.D.

Our Ref: FUT/SOHT/PUH/CS.006/VOL. 1
Your Ref:

October 22, 2021

Dear Sir/Ma,

**LETTER OF INTRODUCTION**

The bearer **Ogini Ikenna Oluebube** with Reg. No. **20184141428** is a bona-fide student of the Department of Public Health, Federal University of Technology, Owerri. As part of requirement for graduating MPH student, every student is required to carry out a well-articulated research.

Accordingly, **Ogini Ikenna Oluebube** is seeking to carry out his research in your Hospital on **FACTORS ASSOCIATED WITH TB-HIV COINFECTION IN CHILDREN RECEIVING ANTIRETROVIRAL THERAPY (ART) IN IMO STATE.** We would appreciate your kind assistance towards the realization of this compulsory requirement for her graduation.

Please give him the necessary assistance he requires for a successful programme.

HEAD OF DEPARTMENT
PUBLIC HEALTH DEPARTMENT
SIGN
DATE 28/10/21

Dr. U. M Chukwuocha
HOD Public Health

## APPENDIX D

## ETHICAL CLEARANCE

**GOVERNMENT OF IMO STATE OF NIGERIA**

Telegrams:
Telephone:
Your Ref: .....
Our Ref: .....

**MINISTRY OF HEALTH**
**PUBLIC HEALTH** DEPT
**OWERRI**
25/11/ 2021

OKINI IKENNA OKUFBUBE
DEPT OF PUBLIC HEALTH
SCHOOL OF POSTGRADUATE STUDIES
FUT, OWERRI

**RE: APPLICATION FOR ETHICAL CLEARANCE CONVEYANCE OF APPROVAL.**

I am directed to convey approval to your application for Ethical Clearance on your research work entitled; "FACTORS ASSOCIATED WITH HIV-TB CO-INFECTION IN CHILDREN RECIEVING ART IN IMO STATE"

With this approval you can carry on with your proposed research while ensuring the observance of consent, confidentiality and other ethical considerations.

You are to submit a copy of your work to the office of the Honourable Commissioner at the end.

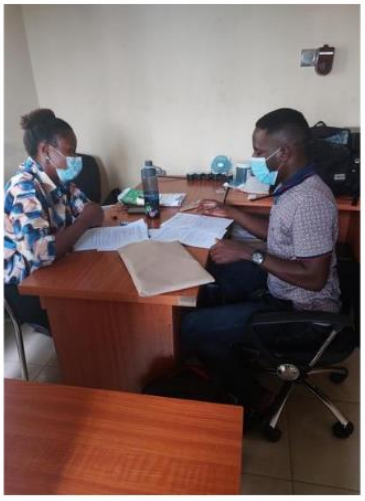
Good luck

DIRECTOR
PUBLIC HEALTH/PRIMARY HEALTH CARE
MINISTRY OF HEALTH
OWERRI

**Dr. Okeji A.C.**
PDH

## APPENDIX E

## TRAINING OF RESEARCH ASSISTANTS



## APPENDIX F

## STUDY PARTICIPANTS