

**SCHOOL OF PUBLIC HEALTH
COLLEGE OF HEALTH SCIENCE
UNIVERSITY OF GHANA**



**PREVALENCE AND RISK FACTORS ASSOCIATED WITH HIV COMORBIDITIES
AMONG CHILDREN AND ADOLESCENTS AT THE EASTERN REGIONAL
HOSPITAL, KOFORIDUA**

BY

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**THIS DISSERTATION IS SUBMITTED TO THE SCHOOL OF PUBLIC HEALTH,
UNIVERSITY OF GHANA IN PARTIAL FULFILLMENT OF REQUIREMENTS FOR
THE AWARD OF THE MASTER OF PUBLIC HEALTH (MPH) DEGREE**

INTEGRI PROCEEDAMUS

AUGUST 2022

DECLARATION

I, Phyllis Otubea Otu, declare the outcome of this work is original, except for references to other investigators' work that have been appropriately acknowledged. This study has not been presented elsewhere for another degree.

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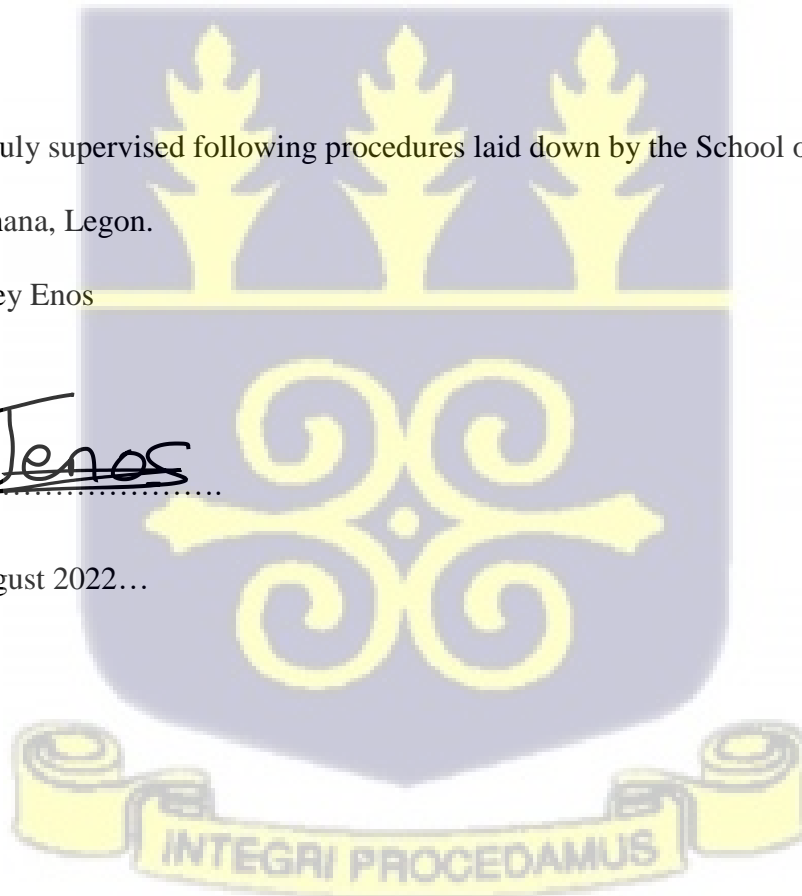
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The thesis was duly supervised following procedures laid down by the School of Public Health,
University of Ghana, Legon.

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Date: ...18th August 2022...



DEDICATION

I dedicate the study to Almighty God for His grace and mercies that enabled me to complete this work.

I again dedicate this work to Rev. and Mrs. Okyere Otu, my parents. Their encouragement and support throughout my stay in school have been immeasurable. I say Almighty God richly bless them.



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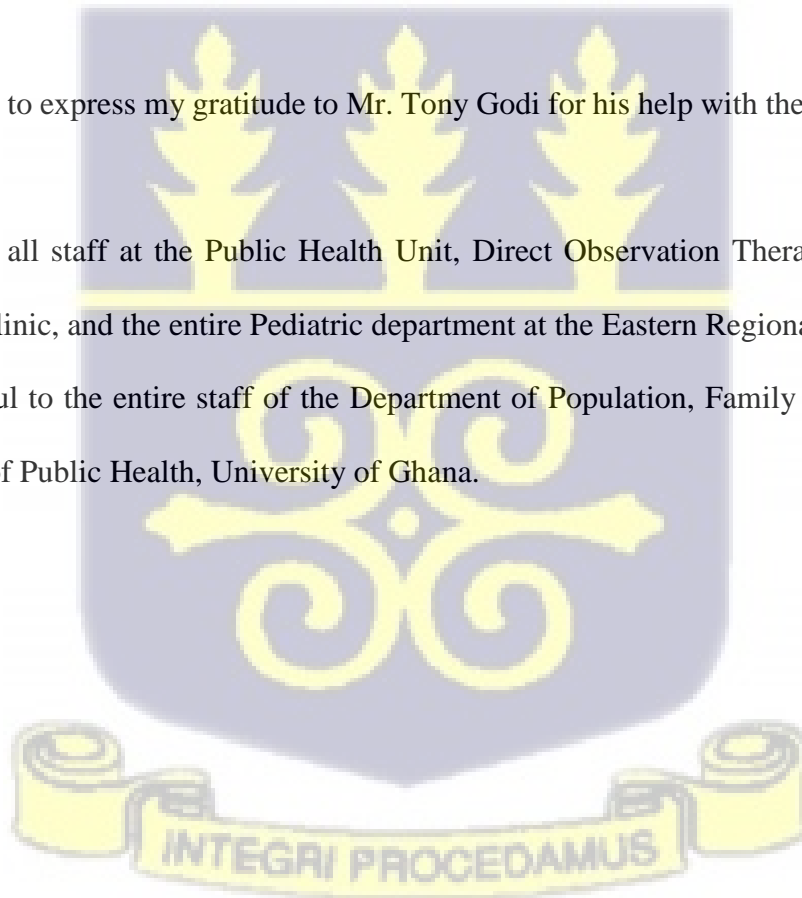


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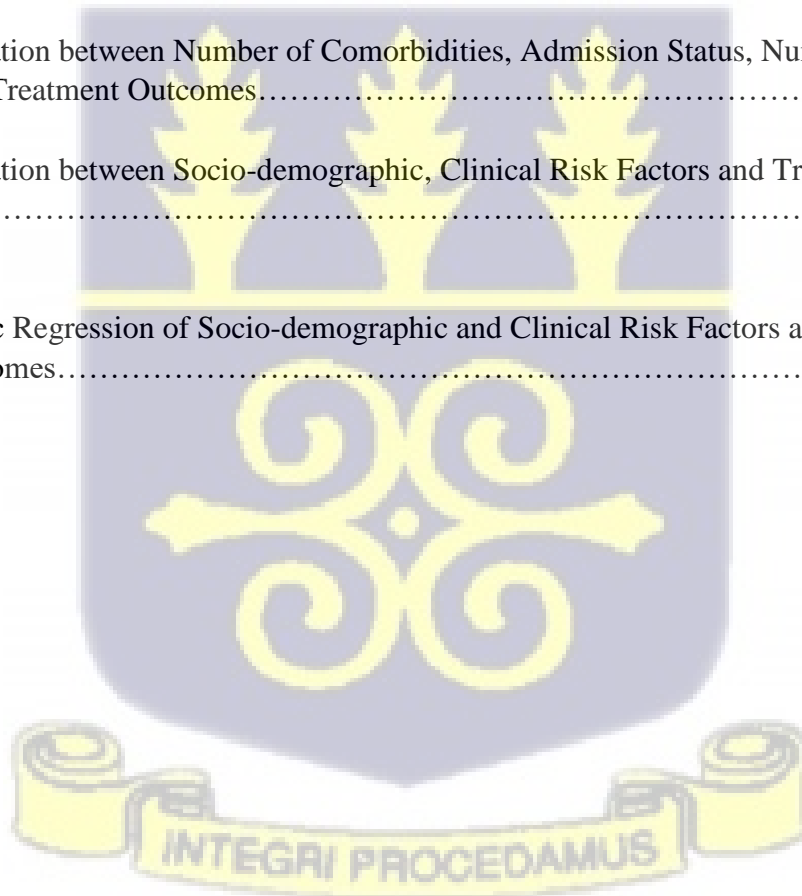
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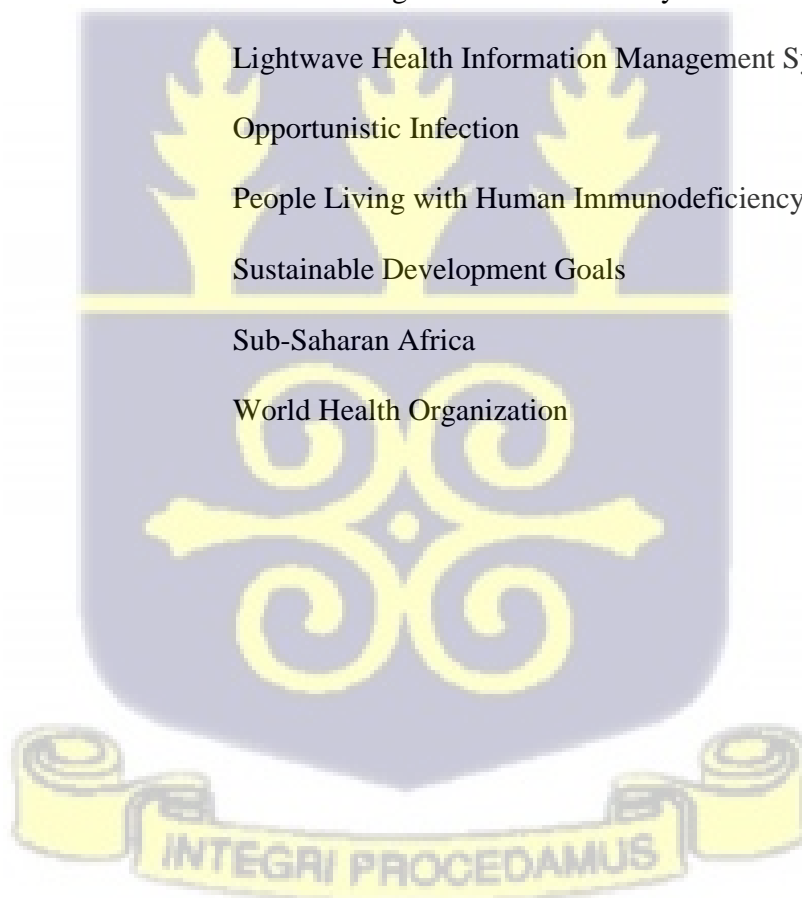
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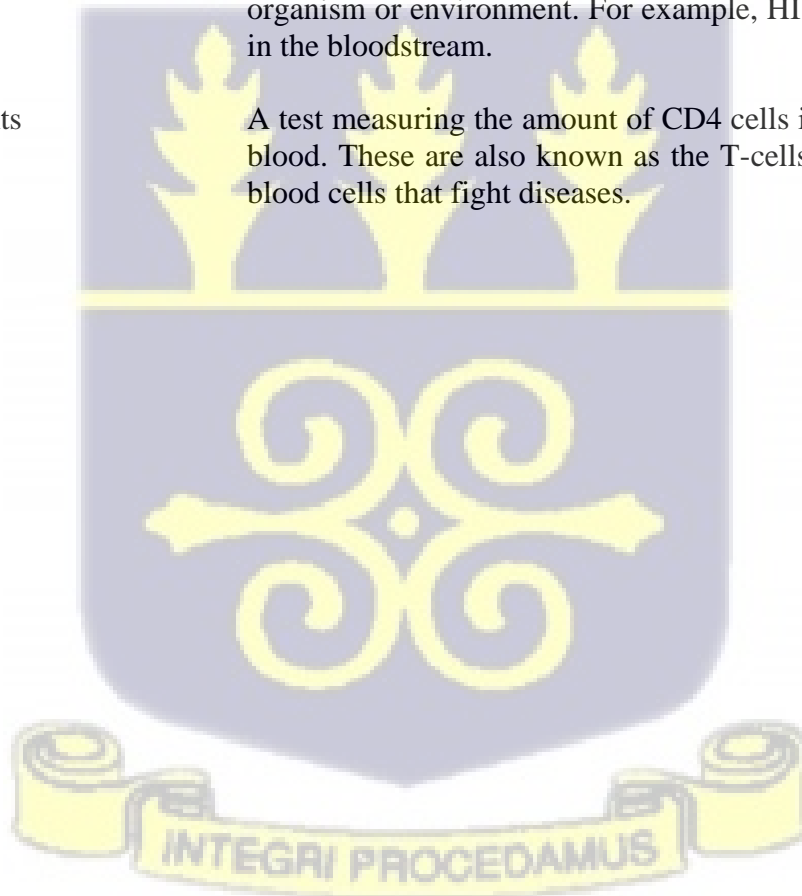
LIST OF ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
CD4	A Cluster of Differentiation 4
CWHIV	Children with Human Immunodeficiency Virus
DOT	Direct Observed Therapy
HIC	High Income Countries
HIV	Human Immunodeficiency Virus
HMIS	Health Management Information System
LHIMS	Lightwave Health Information Management System
OI	Opportunistic Infection
PLHIV	People Living with Human Immunodeficiency Virus
SDGs	Sustainable Development Goals
SSA	Sub-Saharan Africa
WHO	World Health Organization



DEFINITION OF TERMS

HIV	A retrovirus infecting the human immune system by impairing, destroying and damaging its function.
AIDS	A chronic, possibly life-threatening illness caused by the Human Immunodeficiency Virus.
Children with HIV (CWHIV)	Children who have tested positive and been diagnosed with HIV.
People living with HIV (PLWHIV)	Persons who have tested positive and been diagnosed with HIV.
Comorbidities	The presence of one or more infections or diseases, often co-occurring with a primary disease or condition.
Viral load	A measuring of the number of viral particles present in an organism or environment. For example, HIV viruses present in the bloodstream.
CD4 Cell Counts	A test measuring the amount of CD4 cells in an individual's blood. These are also known as the T-cells. They are white blood cells that fight diseases.



ABSTRACT

Background: In the effort to curb HIV/AIDS, children and adolescents remain behind. Children and adolescents living with HIV are primarily at a greater risk of HIV comorbidities because of their susceptibility to infections.

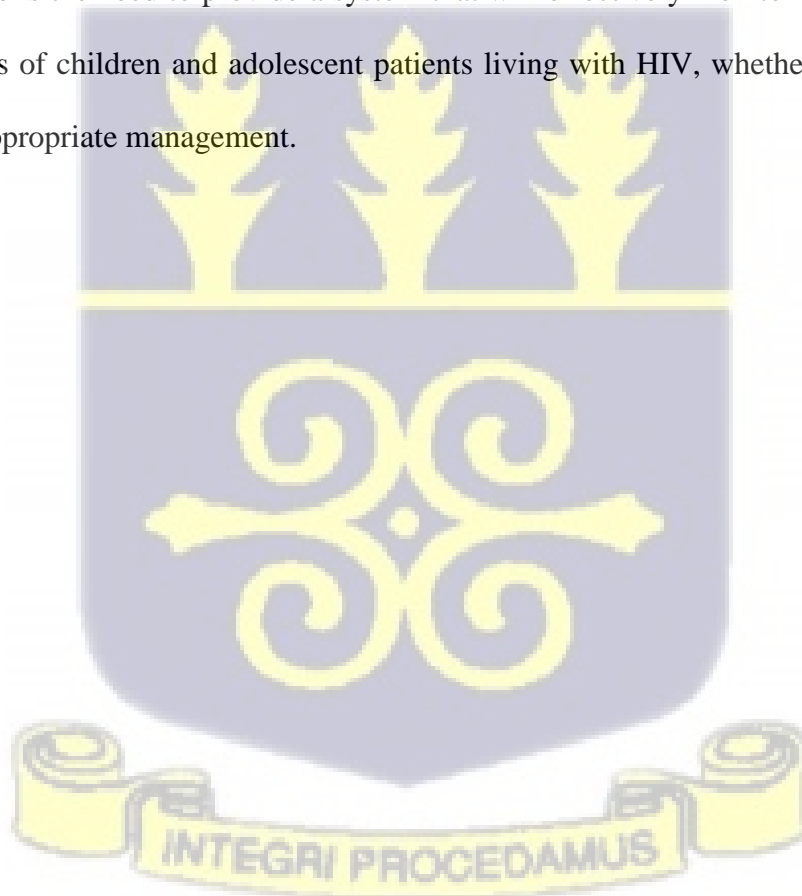
Objective: To determine the prevalence and risk factors associated with HIV comorbidities among children and adolescent patients at the Eastern Regional Hospital, Koforidua.

Method: This is a hospital-based retrospective cross-sectional study, which used clinical record review to obtain retrospective data for 1,437 children and adolescents, from January 2018 to January 2021. Clinical and socio-demographic factors were tabulated and Pearson's chi square test applied to determine associations between risk factors and HIV comorbidities. Logistic regression was used to determine the socio-demographic and clinical factors associated with the presence of HIV comorbidities as well as the treatment outcomes

Results: A majority of the study population (56.9%) were females. The prevalence of HIV comorbidities among the study population was 33.0%. The most frequent comorbidity reported was Bronchopneumonia. Age ($p=0.014$), educational status ($p=0.005$) and adherence to ARTs ($p=0.000$) were significantly associated with HIV comorbidities in bivariate analysis. However, sex ($p=0.063$), level of education of parents or guardians ($p=0.484$), residence ($p=0.845$), viral load detection ($p=0.308$) and viral loads counts ($p=0.973$) were not significantly associated with HIV comorbidities. Children aged 5 - 9 years old were 30% (cOR = 0.70; 95% CI: 0.52 - 0.93; $p=0.017$) less likely to have a comorbidity than children under 5 years old. The odds of having HIV comorbidity was 1.06 (cOR; 95% CI =0.83 - 1.35; $p=0.147$) times higher among children and adolescents whose parents or guardians attained primary education than those whose parents or guardians attained no formal education, but this was not statistically significant. The odds of

having a comorbidity was 45% less likely (cOR = 0.55; 95% CI = 0.42 - 0.71; p= 0.000) among children and adolescents who were not adherent to ARTs than those who were adherent to ARTs. Results from this study showed that there was no significant association between adherence to ARTs and treatment outcomes (p=0.259).

Conclusion: There is a high prevalence of Respiratory comorbidities among children and adolescents with HIV infection. Children and adolescent patients also experience a higher risk of Bronchopneumonia, Pulmonary TB, and Pneumocystis pneumonia. Clinical and Socio-demographic risk factors contribute to the presence of HIV comorbidities and affect their treatment outcomes. There is the need to provide a system that will effectively monitor comorbidities and health conditions of children and adolescent patients living with HIV, whether on admission or not, to inform appropriate management.



CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

The Human Immunodeficiency Virus (HIV) is a virus that attacks the immune system. Over time, HIV weakens a person's immune system, making it challenging to fight other diseases (Rockstroh, 2020). It also causes Acquired Immunodeficiency Syndrome (AIDS), one of the world's most challenging public health issues. Although HIV/AIDS testing capacity has increased over time, enabling more people to learn their status, about one in five people living with the disease is still unaware of the infection (UNAIDS and AIDSinfo, 2021). The epidemic continues to grow worldwide, destroying people's lives, and in many cases, damaging the fabric of societies (Surveillance, 2011).

In 2020, about 37.7 million people were living with HIV globally. Of these, 36.0 million were adults, 1.7 million were children between zero to fourteen years old, and 1.5 million people were newly infected (UNAIDS, 2021). In addition, 84% of people living with HIV (PLHIV) knew their status, and about 6.1 million people were oblivious that they were living with the disease. It is reported that 680,000 and 99,000 deaths due to the disease were among adults and children, respectively. Approximately 15.4 million children and adolescents from the ages of zero to seventeen became orphans (UNAIDS Report, 2021).

The prevalence of HIV infection in high-income countries (HICs) over the past five years has increased, with stable and decreasing death rates (Sullivan et al., 2014). There is evidence that substantial proportions of those diagnosed with HIV infections were people who acquired the infection outside European countries. For example, a large proportion of HIV cases reported in the European Union are largely female migrants from sub-Saharan Africa (SSA) (Sullivan et al., 2014).

According to the update of the epidemic from the Joint United Nations Programme on HIV/AIDS (UNAIDS) 2010, in 2009, 4.9 million adults and children were living with the disease in Asia. This region represents a majority of the world's population (60%). It therefore, has the potential, to influence the course and overall effect of the HIV/AIDS pandemic significantly. Although HIV prevalence is relatively low in most Asian countries, it is reported to be the second highest in the world after SSA (Surveillance, 2011).

An estimated 70% of PLHIV worldwide are in middle-income countries (WHO, 2016). The low and middle-income countries (LMIC) bear the overwhelming burden of the epidemic in terms of the numbers of their citizens living with the disease. In these countries, the epidemic has dramatically disrupted their population structure and economic situation (Loû et al., 2014). Nearly 40 years into the HIV pandemic, SSA where 68% of the world's HIV-positive population lives, remains the global epicenter of transmission. Sub-Saharan Africa has reportedly been with the highest prevalence and accounted for 57% of all new infections in 2019. In parts of the region, one in four adults is infected with the disease. (United Nations Programme on HIV/AIDS. UNAIDS, 2021).

Currently, there are approximately 23.8 million infected persons in sub-Saharan Africa. The impact of the infection is also felt by more than 15 million children who were orphaned - of these; 12.3 million are in SSA (Zewdie, 2005). In 2020, there were 4,000 (60%) reported new HIV infections of adults and children in the SSA. Ten percent of the new HIV infections were in children under 15 years of age (United Nations Programme on HIV/AIDS. UNAIDS, 2021).

The HIV/AIDS epidemic remains a challenge in Ghana. In 1986, the first case of the virus was detected in Ghana by researchers in the Virology Department of the Noguchi Memorial Institute

for Medical Research (NMIMR) of the University of Ghana, Legon (Hardwidge, 2001). Approximately 350,000 Ghanaians were infected with HIV in 2000. This included 330,000 adults and 20,000 children. More than 150,000 Ghanaians have died from the disease since the beginning of the epidemic. Regional HIV prevalence rates ranged from 2.66% in Ahafo as the region with the highest prevalence to 0.39% in North East region, the lowest. At the District level, HIV prevalence ranged from 5.56% in the Lower Manya Krobo, a district in the Eastern Region to 0.07% in Karaga and Tolon, districts with lowest prevalence in the Northern region (Disease Control Unit, 2001).

The 2018 HIV/AIDS estimates reported the national prevalence as 1.69% (Adobebe Y Owusu, 2020). However, prevalence rates varied across all 16 regions of Ghana. Prevalence ranged from 2.5% in the Eastern Region to the lowest of 0.6% in Northern and North East Regions. Since the first case of HIV in Ghana was recorded, the country has systematically responded to the epidemic as it has evolved. Ghana has established appropriate coordination structures and developed policies and action plans to guide the implementation of interventions and activities designed to control the epidemic and eventually end AIDS as a public health concern (Ghana AIDS Commission, 2021).

The 2020 national and sub-national HIV/AIDS report indicated that 346,120 people were living with the disease, with an estimated prevalence of 1.68% (Ghana AIDS Commission, 2021). According to the report, 91.71% adults and 8.29% children are living with the disease, with 18,928 new infections including 80.5% adults and 19.46% children. The infections in adults were considered to be largely sexually transmitted, and in children, vertically transmitted from mothers to their children (Ghana AIDS Commission, 2021). The incidence of new infections among the young population was 0.70% in 2020. Out of an estimated 42,016 youth living with the disease in 2020, 73.91% were females, highlighting the vulnerability of adolescent girls and young women

in this age group to HIV. The report also stated that, of the estimated HIV/AIDS-related deaths, 9,796 were adults and 2,962 were children (Ghana AIDS Commission, 2021). In 2020, the coverage of prevention of mother-to-child transmission (PMTCT) of HIV was 71.59% and the mother-to-child transmission of HIV/AIDS, through breastfeeding period was 20.81% (Owusu, 2021).

HIV/AIDS infection is the leading cause of death among children and adolescents in SSA. Some mothers, who had the infection during pregnancy, infected their children during the birth process or from breastfeeding. (Sandra Fagundes Moreira-Silva et al., 2015). Children could also be infected through sexual abuse or rape. In some low-income countries, where child marriages are culturally accepted, a young girl could get the disease from their older husband, and then infect their babies. For instance, a younger a child is, when they first have sex, the higher the chances of getting the infection are. In some middle and high-income countries, injection drug use spreads HIV among children and adolescents (Fishel et al., 2014).

The HIV/AIDS disease is reported to be associated with comorbidities. Comorbidity, was originally defined by Feinstein as “any distinct additional clinical entity that has existed or may occur during the course of the disease in a patient who has the index disease under study” (Salive, 2013). Comorbidity in HIV is a disease or an illness outside the scope of an AIDS-defining illness. People living with HIV/AIDS are at high risk of developing both related and non-related HIV comorbidities (Christensen et al., 2019).

There is a clear difference between comorbidity and complication of an illness. Comorbidity is a separate illness or disease, along with a primary health concern. A complication on the other hand, may or may not be related to the comorbid disease. A disorder may represent an early manifestation of another. There may be problems of classification, in which the use of same or similar symptoms

define different disorders. Detection artifacts can occur. For example, the presence of one disorder may make another condition more visible. Similarly, the presence of one disorder may influence the observations of clinicians and make them more likely to report the presence of another disorder. Comorbidities can occur by chance. They may be acute or chronic and infectious or non-infectious (Salive, 2013).

HIV comorbidities may or may not interact with each other. They are often due to the infection and its associated risk factors (Lorenc et al., 2014). The risk factors of HIV comorbidities may determine the mortality rate and quality of life of persons living with HIV. Comorbidities increase with severity of the disease, leading to a higher prevalence of comorbidities among people living with HIV/AIDS. Comorbidities may also be due to potential coinfections through overlapping risk factors (Lorenc et al., 2014). The consequences of specific comorbidity combinations, however, depends on several factors. (Schouten et al., 2014). HIV comorbidity is associated with poor health outcomes, more complex clinical management, and increased health care costs (Valderas et al., 2009).

Comorbidities in HIV can occur in relation to treatment, concomitant drugs and the HIV infection. In line with the survival rate, there has been an increase in HIV and non-HIV comorbidities burden, including the overrepresentation of traditional risk factors and chronic immune activation and inflammation among patients living with HIV (Martinez-Iglesias et al., 2019). Comorbidities, co-infections, and side effects are prevalent among HIV-infected patients attending public sector healthcare facilities. Individuals living with HIV may present side effects due to combination antiretroviral therapy (cART) and co-infections and comorbidities pre-existing before starting the cART. Comorbidities may have a prolonged effect on health outcomes of infected individuals and

their survival (Nlooto, 2017). The HIV comorbidities directly interfere with clinical management and further increase the morbidity and mortality of these individuals (Al et al., 2020).

The epidemiology of HIV comorbidities in HICs has had characteristics quite distinct from the situation in SSA. Since the advent of antiretroviral therapy and routine screening of women in pregnancy, the number of infants infected with HIV in HICs has plummeted, although cases still occur (Sullivan et al., 2014).

Risk factors that drive trends in HIV comorbidities may be very different between HICs and LMIC. These include coverage of Anti-Retroviral Therapy, (ART), extent of HIV diagnosis among those living with HIV, access to healthcare services and social structures that facilitate accurate reporting of injection drug use and sex risks. High-income countries have case-based surveillance systems while many lower- and middle-income countries use other systems, such as demographic and household surveys and convenience surveys of key populations to describe epidemiology (Sullivan et al., 2015).

The HIV/AIDS mortality rates are unjustly high in SSA due to HIV comorbidities. The prognosis for persons living with HIV improved since the advent of highly active antiretroviral therapy (HAART), but these improvements have lagged behind in low-income countries. Patients continue to present to inpatient care with the World Health Organization (WHO) Class III and IV illness and undiagnosed or untreated HIV infection because of insufficient case finding, poor linkage to care and treatment failure or default (Phillips et al., 2018).

Out of the 17 Sustainable Development Goals, (SDGs), goal 3 focuses on ‘good health and wellbeing’. In this goal, ending HIV/AIDS epidemic by 2030 is set as one of the priority targets. This underpins the fact that prevention and control of the disease is still an important agenda for the next few years until 2030 (Girma, 2016). The health-related SDG goal 3, addresses a range of

health issues critical for growth. Target 3.3 on infectious illnesses includes ending the epidemic. Interventions to curb HIV/AIDS will influence other health objectives, including maternal mortality reduction (Wynn & Jones, 2019).

Target 3.1, preventing mortality of neonates and children under five years. Target 3.2 is decreasing death from non-communicable infections and promoting mental wellbeing, target 3.4, preventing and treating substance use disorders, target 3.5, sexual and reproductive wellbeing, target 3.7, attaining worldwide health coverage, target 3.8, access to affordable drugs, and treatment (Jones et al., 2017). Ending the epidemic by 2030 will accelerate progress across a range of SDG targets. A core principle of the 17 SDGs and of HIV/AIDS response is to leave no one behind. The epidemic cannot be ended without the needs of people living with and affected by HIV, and the determinants of health and vulnerability, being addressed (Wynn & Jones, 2019).

Other SDGs linked to the HIV/AIDS response are the SDGs 5, 10, 16 and 17. SDG 5, achieve gender equality; gender inequalities, discrimination, violence and harmful practices negatively affect women, girls, men and boys and increase the risk of HIV infection and its impact. HIV is the leading cause of death among women of reproductive age, from 15 to 44 years old. The SDG10 is to reduce inequality. Income inequality is linked to higher HIV prevalence. HIV affects vulnerable and disempowered communities most severely. Stigma and discrimination against key populations is a major contributor to high HIV prevalence among them and is linked to lower access to health care and housing (Morton et al., 2017).

The SDG 16 is to promote peaceful and inclusive societies. Exclusion, stigma, discrimination and violence fuel the HIV/AIDS epidemic among adults and children. The HIV/AIDS response, led by people living with the disease, has demanded access to justice and pioneered people-centred accountability mechanisms, providing lessons on which to build. Participatory governance, which

includes community-led responses, can drive more relevant, rights-based programmes and stronger accountability for health and development (WHO, 2016).

The SDG 17 is to strengthen means of implementation. Global collective action to improve access to affordable HIV commodities is critical to ending the epidemic. Efforts to secure treatment affordability of HIV commodities, including provision of second- and third-line medicines. (Morton et al., 2017). The United Nations Joint Programme on HIV/AIDS focuses on the people in need and reducing the inequalities that drive the HIV epidemic and undermine the abilities of people at risk of, living with the disease to access lifesaving services, social protection and financial support systems and enjoy their human rights through addressing social and structural barriers. In situating its collaborative efforts, within a larger development context, the Joint Programme works to generate and strengthen synergies between HIV-specific actions and broader development, gender equality and human rights initiatives. This contributes to a wide range of areas, including humanitarian responses, social protection, education, efforts to promote more sustainable cities, social justice and innovative financing for development (Morton et al., 2017).

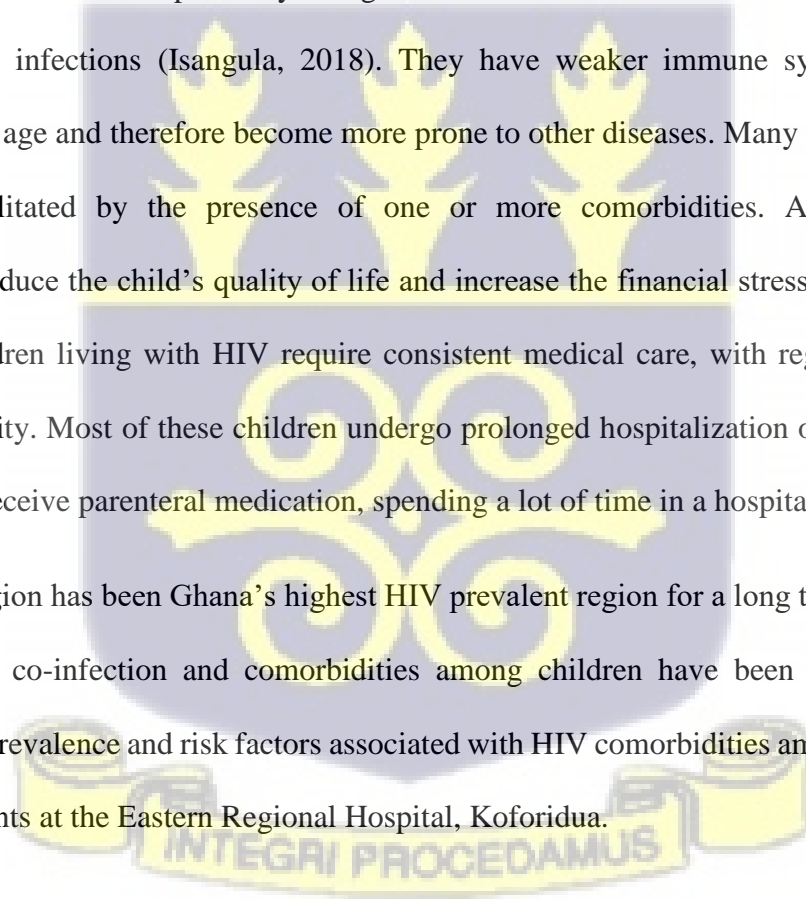
1.2 Statement of the Problem

In the effort to curb HIV/AIDS, children and adolescents continue to fall behind. New cases of the infection are recorded in utero, at birth, during breastfeeding, and in adolescence. (United Nations Children's Fund (UNICEF), 2020). More than 3.4 million children are infected globally. Approximately 30 children die every hour because of the infection and accounts for 3% of deaths in children globally and 6% of those in sub-Saharan Africa, where HIV-AIDS has become one of the critical killers of children (WHO, 2016).

Prevalence studies report the extent of HIV comorbidities and co-infection rates ranging from 2.9% to 72.3% in some regions and countries with a mean rate of 23.5% (Gao et al., 2011). The natural history and clinical manifestations of HIV in children and adolescents differs from adults. Rapid disease progress seen and the opportunistic infections that result from immune deficiency in children and adolescents with the disease are often primary, not reactivation disease, thereby resulting in greater morbidity (Marie et al., 2022). Access to testing and treatment is not enough for children and adolescents living with HIV. This situation results in higher prevalence of comorbidities and hundreds of deaths (United Nations Children’s Fund (UNICEF), 2020).

Children and adolescents are primarily at a greater risk of HIV/AIDS infection because of their susceptibility to infections (Isangula, 2018). They have weaker immune systems than other children of their age and therefore become more prone to other diseases. Many of these cases and deaths are facilitated by the presence of one or more comorbidities. Apart from death, comorbidities reduce the child’s quality of life and increase the financial stress on the parents or guardians. Children living with HIV require consistent medical care, with regular visits to the health care facility. Most of these children undergo prolonged hospitalization or regularly attend the hospital to receive parenteral medication, spending a lot of time in a hospital environment.

The Eastern Region has been Ghana’s highest HIV prevalent region for a long time. However, no studies on HIV co-infection and comorbidities among children have been done. This study determines the prevalence and risk factors associated with HIV comorbidities among pediatric and adolescent patients at the Eastern Regional Hospital, Koforidua.



1.3 Justification and significance of study

Despite the availability of the measures and interventions to control HIV, the risk of mortality due to HIV comorbidities among children and adolescents have not been thoroughly investigated in Ghana. Morbidity related to HIV infection is not well understood, particularly in low resource settings such as Ghana, where laboratory or diagnostic competencies are limited. This study is thus, designed to investigate the prevalence and risk factors associated with HIV comorbidities among children and adolescents living with HIV.

The study will add to the knowledge and information concerning challenges in healthcare needs among HIV-positive children and adolescents. The data that will be collected will be a vital component in the assessment of the effectiveness of both comorbid and HIV control interventions. It will encourage synergized efforts between HIV programs and, in so doing, recalibrate their efficiency in effectively reducing HIV comorbidities burden, reinforce existing recommendations and fight against major preventable infectious diseases among children and adolescents living with HIV. This study will enable public health surveillance to improve efforts in addressing the treatment regime for HIV comorbidities among children and adolescents.

Every child has the right to live, not to have their lives arbitrarily taken, and benefit from every economic and social policy that will allow them to continue into adulthood, whether HIV positive or not, children have the right to quality of life.



1.4 Objectives of the study

1.4.1 General Objective

To determine the prevalence and risk factors associated with HIV comorbidities among children and adolescent patients at the Eastern Regional Hospital, Koforidua.

1.4.2 Specific Objectives

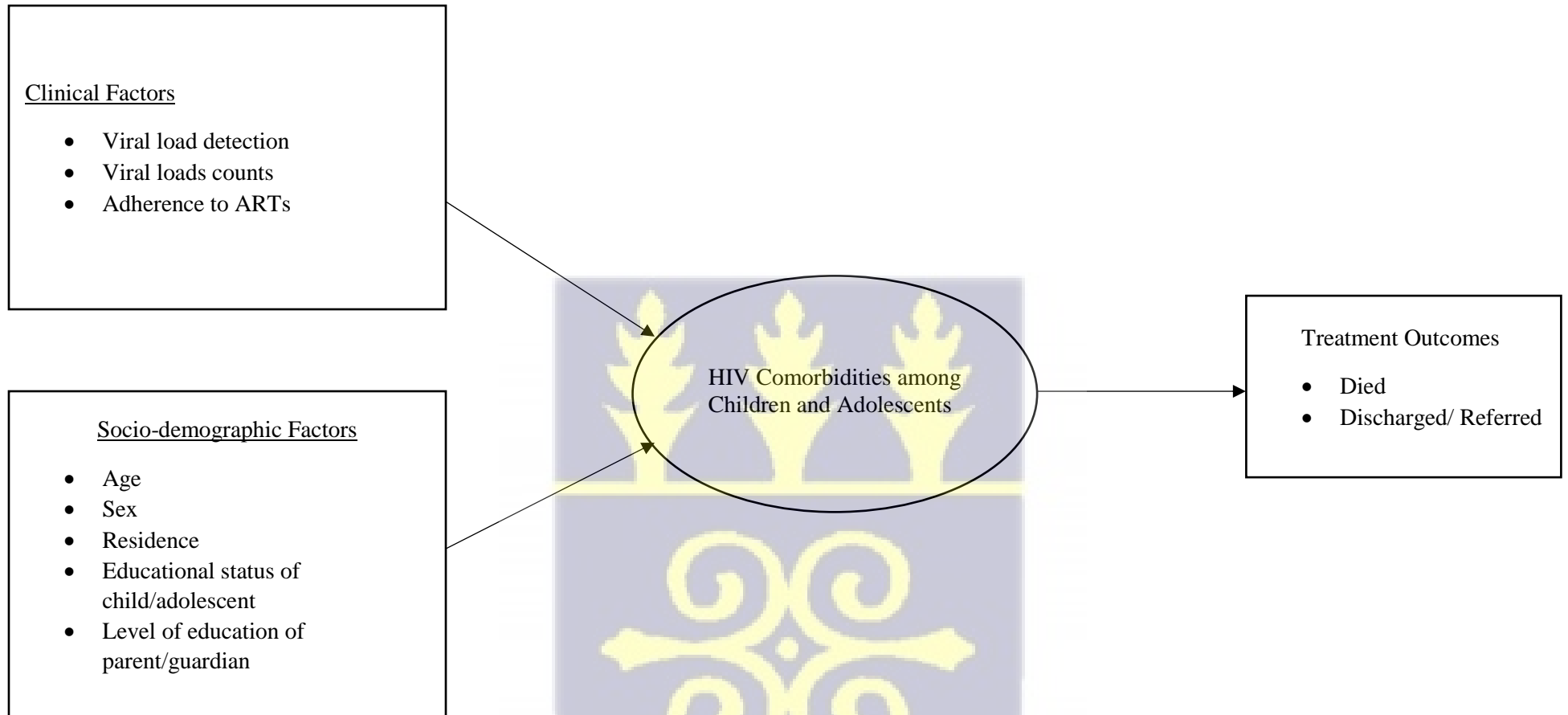
1. To estimate the prevalence of HIV comorbidities among children and adolescents at the Eastern Regional Hospital, Koforidua.
2. To determine the clinical and socio-demographic risk factors associated with HIV comorbidities among children and adolescents at the Eastern Regional Hospital, Koforidua.
3. To determine the clinical and socio-demographic risk factors associated with treatment outcomes of HIV comorbidities among children and adolescents at the Eastern Regional Hospital, Koforidua.

1.5 Research Questions

1. What is the prevalence of HIV comorbidities among children and adolescents at the Eastern Regional Hospital, Koforidua?
2. Which clinical and socio-demographic risk factors are associated with HIV comorbidities among children and adolescents at the Eastern Regional Hospital?
3. Which are the clinical and socio-demographic risk factors associated with treatment outcomes of HIV comorbidities among children and adolescents at the Eastern Regional Hospital?



1.6 Conceptual Framework for Risk factors associated with HIV Comorbidities and Treatment Outcomes among Children and Adolescents



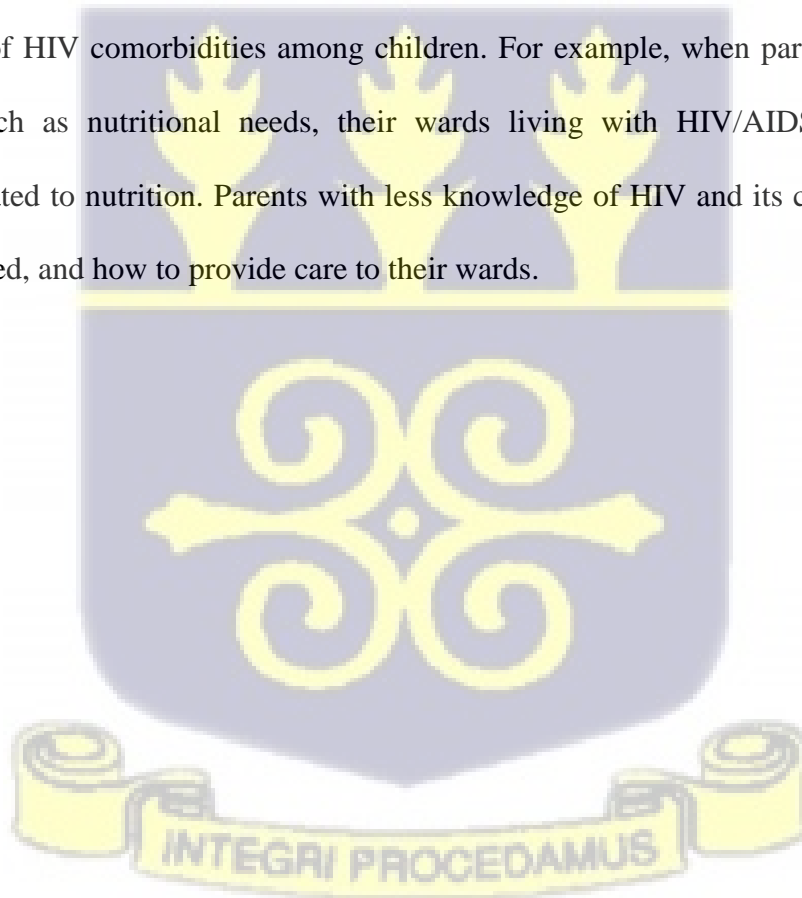
Author's own construct

Figure 1. Conceptual Framework for Risk Factors associated with HIV Comorbidities and Treatment Outcomes among Children and Adolescents.

1.6.1 Narrative of Conceptual Framework for Risk Factors associated with HIV Comorbidities and Treatment Outcomes among Children and Adolescents.

Figure 1 shows a conceptual framework of risk factors associated with HIV comorbidities among children and adolescents and treatment outcomes. Several factors may be associated with HIV comorbidities among children and adolescents. Clinical risk factors of HIV comorbidities include HIV RNA plasma (viral load), and adherence to anti-retroviral therapy (ARTs). The level of viral loads notwithstanding, children and adolescents are at higher threat of death and advancement to AIDS than adults are (Tobinet et al., 2014).

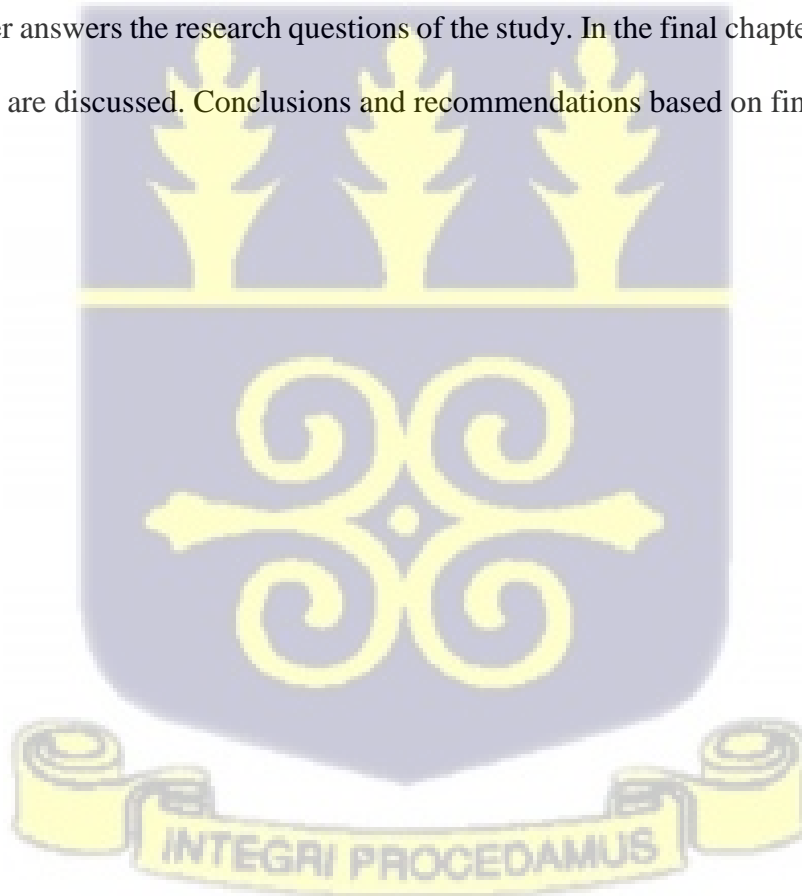
Socio-economic factors such as the age, sex, educational status of the child or adolescents, residence and even the level of education of the parent or guardian may also increase or decrease the prevalence of HIV comorbidities among children. For example, when parents are unable to meet needs, such as nutritional needs, their wards living with HIV/AIDS may acquire a comorbidity related to nutrition. Parents with less knowledge of HIV and its comorbidities may not know the need, and how to provide care to their wards.



1.7 Outline of Dissertation

This dissertation is organized in six chapters. The key concepts of the study are described from the literature in chapter two. These include prevalence of HIV comorbidities, age distribution of HIV comorbidities among children and adolescents, risk factors and treatment outcomes of HIV comorbidities among children and adolescents. Chapter three of the study describes the study design, study location, study variables, study population, sampling determination, data collection tool, data analyses and ethical considerations.

The fourth chapter of the study has results obtained from data analysis. The results are presented with aid of tables and graphs. Chapter five of the study provides interpretation of results in chapter four. This chapter answers the research questions of the study. In the final chapter, the significance and implications are discussed. Conclusions and recommendations based on findings of the study are made.



CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

The chapter examined studies on the prevalence and risk factors related to HIV comorbidities in children and adolescents. It involved researching and gathering relevant information from published works and other data that supported the study. The literature looked at the prevalence, kinds and distribution of HIV comorbidities among children and adolescents living with HIV. Based on the study's objectives, the literature review looked at works relevant to risk factors associated with comorbidities, clinical, psychological, and socio-economic factors. The literature review also looked at results pertinent to the treatment outcomes of these comorbidities among children and adolescents living with HIV.

2.1 Prevalence of HIV Comorbidities among Children and Adolescents

The initial diagnosis of HIV disease in children and adolescents can be a challenge (Sandra F. Moreira-Silva et al., 2013). The spectrum of HIV comorbidities in children may differ from those in adolescents and even adults, likely related to the timing of HIV infection and or anti-retroviral therapy (ART) initiation (Frigati et al., 2020). Clinical presentations resemble other common childhood diseases. Clinical manifestations include prolonged or recurrent fever (often considered to be of unknown origin); recurrent or chronic diarrhoea; generalized lymphadenopathy; persistent or chronic cough; recurrent upper respiratory tract infections (URTI), including sinusitis and otitis; recurrent pneumonia; persistent oral candidiasis; delayed somatic growth; skin lesions, especially eczema; hepatosplenomegaly; and delayed neuropsychomotor development (Sandra F. Moreira-Silva et al., 2013).

Circulatory diseases

In low-income countries, it is reported that a high burden of HIV-associated cardiac abnormalities in children with HIV (CWHIV) taking ART, has a prevalence estimated between 14% to 89% (Frigati et al., 2020). A study on cardiovascular anomalies among African children below 12 years reported a prevalence of cardiac abnormalities in HIV-infected children of 75.9%. Abnormalities included heart failure, dilated cardiomyopathy (33.7%), increased left ventricular mass (20.5%), and pericardial effusion (14.5%). The study concluded that there was no significant association between occurrence of cardiovascular abnormalities and variables such as age and gender (Okoromah et al., 2012).

Genitourinary Diseases

With renal diseases among children and adolescents, microalbuminuria is an early marker of glomerular injury and predicts further proteinuria development. Two studies from Tanzania and South Africa reported a variable prevalence of 20.4% and 8.5% respectively for microalbuminuria in CWHIV (Frigati et al., 2020). Microalbuminuria, proteinuria and renal dysfunction were noted to be prevalent among HIV infected children. Another study on renal abnormalities among HIV infected children reported microalbuminuria and proteinuria were present in 20.4 % and 7.1 % respectively. Significantly higher prevalence of microalbuminuria ($p < 0.01$) and proteinuria ($p < 0.01$) were noted with undetectable viral load (Fredrick et al., 2016).

Neurological Diseases

Considering developmental delay, neurocognitive disease, and mental health, severe neurodevelopmental delay and HIV encephalopathy were common in children with HIV. The prevalence of HIV-associated neurocognitive impairment has declined in the ART era (Frigati et al., 2020).

Prevalence rates for psychiatric disorders in perinatally-infected children vary from 55% to 61%. The most common disorders found are anxiety disorders, followed by attention-deficit hyperactivity disorders, conduct disorders, oppositional defiant disorders, and mood disorders (Narasimha & Science, 2019).

Among adolescents living with HIV, studies report a high prevalence of mental health disorders. A large Ugandan study that recruited more than 1300 children and adolescents with HIV reported a prevalence of 17% of any psychiatric disorder and a 10% prevalence of a behavioural disorder, most commonly attention deficit hyperactivity disorder. These disorders were more common in adolescents (Frigati et al., 2020). A study carried out in a pediatric clinic in Nairobi, included 162 HIV-infected children and adolescents (six to eighteen years of age). The most common psychiatric diagnoses were major depression (17.8%), social phobia (12.8%), and oppositional defiant disorder (12.1%). Meanwhile, in northern Nigeria, a relatively low prevalence of psychiatric comorbidities including depression and psychosis has been reported (Dias et al., 2021).

Respiratory Diseases

Respiratory infection is the major cause of morbidity and mortality in children and adolescents infected with human immunodeficiency virus. The initial presentation of respiratory infection is usually in infancy or early childhood (Graham & Gibb, 2002). Several studies in sub-Saharan Africa have reported high prevalence of respiratory diseases among children and adolescents living with HIV, including both those with delayed HIV diagnosis and treatment and those already established on ART. Prevalence of respiratory diseases can be as high as 25- 37.5% (McHugh et al., 2020). In the absence of ARTs, up to 90% of HIV infected children and adolescents develop a severe respiratory illness in the course of their HIV disease. Pneumonia is the commonest cause

of hospitalization in African HIV infected children with pneumonia-specific mortality rates 3-6 times higher than those of HIV negative patients (Becker et al., 2015).

A study in Zimbabwe reported a prevalence of 25% on children and adolescents with HIV infected on ART and receiving co-trimoxazole prophylaxis (Desai et al., 2018). Another study reported fourteen percent (14%) of children presented with tuberculosis (TB). The severe state of immunosuppression in these cases was significant ($p=0.001$), and tuberculosis was significantly associated with an age at admission to an infectious diseases ward of less than five years ($p=0.02$).

A previous study on the prevalence of HIV/AIDS in children diagnosed with active TB in the state of Espírito Santo showed 411 cases of pediatric TB from 2000 to 2006, and 27 (7%) children were living with HIV/AIDS. Again, in a Chilean study, of 246 children with the disease due to vertical transmission, six presented with TB/HIV co-infection (Sandra F. Moreira-Silva et al., 2013).

Infectious Diseases

On infectious comorbidities, eighteen studies reported a low prevalence of 2% with Hepatitis B in SSA and the highest of 13% in the eastern Mediterranean region among adolescents living with HIV (Ford et al., 2015). A study reported that 177 children, between the ages of 6 to 15 years living with the HIV infection were admitted in a hospital, due to other infectious comorbidities. Regarding clinical-immunological classification, 146 (82.5%) patients of these children showed acute and chronic forms of the infectious comorbidities at the time of admission into the ward during the study. The most common clinical signs were hepatomegaly (81.62%), splenomegaly (63.8%), lymphadenopathy (68.4%) and, persistent fever (32.8%). (Kukoyi et al., 2016). A study in Tanzania reported prevalence of oral candidiasis as 42.0% (132/314) among children and adolescents. Oral candidiasis remains the most frequently HIV-associated oral lesion in Tanzania (Ngasala et al., 2016).

Blood Diseases

HIV affect different hematological parameters, like hemoglobin percentage, total WBC count, absolute neutrophil count, total lymphocyte count and platelet count. These parameters change with change in disease severity. A study done in Kolkata hospital, India reported the frequency of anemia as 69 out of 100 study population (Bhowmik & Banerjee, 2015). Another study in China reported that prevalence of anemia was 39.7% (95% CI: 31.4%-48.0%) among children and adolescents living with HIV (Cao et al., 2022).

Chronic Diseases

A study reported a high burden of comorbidities such as hypertension and diabetes with prevalence of (39.2%) and (12.4%) among adolescents. These co-infect with tuberculosis as side effects due to combination of Antiretroviral Therapy (cART) was observed among HIV-infected adolescents attending public sector healthcare facilities in KwaZulu-Natal. This study further reported the prevalence of some comorbidities, asthma (5.8%), epilepsy (5.8%), gastric ulcers (1.9%), herpetic skin rash (1.3%), oral candidiasis (0.4%), and, renal disorders (2.1%). The observed prevalence of comorbidities in this study is consistent with a report on the rate of comorbidities among adolescents living with the HIV infection in sub-Saharan Africa. A similar study conducted in Canada showed same comorbidities are prevalent among HIV infected adolescents on cART. This study found that comorbidities were mainly chronic diseases affecting the cardiovascular (hypertension, heart disease) and endocrine (diabetes) systems (Nlooto, 2017).

Neoplasms

Children and adolescents with HIV have an increased risk of malignancy. Non-Hodgkin's lymphoma (NHL) occurs most commonly, followed by Kaposi's sarcoma, Leiomyoma-sarcoma

and Hodgkin's lymphoma. In African HIV-infected children, Kaposi's sarcoma is a common AIDS-defining malignancy probably due to the prevalence of human herpes virus infection (Frigati et al., 2020).

Skin Diseases

Skin disease is severe and atypical, responds less well to treatment, and relapse more frequently compared with HIV- uninfected children. Although incidence has declined in the ART era, HIV-related skin conditions remain one of the most common management problems faced by health care workers caring for children and adolescents with HIV. It is reported that ART is associated with risk of drug reactions and immune reconstitution inflammatory syndrome skin disease. These conditions receive little attention as they may not be "life-threatening" but lead to complications and disability, reduced quality of life and frequent clinic attendances placing an additional burden on health services (Frigati et al., 2020).

Musculoskeletal Diseases

Adolescence is a critical period for musculoskeletal development and bone mass accrual. Impaired growth may have a deleterious effect on musculoskeletal development and health across the life course. After cessation of linear growth and skeletal maturation, bone mass reaches a peak (peak bone mass [PBM]), after which bone mass declines at varying rates through adulthood. Peak bone mass accounts for 60% of lifetime osteoporosis risk, with a 10% decrease in PBM doubling adult fracture risk. Pubertal delay predicts lower adult bone mass and increases future osteoporotic fracture risk. It is reported that there is an increased prevalence of 15% to 20% of low bone density in adolescents living with HIV, and the disease appears to be associated with decreased bone accrual throughout adolescence. A recent study from Zimbabwe showed reduced size-adjusted (Z-

Score ≤ -2.0) lumbar spine total-body-less head bone density measurements in 15% and 13% of children and adolescents aged 8 to 16 years taking ART (Frigati et al., 2020).

2.2 Risk Factors associated with HIV Comorbidities among Children and Adolescents

2.2.1 Clinical Risk Factors

The clinical course of HIV/AIDS is faster in children and adolescents than in adults due to their immunological immaturity (Sandra F. Moreira-Silva et al., 2013). Unlike adults, children and adolescents often experience a rapid progression of HIV disease and persistently high levels of plasma virus (Kwara et al., 2010). HIV viral load has been found in several studies to be the main determinant of HIV disease progression. For example, in a resource-limited setting, the two immediate deleterious effects of persistent viremia will be virological treatment failure. Again, it is reported that children and adolescents with high viral loads show moderate and severe manifestations of HIV comorbidities. (Kukoyi et al., 2016).

Annual mortality estimated without treatment in HIC ranged from 1.2–12.0% to 0.2–2.1% in 2015 among children and adolescents living with HIV. A Cluster of Differentiation 4, CD4, and HIV RNA plasma (viral load) were poorer predictors of mortality among children and adolescents. In middle and low-income countries, where the mortality rate is higher among children and adolescents, viral load is highly associated with HIV related illness and high mortality rate. Therefore, the annual mortality estimated without treatment among children and adolescents ranged from 2.6–32.5% in children and 0.6–23.0% in adolescents (Davies et al., 2016).

It is reported that in SSA, children and adolescents with moderate and severe manifestations of HIV comorbidities have high HIV viral loads followed by low body weight for age and hemoglobin level (Sandra F. Moreira-Silva et al., 2013). The severity of HIV comorbidities, for

example, neurological and neuropsychological problems and developmental delays is reported to have an association with higher viral loads and the most severe non-neurological health-related symptoms (Narasimha & Science, 2019). In some extreme cases, children and adolescents taking ART may not control HIV replication. Poorly controlled HIV can be due to, lack of health care, poor medication adherence, drug resistance, and drug toxicity (Shiferaw et al., 2019).

Viral suppression was defined as recording at least one viral load less than 50 copies/mL after commencement of treatment (Opoku et al., 2022) A study conducted in Ho in the Volta Region of Ghana reported a virological failure of 80 (31.3%) out of 284 HIV-positive patients (Lokpo et al., 2020). Another study on virological failure in Kumasi, Ashanti Region reported viral suppression rate of 76.4% among patients on ARTs. (Ansah et al., 2021). A study on the association between viral load detection and HIV comorbidities in Western Cape, South Africa found no association between a detectable HIV viral load and HIV comorbidity ($p = 0.92$). However, significantly, higher odds of a detectable HIV viral load were associated with being female (OR 3.26; $p = 0.02$) (George et al., 2019). Another study done on HIV virology and associated factors reported that out of 250 study participants, 74 (30%) had baseline VL documented. Of the 74 study participants that had records of baseline VL, the median (range) log₁₀ copies/ml was 4.8 (1.7–6.9). Females were more likely to have virological non-suppression in comparison to males (54.2% vs 32.2%, $p = 0.035$). (Afrane et al., 2021).

Adequate adherence to antiretroviral therapy (ART) is key to the successful treatment of children and adolescents living with HIV. Continuous ART Adherence is the key factor for virology suppression and stability of the immune system and prevents the occurrence of opportunistic infections. Children and adolescents struggle with adherence to ART for various reasons, including a poor psychosocial support system and clinic attendance (Tanyi et al., 2021). A study conducted

in Nigeria on ARTs adherence revealed varied knowledge levels about ART, adherence level, causes of non-adherence. Out of 34 participants involved in the study, 20 (58.8%) were adhering to treatment, even though 22 (64.7%) knew what adherence means and 26 (76.5%) knew that not adhering will affect their immune system which would make their health worse (Aderemi-Williams et al., 2021). Another study on adherence to ARTs reported that the overall rate of adherence to ART was 88.2% (95% CI=85.2 - 91.1) was significantly associated with HIV comorbidities (Molla et al., 2018).

2.2.2 Socio-demographic Risk Factors

The SSA and the world's social and economic inequalities are rooted in the Human Immunodeficiency Virus (HIV). Poor neighborhoods and those with lesser socioeconomic status are disproportionately affected. According to studies on the sociodemographic status and HIV/AIDS, one's status may have an impact on their risk of obtaining HIV, AIDS, or an HIV comorbidity. Additionally, socio-demographic status is a significant factor in determining a person's quality of life after contracting the virus. (Bradley, 2016).

Socio-demographic factors are as important as physical health variables in affecting a person's ability to function normally in their everyday life (Fletcher & Schofield, 2007). There is an interplay of these factors; gender, age, residence, level of education, employment status, profession, marital status, and the prevalence of HIV and its associated comorbidities (Ibrahim et al., 2019). Age and gender are important factors that determine HIV infection and its comorbidities. It is reported that most adolescents are likely to be infected with HIV because they are sexually active and more prone to risky sexual behaviours compared to the older age group (Ibrahim et al., 2019). A study on sociodemographic and HIV comorbidities reported that, out of

402 participants, 42.1% were children and adolescents and 66.3% were females. It further reported that among the children and adolescents, age was ($p=0.01$) significantly associated with non-infectious and chronic HIV comorbidities. In the study, sex ($p=0.08$) was not significantly associated with the comorbidities (Yang et al., 2020). Another study reported that among the study's population of 3,755, those belonging to the age group 25 years and older had almost five times the odds of having an HIV comorbidity compared to those in the under 25 years age group (OR: 4.7, (95% CI: 3.1–7.0)). Females had almost double the odds of having comorbidity compared to males (OR: 1.6, (95% CI: 1.1–2.4)) (Roomaney et al., 2022).

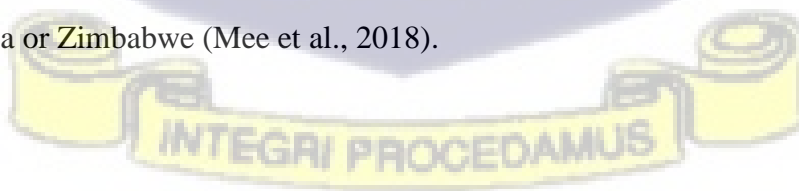
Residence is also a sociodemographic factor, affecting HIV comorbidities. Residents of poor urban settings are more likely to be HIV positive. For example, in 2004, the demographic and health survey in Malawi showed that HIV prevalence was more among females in urban settings. Again, a study among severely malnourished (SAM) children and adolescents at a nutrition center in Malawi showed that HIV prevalence is highest among urban children and adolescents (Ibrahim et al., 2019). A study reported that among of 3,755, those living in urban areas were more likely to have an HIV comorbidity compared to those living in rural areas (cOR: 2.6, (95% CI: 1.8–3.7)) (Roomaney et al., 2022).

It is documented that people living with HIV and are employed are less likely to have comorbidities of the infection. Being financially independent enables one to afford healthy meals and access to health services (Ibrahim et al., 2019). The costs of health associated with HIV comorbidities, for example, tuberculosis (TB), are directly from the user fee charges at the healthcare center and indirectly from the cost of the visit. Money spent on transportation, medication, and medical appointments are all indirect costs associated with the use of healthcare services (Centis, 2018). However, having employment may also allow them to afford a certain standard of living, such as

alcoholism, and promiscuity, that may increase their chances of getting HIV comorbidities (Ibrahim et al., 2019).

Antiretroviral therapy (ART) has shown to be highly successful in reducing mortality in infected children and adolescents in HIC. In middle and low-income countries, the provision of ART is not enough to reduce comorbidities and mortality rate due to the presence of tropical diseases. For example, malnutrition is common in both infected and uninfected children and adolescents in low-income countries; therefore, nutritional support may also be important in the treatment and management of the disease (Kwara et al., 2010.).

Attaining a level of education allows an individual to have clear perspective about life issues including disease prevention. For example, a study in Zimbabwe reported that the prevalence of HIV comorbidities fell steeply among educated people. A hospital-based study in India on socio-demographic factors associated with HIV showed that level educational attainment was associated with HIV comorbidities. Another study in Thailand showed that those with more schooling remain at a lower risk of HIV comorbidities (Ibrahim et al., 2019). Another study conducted in some countries of Africa reported a strong evidence that attaining some level of education was associated with a reduced odds of being HIV positive and getting other comorbidities in Lesotho (aOR: 0.37; 95%CI: 0.17±0.79), Swaziland (aOR: 0.32; 95%CI: 0.17±0.59), and Uganda (aOR: 0.48; 95%CI: 0.29±0.80). No statistically significant evidence for this in Kenya, Malawi, Mozambique, Tanzania, Zambia or Zimbabwe (Mee et al., 2018).



2.2.3 Psychological Risk Factors

A major factor that distinguishes HIV/AIDS from other chronic or terminal illnesses is the stigma.

Too often, many HIV infected children and adolescents, and their families live in a “conspiracy of silence” and shame associated with AIDS. The illness is often kept a secret (Narasimha & Science, 2019). One of the disturbing consequences of “conspiracy silence” is that the families may be withdrawn, become socially isolated and become emotionally cut off from traditional support systems. Parents delay disclosing the children as well as their own HIV/AIDS illness status due to stigma and possible social consequences (Narasimha & Science, 2019).

Children living with HIV/AIDS, especially adolescents, have poorer functional competence, self-concept and motivation and higher levels of depression, disruptive behaviour, attention-deficit hyperactivity disorder symptoms and clinically significant anger, compared to their HIV-negative peers. They face recurrent and cumulative psychosocial stressors that differ from other chronic childhood and adolescent illnesses such as stigma and discrimination, the responsibility for welfare of siblings or other ill family members, illness and the death of their parents and unstable guardianship. This may hamper development of protective mechanisms and leave these children and adolescents psychologically vulnerable and ill equipped for coping with challenges. For example, increasing the risk of development of mental disorders. Mental health disorders affect adherence to ART and are associated with an impaired quality of life, yet they typically receive little attention in the face of physical health concerns (Frigati et al., 2020).



Perinatally acquired HIV occurs in the context of an immature brain with human brain development typically continuing into the third decade of a person's life. Without antiretroviral therapy, around 10% of infected infants present with progressive severe HIV encephalopathy (damage to the brain), which although arrested by ART, leaves residual cognitive and motor deficits with a significant impact on independent mobility and daily living (Services, 2016.)

2.3 Treatment Outcomes of HIV Comorbidities among Children and Adolescents

Antiretroviral therapy (ART) is a critical component of the overall management plan for HIV infection. The primary goal of ART is to suppress viral replication, which ultimately results in restoration of the immune system, reduction in HIV transmission and a general improvement in the quality of life of people infected with HIV (Afrane et al., 2021). The global expansion of access to ART over the past decade has led to substantial declines in HIV comorbidities and mortality, especially in low-income and middle-income countries in which HIV prevalence is highest (Ford et al., 2015.).

Initiatives to increase access to ART for children and adolescents in resource-limited settings, particularly the integration of HIV treatment, and care into existing adult ART centers as well as maternal newborn and child health services, have resulted in a significant increase in the numbers of children and adolescents starting treatment over the last couple of years (Okomo et al., 2012). The effort to implement a “test and treat” strategy in pediatric HIV care began a decade ago (Moreira-Silva et al., 2013). Ghana was one of the first pilot sites to provide therapy and treatment to HIV- infected children and adolescents (Kwara et al., 2010.).

According to Ghana's National AIDS Control Programme (NACP) guidelines, viral load testing is recommended six months after initiating ART and thereafter annually for people who have achieved virological suppression. However, people with HIV viral load (HIV VL) levels > 1000

copies/ml are required to undergo intensified adherence support after which the viral load is repeated 3 months later in order to differentiate poor adherence from treatment failure (Afrane et al., 2021).

The identification and appropriate management of people with the HIV disease is a key component in the response to further reduce HIV-related comorbidities and mortality (Ford et al., 2022). HIV treatment and management are currently in an era of effective anti-retroviral therapy (ART). In the past years, modern drug discovery and development has transformed the disease into a treatable chronic infectious disease. In 2009, 1.2 million people received ART for the first time globally. There was an increase in the number of people receiving treatment by 30 % in a single year. Overall, the number of people being managed and receiving therapy has grown 13-fold (Ayele et al., 2015). However, with the improvement of prognosis for persons living with HIV since the advent of highly active antiretroviral therapy (HAART), these improvements have lagged behind in resource-limited settings (Phillips et al., 2018).

The use of ART has reduced the morbidity and mortality of the disease cases and has altered the pattern of the causes of death in children and adolescents (Sandra F. Moreira-Silva et al., 2013). However, treatment and management of HIV may fail. The failure can be clinical, immunologic, viral, or any combination of the three. Following treatment failure, therapy aims to attain and continue viral suppression as measured by a plasma viral load below the detection limits using the most sensitive assay (Shiferaw et al., 2019). Although programs for the prevention of mother-to-child transmission of HIV are being scaled up at all levels of care, the need to improve HIV/AIDS care, treatment, and counseling for infected children remains critically important. Challenges to optimal care and treatment in SSA include limited resources, staff, and laboratory support. The human professional capacity for delivering HIV/ AIDS care is constrained across much of SSA,

where per capita numbers of physicians and nurses are only 1% to 2% of those of the United States (Kwara et al., 2010.)

According to the World Health Organization (WHO)'s recommendations, any HIV-infected child below two years of age should be treated with antiretroviral therapy (ART) as soon they test positive, even when no symptoms are present and irrespective of viral load detection. Children and adolescents infected with the disease present clinical signs in the first year of life. In most cases of these children and adolescents, without effective treatment they die even before completing the year (Sandra Fagundes Moreira-Silva et al., 2015).

A study reported 3,340 patient admissions recorded in medical wards in 2020. Among, 390 patients 11.7% had died and 302 (9.0%) were discharged before being seen by the HIV counselor, due to admission during weekends. The total number of admissions in medical wards was almost twice as high in 2017 compared with 2020. Forty-four (22.0%) of the patients were children and adolescents below 20 years (Heller et al., 2022).

Children and adolescents living with HIV on admission are at a higher risk of death. The risk might persist after being discharge from the hospital. For example, a systematic review of post-discharge mortality among general paediatric admissions in low-income settings found that post-discharge mortality rates often exceeded in-patients mortality rates (Ford et al., 2022). HIV comorbidities, particularly tuberculosis and bacterial infections such as particularly pneumonia and bacteremia continue to be leading causes of hospital admission and in-patient mortality in children and adolescents living with HIV globally (Ford et al., 2015.). Malnutrition, wasting, and hematological disorders are other illnesses-causing children's hospitalization. Majority of admissions among children and adolescents are for pneumonia, gastroenteritis, pulmonary TB, malnutrition, and malaria (Kwara et al., 2010.). Risk factors for readmission among children and adolescents

included discharge against medical advice not being on ART, having an AIDS- defining illness, high viral load, and no support for linkage to care (Ford et al., 2022).

It is reported that mortality is associated with a high viral loads and lower CD4 counts whereas initiation of ART in hospital was associated with decreased mortality (Ford et al., 2022). However, suboptimal retention on combined antiretroviral therapy (cART) in routine programs threatens good survival outcomes and even on treatment, children and adolescents continue to experience high comorbidity risk; infections remain the major cause of death (Davies et al., 2016).

In 2015, global estimates showed that up to 30% of HIV-infected child and adolescent deaths may be tuberculosis-related. HIV-infected children and adolescents are more than twice as likely to die from tuberculosis compared to HIV-uninfected children and adolescents; within pediatric HIV cohorts tuberculosis increases mortality risk 2–4 times. Treatment outcomes for children with drug resistant tuberculosis (DR-TB) vary widely. A South African study of DR-TB (55% of children HIV-infected) found 20% overall mortality, while a systematic review found mortality was twice as high in HIV-infected compared to uninfected children (11.5% vs. 6%) (Davies et al., 2016).

In the report of a study on treatment outcomes in West Africa, one out of 65 children and adolescents, less than 15 years was transferred to another ART center for continued care and 8 (12.3%) were lost to follow-up of whom one was withdrawn from the programme to seek alternative (herbal) treatment. Six (9.2%) HIV-infected children and adolescents died during hospitalization. Children and adolescents who died had significantly higher viral loads at baseline than those who survived (3.5% vs. 13% respectively; $P = 0.004$) (Okomo et al., 2012). A study in Ghana also reported that out of 102 admissions among 76 children, age ($p= 0.938$), gender ($p=0.841$) and ART adherence ($p= 0.685$) were not significantly associated with treatment outcomes (Kwara et al., 2010.)

For a class of disease such as malignancies, occurrence is five to ten times more common in HIV-infected children and adolescents compared to those uninfected. In the combination Antiretroviral Therapy (cART) era, HIV/AIDS-defining cancers (ADCs) have reduced dramatically. Treatment outcomes are worse in HIV-infected children and adolescents. In South Africa less than 80% of children and adolescents with the disease with cancer presented with advanced disease, only a third survived. Survival was higher (57.8%) after treatment with cART and chemotherapy. In Uganda, half of HIV-infected children and adolescents with cancer died. Mortality was at least three-fold higher than the clinic crude mortality rate (33% vs 5–10%) (Davies et al., 2016).

There is a relation of HIV comorbidities and their treatment outcomes. For example, a study on HIV comorbidities among children and adolescents in Victoria, Brazil, reported on nineteen (19) comorbidities. Out of these, twelve comorbidities were significantly associated with treatment outcome; anemia ($p=0.001$), dermatosis ($p=0.04$), diarrhoea and gastroenteritis ($p=0.000$), hepatitis ($p=0.020$), thrombocytopenia ($p=0.015$), septicemia ($p=0.000$), tuberculosis ($p=0.001$), encephalopathy ($p=0.000$), severe bacterial infection ($p=0.000$), PJP ($p=0.000$), candidiasis ($p=0.000$) and cytomegalovirus (0.046) (Sandra F. Moreira-Silva et al., 2013).

2.4 Chapter Summary

The chapter reviewed literature relevant to the study. The sections of the chapter elaborated on the literature on prevalence of HIV and age distribution among children and adolescents, clinical, socio-demographic, and psychological risk factors associated with HIV comorbidities and treatment outcomes of HIV comorbidities. From the reviews, HIV comorbidities in children may differ from those in adolescents. In addition, the use of ART has reduced the morbidities and co-infections. Mortality rate of the disease cases and has altered the pattern of the causes of death in children and adolescents.

CHAPTER THREE

METHODS

3.0 Introduction

This chapter presents methods that were employed in the gathering of data for the study. It comprises sections addressing the study design, study location, study population, study variables, sample size determination, sampling procedure, data analysis, and ethical consideration. A summary of the chapter is provided at the end of these sections.

3.1 Study Design

A hospital-based retrospective cross-sectional study was carried out. The study used a clinical record review to obtain retrospective data. Clinical records of children and adolescents infected with HIV and registered at the hospital from January 2018 to January 2021 were assessed. A specially designed tool was used to extract the data from the clinical records. The prevalence of HIV comorbidities was determined along with factors associated with the presence of the comorbidities.

3.2 Study Location

The study was conducted at the Eastern Regional Hospital, Koforidua. The Eastern region has consistently had the highest HIV prevalence in the country. The Regional Hospital serves as a referral center for the Eastern Region. The Eastern Regional Hospital was established in 1926 in the regional capital city, Koforidua. The 356-bed capacity hospital is currently the region's second-level referral facility, serving as a central referral point for about eighteen district hospitals. It is also the Municipal Hospital for the New Juaben Municipality. The hospital offers these services: Internal Medicine including Anti-Retroviral Therapy, Paediatric, Surgery, Medicine, Dental,

Ophthalmology, Physiotherapy, Ear, Nose and Throat, Pharmacy, Laboratory, X-ray, Ultrasound, Catering and Hospitality, Laundry, Mortuary, and Primary Healthcare Services. It is a Ghana Health Service facility, a not-for-profit healthcare organization.

3.3 Study Population

The study's target populations were children and adolescent patients between the ages of 0 and 19 years reporting to the Eastern Regional Hospital, Koforidua.

3.3.1 Inclusion criteria

Children and adolescent patients from 0 to 19 years old, who had been tested, diagnosed with HIV, and registered at the hospital from January 2018 to January 2021, who consented to participate in the study.

3.3.2 Exclusion criteria

Patients diagnosed with HIV, aged 20 years and above registered at the hospital, and those between 0 to 19 years who did not consent to participate in the study.

3.4 Study Variables

3.4.1 Outcome variable

- HIV comorbidities among children and adolescents
- Treatment outcomes of patients with HIV comorbidities

3.4.2 Exposure variables

- Clinical factors: viral load detection, viral load counts, adherence to ARTs
- Socio-demographic factors: Age, Sex, Residence, Educational status of child/ adolescent, Level of education of parent or guardian

3.5 Sample Size Determination and Sampling Procedure

For this study, no actual sample size was calculated. Clinical records of the total population of children and adolescents with HIV/AIDS registered at the hospital were extracted for the period January 2018 to January 2021.

3.6 Data Collection

Data were collected using a specially designed tool. The tool was composed of five (5) sections. The first section of the form had the patient's details. These included the patient's initials, folder number, age, sex, residence, and date of registration at the hospital. The second section had details of the parent or guardian. This captured the level of education of the parents or guardians. Data obtained from the records were gathered from folders and the hospital's database, Hospital Administration Management System (HAMS), and Lightwave Hospital Information Management System (LHIMS).

3.7 Data Analysis

Data were entered and cleaned using Microsoft Excel plus 2016 and imported into STATA version 16 software for analysis. Descriptive statistics were used to describe the socio-demographic characteristics of the study population expressing the results in percentages. Descriptive statistics were also used to describe the profile of HIV comorbidities experienced by the study population during the specified period. Categorical variables were summarized in the form of frequencies and proportions. Bivariate analyses between socio-demographic factors, clinical factors and treatment outcomes of HIV comorbidities were compared using chi-square. Logistic regression was used to determine the socio-demographic and clinical factors associated with the presence of HIV comorbidities as well as the treatment outcomes. Odds ratios, P-values and confidence intervals

were reported. Statistical significance was determined at a p-value of less or equal to 0.05 (p-value ≤ 0.05).

3.8 Ethical Considerations

Ethical approval with a protocol ID number GHS-ERC: 023/10/21 was obtained from the Ghana Health Service Ethics Review Committee (GHS-ERC) in conformity with ethical considerations. The approval letter from the GHS-ERC and an introductory letter from the Department of Population, Family and Reproductive Health, School of Public Health, University of Ghana, were sent to the Medical Director of the Eastern Regional Hospital, Koforidua for permission to start data collection and cleaning. For anonymity and confidentiality of patient information, patients' names were replaced with identification numbers.

3.9 Chapter Summary

This was a clinical record review retrospective study. The study was conducted at the Eastern Regional Hospital, Koforidua. The Eastern region has consistently had the highest HIV prevalence in the country. The Regional Hospital serves as a referral center for Eastern Region. One thousand, four hundred and thirty-seven (1,473) HIV-infected children and adolescents who had been registered with the hospital were used as the study's population.

Data from the clinical records extracted was done using a specially designed tool. Data analysis was done using STATA version 16. Descriptive analysis was conducted. Categorical variables were summarized in the form of frequencies and proportions. Bivariate analyses and multivariable logistic regression were used to determine the clinical and socio-demographic factors associated

with HIV comorbidities as well as the treatment outcomes. Odds ratios, P-values and confidence intervals were reported.



CHAPTER FOUR

RESULTS

4.0 Introduction

This presents the results of statistical analysis of data gathered from clinical records or folders of patients and the database system. The chapter is structured into three sections; the prevalence of HIV comorbidities among children and adolescents, clinical and socio-demographic risk factors associated with HIV comorbidities, and treatment outcomes of these comorbidities. The prevalence of HIV comorbidities covers the presence of and the number of comorbidities among the study population.

4.1 Demographic Characteristics of Study Population

This study reviewed one thousand four hundred and thirty-seven (1,437) patient records. Four hundred and eighty-one (33.5%) of the study population were below 5 years of age. Two hundred and twenty-five (15.7%) patients were aged 5 – 9 years; 400 (27.8%) were aged 10 – 14 years; and 319 (22.2%) patients were aged 15 – 19 years. More than half of the patients (816, 56.9%) were female and 572 (39.8%) were males (Table 1).

Regarding the educational status of the study population, 470 (32.7%) had no formal education, 435 (31.7%) were in primary school, and 500 (34.8%) were in secondary school. For the level of education of the parents or guardians of participants, 199 (13.9%) had no formal education, 432 (28.0%) attained primary education, with secondary and tertiary education being 499 (34.7%) and 216 (15.0%) respectively. Six hundred and ninety-three (48.2) of the study population lived in urban areas and 734 (51.1%) lived in rural areas of the Eastern region.

More than half of the study population (782, 54.4%) had their viral loads undetected. Four hundred and fifty-three (31.5%) children and adolescents had their viral loads detected. Viral load results

of 202 (14.1%) were not recorded. Three hundred and forty-eight (24.2%) participants had viral load counts below 100 copies/mls, 62 (4.3%) had viral loads from 101 - 500 copies /mls, 31 (2.2%) had viral load counts from 501 - 1000 copies /mls, and 8 (0.6%) had viral loads above 1000 copies/mls. (Figure 2).

Six hundred and two (41.9%) of the study population adhered to anti-retroviral therapy (ARTs) and 450 (31.3%) were non-adherents. About 33.0% (474/1,437) of the study population had HIV comorbidities.



Table 1. Socio-demographic and Clinical Characteristics of Study Population (N=1,437)

Variable	n	%
Socio-demographic Characteristics		
Age (Years)		
<5	481	33.5
5 - 9	225	15.7
10 - 14	400	27.8
15 - 19	319	22.2
Missing values	12	0.8
Sex		
Male	572	39.8
Female	819	57.0
Missing values	46	3.2
Educational Status		
No formal education	470	32.7
Primary	455	31.7
Secondary	500	34.8
Missing values	12	0.8
Educational level (Parent/ Guardian)		
No formal education	199	13.9
Primary	402	28.0
Secondary	499	34.7
Tertiary	216	15.0
Missing values	121	8.4
Residence		
Urban	693	48.2
Rural	734	51.1
Missing values	10	0.7
Clinical Characteristics		
Viral load detection		
Detected	449	31.3
Not detected	782	54.4
Missing values	206	14.3
Viral load counts		
< 100	348	24.2
101 - 500	62	4.3
501 - 1000	31	2.2
>1000	8	0.6
Missing values	988	68.7
Adherence to ARTs		
Adherent	602	41.9
Non- adherent	450	31.3
Missing values	385	26.8
Presence of comorbidities		
Present	474	33.0
Absent	963	67.0

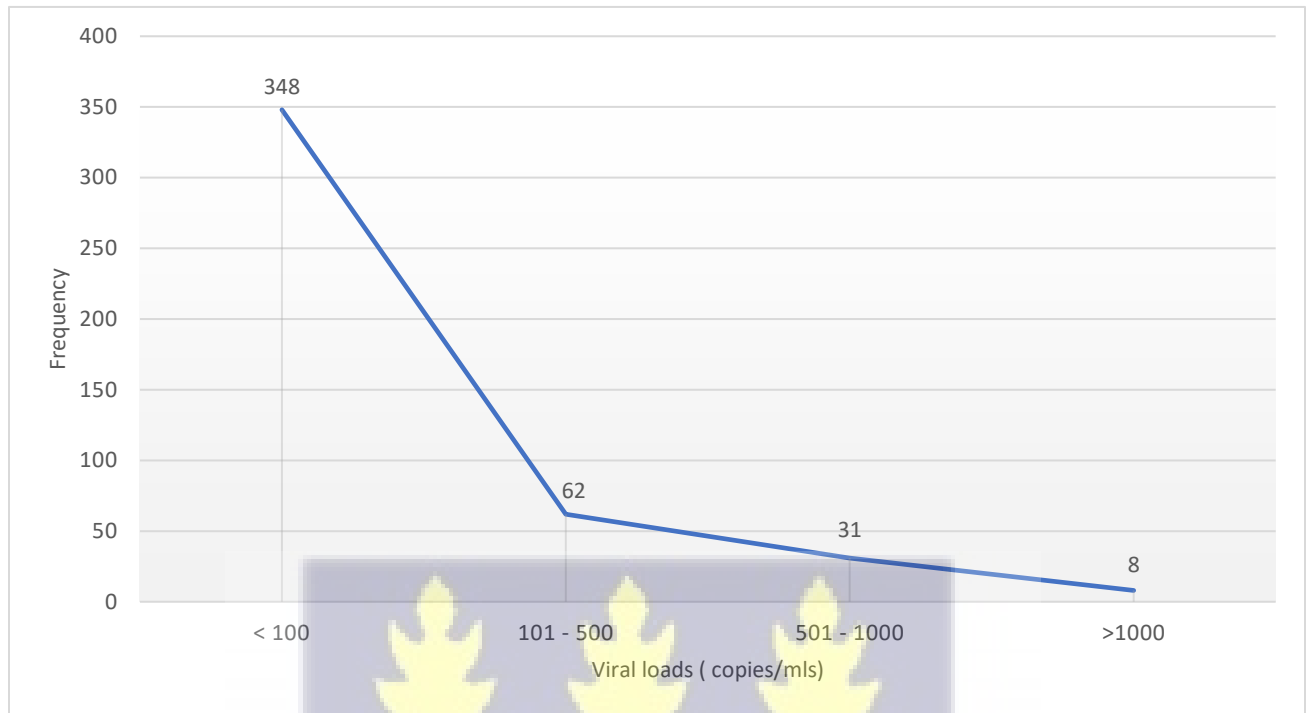


Figure 2. Frequencies of Viral load counts of Children and Adolescents

4.2 Prevalence of HIV Comorbidities among Children and Adolescents

4.2.1 HIV Comorbidities among Children and Adolescents

Forty-eight comorbidities were recorded among 474 children and adolescents of 1,437-study population. Figure 2 shows the comorbidities recorded and their frequencies. Bronchopneumonia was the comorbidity with the highest frequency of 106. Comorbidities were grouped into 12 classifications using the International Classification of Disease (ICD) version 11. Figure 3 shows the frequencies of the comorbidities by ICD 11 classifications. Respiratory diseases had the highest frequency of 202.

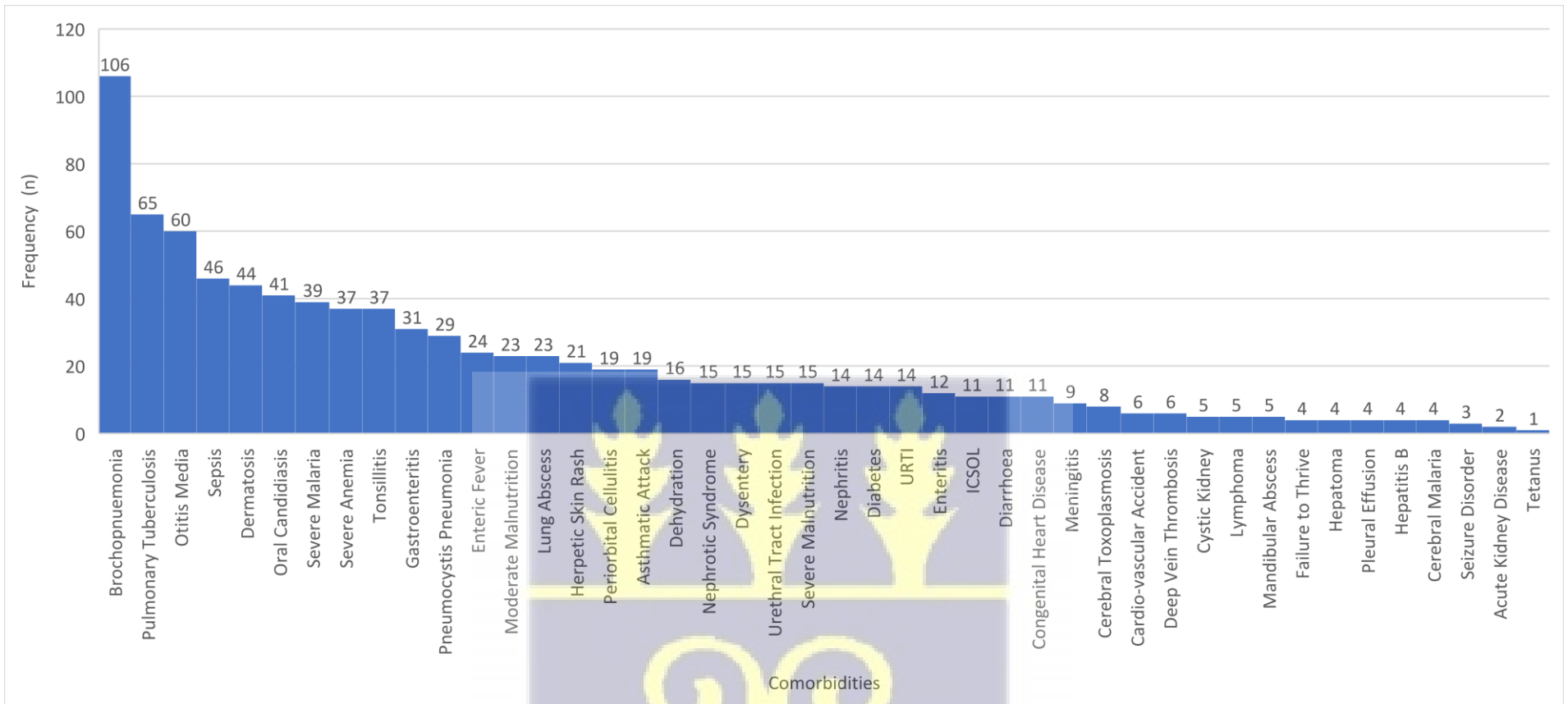
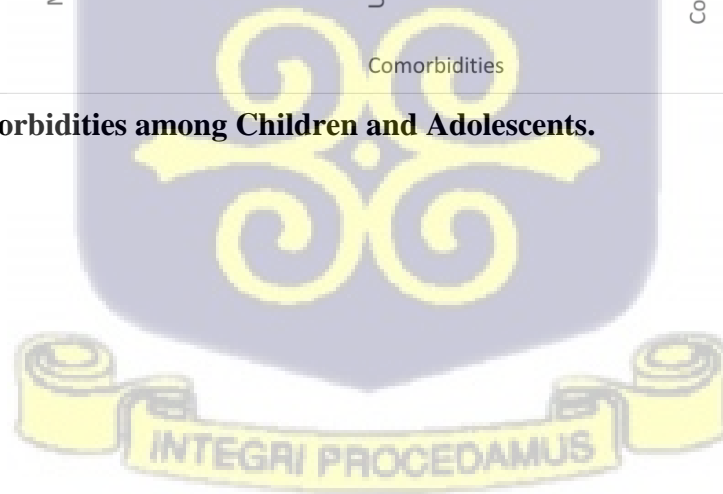


Figure 3. Frequencies of HIV Comorbidities among Children and Adolescents.



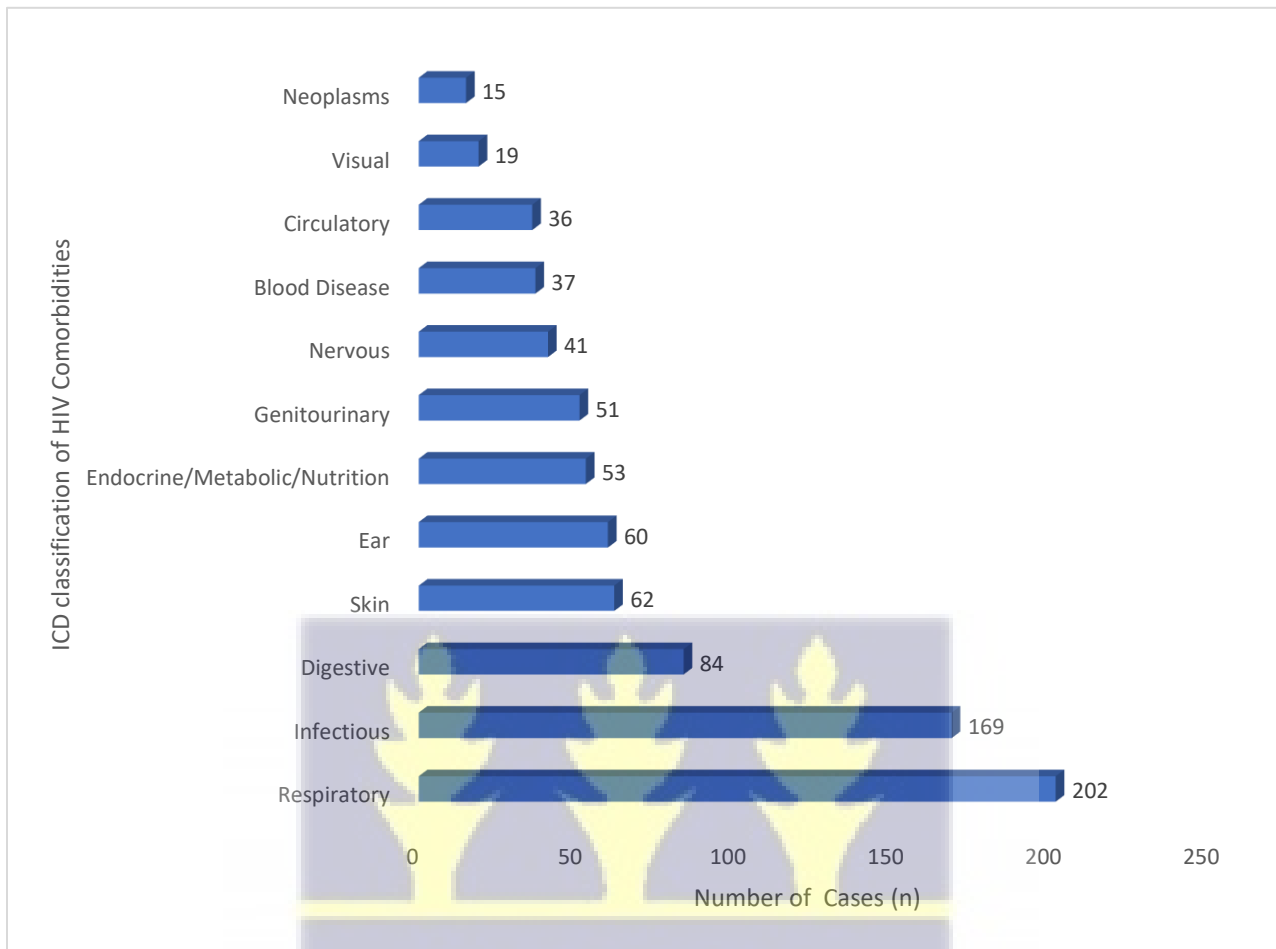


Figure 4. Frequencies of HIV Comorbidities among Children and Adolescents using ICD 11 Classification.



4.2.2 Prevalence of HIV Comorbidities

Prevalence of the HIV comorbidities recorded in the study was calculated using the formula below.

$$\text{Prevalence} = \frac{\text{Number of cases with HIV comorbidities}}{\text{Total Number of individuals in the study}} \times 100\%$$

Number of cases with HIV comorbidities (n) = 474

Total Number of individuals in the study (N) = 1,437

Prevalence of HIV comorbidities = 33.0%

Respiratory diseases including bronchopneumonia, pleural effusion, airway obstruction, pulmonary tuberculosis, pneumocystis pneumonia, lung abscess, asthmatic attack, and upper respiratory tract infection had the highest prevalence of 14.1%, followed by infectious diseases at 11.8%. The infectious diseases reported included sepsis, oral candidiasis, tonsillitis, dysentery, hepatitis B, and tetanus. Neoplasms, including Kaposi sarcoma, lymphoma, and Hepatoma, recorded the lowest prevalence of 1.0%.

The study recorded a prevalence of 5.3% for digestive diseases, which included mandibular abscess, diarrhoea, gastroenteritis, enteritis, and enteric fever. Prevalence of 3.5% and 2.9% were recorded for genitourinary diseases and neurological diseases respectively. Neurological diseases reported included meningitis, cerebral toxoplasmosis, Cerebro-vascular accident, cerebral malaria, failure to thrive, seizure, and intra-cranial space occupying lesion. Anemia was the only comorbidity recorded under blood diseases, with a prevalence of 2.6%. Circulatory diseases including deep vein thrombosis, congenital heart disease recorded a prevalence of 2.5%. Prevalence of 4.2% and 1.3% were recorded for ear diseases and visual diseases respectively.

Table 2. Prevalence of HIV Comorbidities among Children and Adolescents

HIV Comorbidities by ICD Classifications	n	Prevalence (%)
Respiratory Diseases Bronchopneumonia, Pleural Effusion, Airway Obstruction, Pulmonary Tuberculosis, Pneumocystis Pneumonia, Lung Abscess, Asthmatic Attack, Upper Respiratory Tract Infection	202	14.1
Infectious Diseases Sepsis, Oral Candidiasis, Tonsillitis, Dysentery, Hepatitis B, Tetanus	169	11.8
Digestive Diseases Mandibular Abscess, Diarrhoea, Gastroenteritis, Enteritis, Enteric Fever	84	5.8
Skin Diseases Dermatosis, Herpetic Skin Rash	62	4.3
Ear Diseases Otitis Media	60	4.2
Endocrine/ Metabolic/ Nutritional Diseases Severe Malnutrition, Moderate Malnutrition, Dehydration	53	3.7
Genitourinary Diseases Nephrotic Syndrome, Acute Kidney Disease, Nephritis, Cystic Kidney, Urethral Tract Infection	51	3.5
Neurological Diseases Meningitis, Cerebral Toxoplasmosis, Cerebro-vascular Accident, Cerebral Malaria, Failure to Thrive, Seizure, Intra-cranial Space Occupying Lesion	41	2.9
Blood Diseases Severe Anemia	37	2.6
Circulatory Deep Vein Thrombosis, Congenital Heart Disease	36	2.5
Visual Diseases Periorbital Cellulitis	19	1.3
Neoplasms Kaposi sarcoma, Lymphoma, Hepatoma	15	1.0

4.3 Socio-demographic and clinical Factors associated with HIV Comorbidities

4.3.1 Association between Socio-demographic and Clinical Factors and HIV Comorbidities

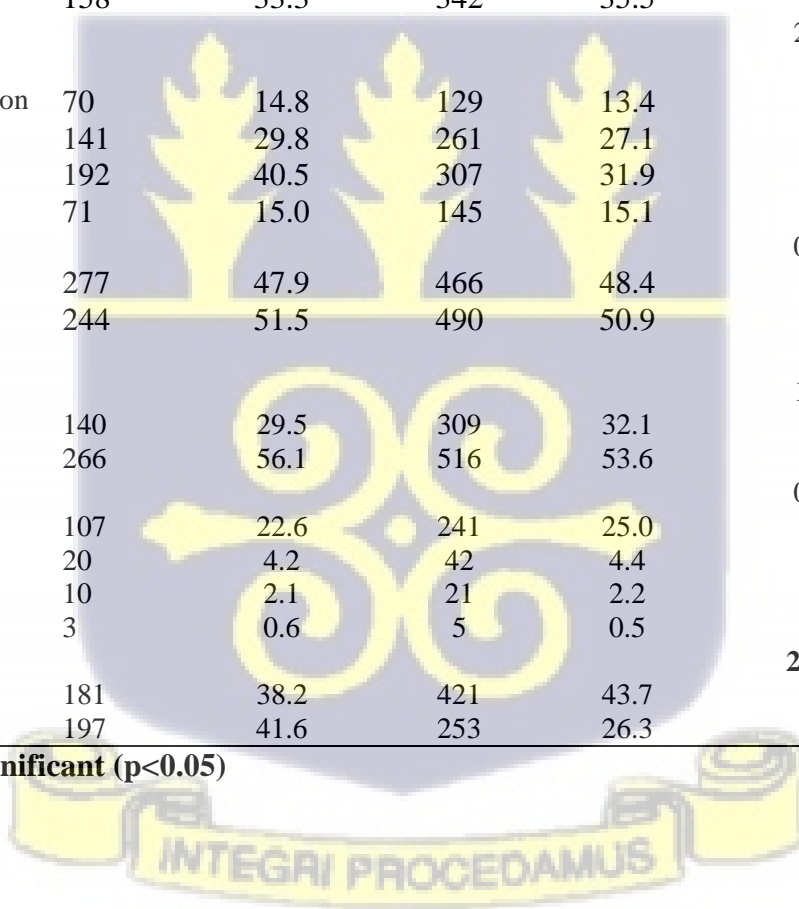
Table 4 shows a bivariate analysis of the association between socio-demographic and clinical risk factors and HIV comorbidities. Results showed that age ($p=0.014$), educational status ($p=0.005$) and adherence to ARTs ($p=0.000$) were significantly associated with HIV comorbidities. However, sex ($p=0.063$), level of education of parents or guardians ($p=0.484$), residence ($p=0.845$), viral load detection ($p=0.308$) and viral loads counts ($p=0.973$) were not significantly associated with HIV comorbidities.



Table 3. Association between Socio-demographic and Clinical Factors and HIV Comorbidities

Variable	Patients with comorbidities		Patients without comorbidities		Chi-square	p-value
	n = 474	%	n = 963	%		
Sociodemographic factors						
Age (Years)					12.5227	0.014
<5	144	30.4	337	35.0		
5 - 9	90	19.0	135	14.0		
10 - 14	93	19.6	226	23.5		
15 - 19	145	30.6	255	26.5		
Sex					5.5152	0.063
Male	279	58.9	540	56.0		
Female	187	39.5	385	40.0		
Educational Status					10.7321	0.005
No formal education	137	29.0	333	34.6		
Primary	177	37.3	278	28.9		
Secondary	158	33.3	342	35.5		
Educational level (Parent/ Guardian)					2.4544	0.484
No formal education	70	14.8	129	13.4		
Primary	141	29.8	261	27.1		
Secondary	192	40.5	307	31.9		
Tertiary	71	15.0	145	15.1		
Residence					0.0381	0.845
Urban	277	47.9	466	48.4		
Rural	244	51.5	490	50.9		
Clinical Factors						
Viral load detection					1.0371	0.308
Detected	140	29.5	309	32.1		
Not detected	266	56.1	516	53.6		
Viral load counts					0.2297	0.973
< 100	107	22.6	241	25.0		
101 - 500	20	4.2	42	4.4		
501 - 1000	10	2.1	21	2.2		
>1000	3	0.6	5	0.5		
Adherence to ARTs					21.0297	0.000
Adherent	181	38.2	421	43.7		
Non- adherent	197	41.6	253	26.3		

***statistically significant (p<0.05)**



4.3.2 Logistic Regression of Socio-demographic and Clinical Risk Factors associated with HIV Comorbidities

Table 5 shows the socio-demographic and clinical risk factors associated with HIV comorbidities using multiple logistic regression. At a 95% confidence interval, children aged 5 - 9 years old are 30% (OR = 0.70; 95% CI: 0.52 - 0.93) less likely to have a comorbidity than children under 5 years old and this was statistically significant ($p = 0.017$). After adjusting for all other factors, at 95% CI, children aged 5 - 9 ($p = 0.008$) and 15 - 19 ($p = 0.047$) years old are 36% (OR = 0.64 95% CI; 0.40 - 0.89) and 25% (OR = 0.75 95% CI; 0.56 - 0.99) less likely to have a comorbidity. These were statistically significant.

The odds of having HIV comorbidity was 32% (cOR = 0.68; 95% CI = 0.54 - 0.86; $p = 0.002$) less among children and adolescents who were in primary school than those who had no formal education. After adjusting for all risk factors, at 95% confidence interval, children and adolescents in primary school were 28% (aOR = 0.72 95% CI; 0.55 - 0.94) less likely to have a comorbidity than children and adolescents with no formal education and this was statistically significant ($p = 0.018$).

The odds of having a comorbidity was 45% (cOR = 0.55; 95% CI = 0.42 - 0.71; $p = 0.000$) less among children and adolescents who were non-adherent to ARTs than those who were adherent to ARTs and this was statistically significant ($p = 0.000$). After adjusting for all other factors, at 95% confidence interval, children and adolescents who were not adherent to ARTs were 45% (aOR = 0.55; 95% CI = 0.42 - 0.71; $p = 0.000$) less among children and adolescents who were non-adherent to ARTs than those who were adherent to ARTs and this was statistically significant ($p = 0.000$).

Table 4. Logistic Regression of Socio-demographic and Clinical Risk Factors associated with HIV Comorbidities

Variable	Unadjusted		Adjusted	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value
Socio-demographic factors				
Age (Years)				
<5 (Ref.)	1.00		1.00	
5 - 9	0.70 (0.52 - 0.93)	0.017*	0.64 (0.40 - 0.89)	0.008*
10 - 14	1.26 (0.96 - 1.66)	0.088	1.03 (0.56 - 1.41)	0.812
15 - 19	0.82 (0.64 - 1.04)	0.117	0.75 (0.56 - 0.99)	0.047*
Sex				
Male	1.06 (0.84 - 1.33)	0.593	0.94 (0.74 - 1.17)	0.593
Female (Ref.)	1.00		1.00	
Educational Status				
No formal education (Ref.)	1.00		1.00	
Primary	0.68 (0.54 - 0.86)	0.002*	0.72 (0.55 - 0.94)	0.018*
Secondary	1.11 (0.88 - 1.40)	0.369	1.12 (0.85 - 1.47)	0.407
Educational level (Parent/ Guardian)				
No formal education (Ref.)	1.00		1.00	
Primary	1.06 (0.83 - 1.35)	0.636	0.90 (0.63 - 1.28)	0.582
Secondary	0.84 (0.66 - 1.06)	0.147	0.78 (0.55 - 1.09)	0.154
Tertiary	1.18 (0.86 - 1.60)	0.292	0.90 (0.60 - 1.35)	0.620
Residence				
Urban	1.02 (0.81 - 1.27)	0.845	1.02 (0.81 - 1.27)	0.845
Rural (Ref.)	1.00		1.00	
Clinical factors				
Viral load detection				
Detected	1.13 (0.88 - 1.45)	0.309	1.13 (0.88 - 1.45)	0.309
Not detected (Ref.)	1.00		1.00	
Viral load counts				
< 100 (Ref.)	1.00		1.00	
101 - 500	0.94 (0.53 - 1.67)	0.844	1.26 (0.27 - 5.80)	0.767
501 - 1000	0.94 (0.43 - 2.06)	0.893	1.26 (0.25 - 6.35)	0.779
>1000	0.75 (0.17 - 3.18)	0.698	1.35 (0.31 - 5.75)	0.684
Adherence to ARTs				
Adherent (Ref.)	1.00		1.00	
Non- adherent	0.55 (0.42 - 0.71)	0.000*	0.55 (0.42 - 0.71)	0.000*

*statistically significant (p<0.05)

4.3.3 Number of Comorbidities, Admission Status, and Number of Days on Admission among Study Population with HIV Comorbidities

Out of the 474 individuals with HIV comorbidities, 142 (29.9%), 169 (35.7%), 139 (29.3%), 18 (3.8%), 5 (1.1%) and 1 (0.2%) had 1, 2, 3, 4, 5 and comorbidities respectively. Three hundred and sixty-six (77.2%) were admitted and 108 (22.8%) were seen as Outpatient Department (OPD) cases. Fifty (10.6%) of the study population spent from 1 - 5 days on admission. One hundred and fifty-two (32.1%) spent 6-10 days on admission. Eighty-nine (18.8%) spent 11 - 15 days on admission. Forty-four (9.3%) spent 16 - 20 days on admission. Twenty-six (5.4%) and five (1.0%) spent 21 - 25 and 26 - 30 d days on admission respectively.

Table 5. Number of Comorbidities, Admission Status, and Number of Days on Admission among Study Population with HIV Comorbidities

Variable	n=474	%
Number of comorbidities		
1	142	29.9
2	169	35.7
3	139	29.3
4	18	3.8
5	5	1.1
6	1	0.2
Admission status		
Admitted	366	77.2
OPD cases	108	22.8
Number of days on admission		
1 - 5	50	10.6
6 - 10	152	32.1
11 - 15	89	18.8
16 - 20	44	9.3
21 - 25	26	5.4
26 - 30	5	1.0
OPD cases	108	22.8

4.4 Treatment Outcomes of HIV Comorbidities among Children and Adolescents

Out of the 474 patients with HIV co-morbidities, 421 (88.8%) were discharged after treatment or referred to Teaching Hospitals for further management. Fifty-three (11.2%) died while on admission.

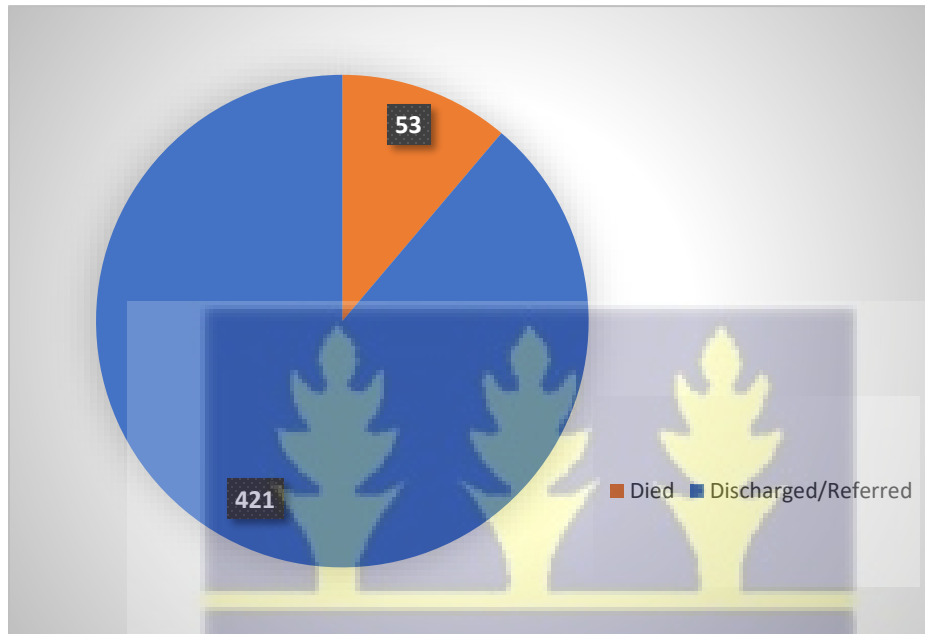


Figure 5. Treatment Outcomes of HIV Comorbidities among Children and Adolescents

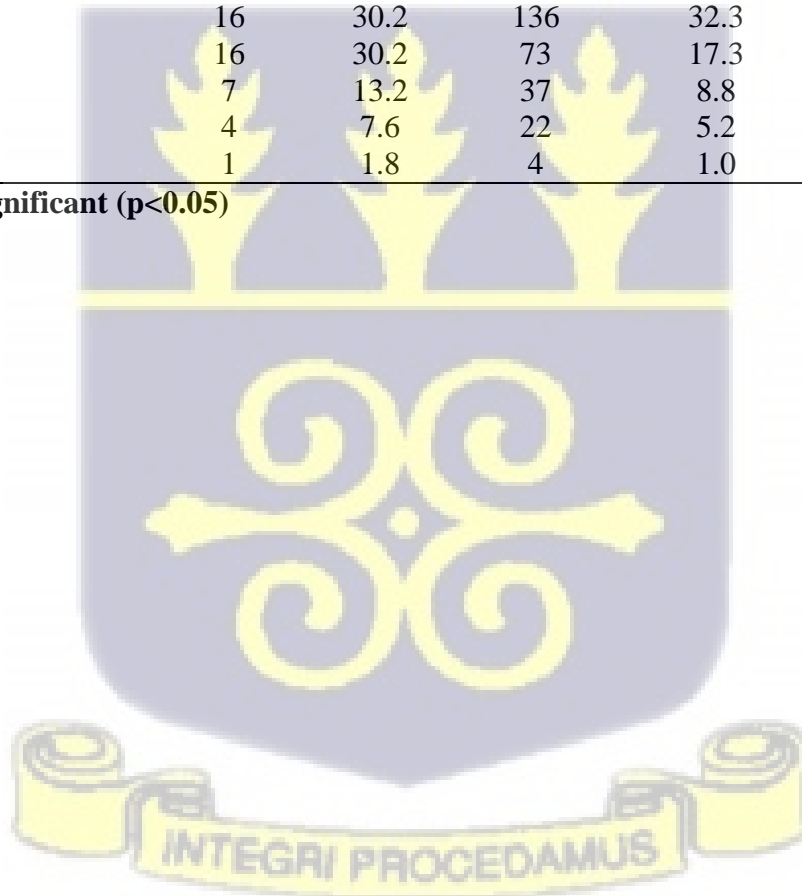
4.4.1 Association between Numbers of Comorbidities, Hospital Admission, Number of Days on Admission and Treatment Outcomes

Table 7 below presents a bivariate analysis showing the relationships between numbers of comorbidities experienced, admission status, number of days on admission, and treatment outcomes. The results show that hospital admission ($p=0.000$) was significantly associated with treatment outcomes of HIV comorbidities. However, number of comorbidities ($p=0.179$) and number of days on admission ($p=0.622$) were not significantly associated with treatment outcomes of HIV comorbidities.

Table 6. Association between Number of Comorbidities, Hospital Admission, Number of Days on Admission and Treatment Outcomes

Variable	Treatment Outcomes				Chi-square	p-value
	Died		Discharged/ Referred			
	n=53	%	n=421	%		
Number of comorbidities					7.6178	0.179
1	10	18.9	132	31.4		
2	18	33.9	151	35.9		
3	23	43.4	116	27.6		
4	1	1.9	17	4.0		
5	1	1.9	4	0.9		
6	0	0.0	1	0.2		
Hospital admission					17.6082	0.000*
Admitted	53	100.0	313	74.3		
OPD cases	0	0.0	108	25.7		
Number of days on admission					3.5108	0.622
1 - 5	9	17.0	41	9.7		
6 - 10	16	30.2	136	32.3		
11 - 15	16	30.2	73	17.3		
16 - 20	7	13.2	37	8.8		
21 - 25	4	7.6	22	5.2		
26 - 30	1	1.8	4	1.0		

*statistically significant (p<0.05)



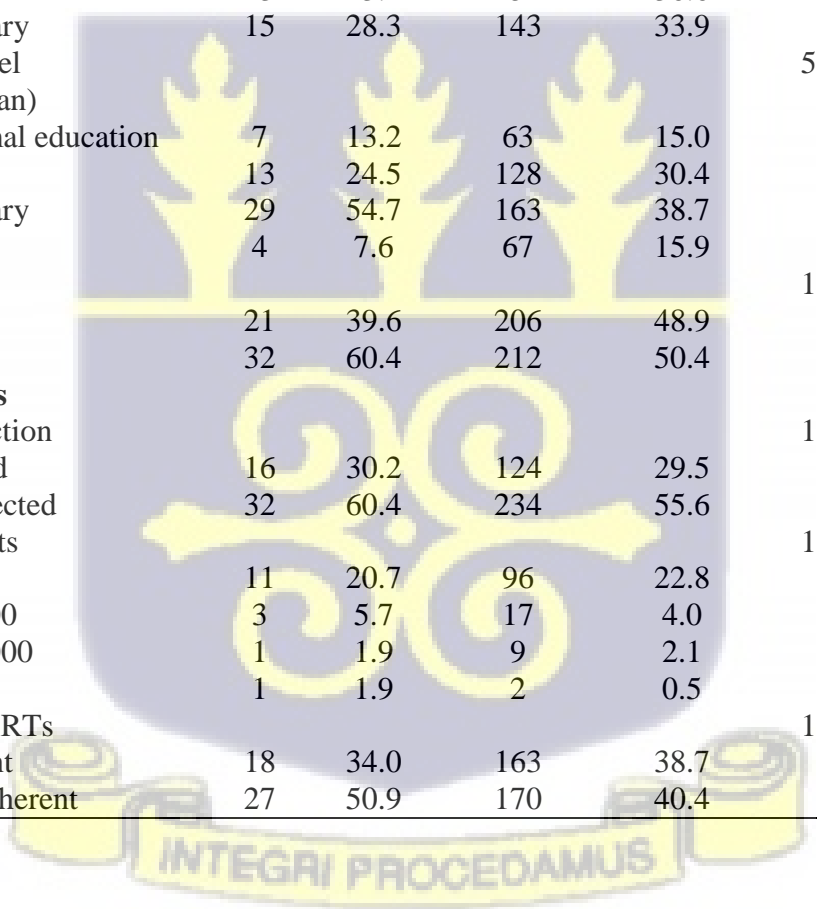
4.4.2 Association between Socio-demographic and Clinical Risk Factors and Treatment Outcomes

Table 8 shows a bivariate analysis between socio-demographic and clinical factors and treatment outcomes of HIV comorbidities. Results showed no statistically significant association between socio-demographic; age ($p=0.079$), sex ($p=0.347$), educational status ($p=0.594$), level of education of parents or guardians ($p=0.121$), residence ($p=0.185$) and clinical factors; viral load detection ($p=0.608$), viral load counts ($p=0.608$), adherence to ARTs ($p=0.259$) and treatment outcomes.



Table 7. Association between Socio-demographic and Clinical Factors and Treatment Outcomes

Variable	Treatment Outcomes				Chi-square	p-value
	Died		Discharged/ Referred			
	n=53	%	n=421	%		
Socio-demographic factors						
Age (Years)					6.7893	0.079
<5	17	32.0	127	30.2		
5 - 9	10	18.9	80	19.0		
10 - 14	22	41.5	89	21.1		
15 - 19	4	7.6	123	29.2		
Sex					0.8844	0.347
Male	24	45.3	163	38.7		
Female	28	52.8	251	59.6		
Educational Status					1.0415	0.594
No formal education	15	28.3	122	29.0		
Primary	23	43.4	154	36.6		
Secondary	15	28.3	143	33.9		
Educational level (Parent/ Guardian)					5.8199	0.121
No formal education	7	13.2	63	15.0		
Primary	13	24.5	128	30.4		
Secondary	29	54.7	163	38.7		
Tertiary	4	7.6	67	15.9		
Residence					1.7578	0.185
Urban	21	39.6	206	48.9		
Rural	32	60.4	212	50.4		
Clinical factors						
Viral load detection					1.8336	0.608
Detected	16	30.2	124	29.5		
Not detected	32	60.4	234	55.6		
Viral load counts					1.8336	0.608
< 100	11	20.7	96	22.8		
101 - 500	3	5.7	17	4.0		
501 - 1000	1	1.9	9	2.1		
>1000	1	1.9	2	0.5		
Adherence to ARTs					1.2722	0.259
Adherent	18	34.0	163	38.7		
Non- adherent	27	50.9	170	40.4		



4.4.3. Logistic Regression of Socio-demographic and Clinical Risk Factors associated with Treatment Outcomes

Table 10 shows the socio-demographic and clinical risk factors associated with treatment outcomes using multiple logistic regression. Children and adolescents aged 10 - 14 ($p=0.029$) years old are 47% ($cOR = 0.53$; 95% $CI= 0.30 - 0.93$) less likely to die, be discharged or referred than children under 5 years old. However, after adjusting for all other factors, the association was found not to be statistically significant ($p=0.161$). The odds of dying, being discharged or referred among children and adolescents aged 15 - 19 ($p=0.013$) years old was 3.65 (cOR ; 95% $CI= 1.30 - 10.19$) times higher than children under 5 years old. After adjusting for all other factors, this was not statistically significant ($p=0.059$).

The odds of dying, being discharged or referred among children and adolescents whose parents or guardians attained secondary education was 51% ($cOR= 0.49$; 95 $CI= 0.28 - 0.85$, $p=0.012$) less than those whose parents or guardians had no formal education. However, after adjusting for all other factors, the odds was not statistically significant 41% ($aOR=0.59$, 95% $CI=0.25-1.37$, $p=0.221$).

Children and adolescents who were non-adherent to ARTs were 52% ($cOR = 0.48$; 95% $CI= 0.26 - 0.88$, $p=0.019$) less likely to die, be discharged or referred than children and adolescents who adhered to ARTs. This was statistically significant. After adjusting for all other factors, the odds of dying, being discharged or referred among children and adolescents who were non-adherent to ARTs was 2.07 (aOR ; 95% $CI= 1.12 - 3.80$, $p=0.019$) times higher than children and adolescents who were adhered to ARTs, and this was statistically significant.

Table 8. Logistic Regression of Socio-demographic and Clinical Risk Factors associated with Treatment Outcomes

Variable	Unadjusted		Adjusted	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value
Socio-demographic factors				
Age (Years)				
<5 (Ref.)	1.00		1.00	
5 - 9	0.79 (0.39 - 1.61)	0.532	0.78 (0.35 - 1.74)	0.558
10 - 14	0.53 (0.30 - 0.93)	0.029*	0.62 (0.32 - 1.20)	0.161
15 - 19	3.65 (1.30 - 10.19)	0.013*	2.88 (0.96 - 8.65)	0.059
Sex				
Male	1.23 (0.70 - 2.15)	0.453	0.80 (0.46 - 1.40)	0.453
Female (Ref.)	1.00		1.00	
Educational Status				
No formal education (Ref.)	1.00		1.00	
Primary	0.59 (0.34 - 1.04)	0.071	0.58 (0.29 - 1.12)	0.108
Secondary	1.38 (0.75 - 2.54)	0.293	0.93 (0.45 - 1.94)	0.863
Educational level (Parent/ Guardian)				
No formal education (Ref.)	1.00		1.00	
Primary	1.36 (0.72 - 2.58)	0.333	1.09 (0.42 - 2.77)	0.855
Secondary	0.49 (0.28 - 0.85)	0.012*	0.59 (0.25 - 1.37)	0.221
Tertiary	2.47 (0.88 - 6.92)	0.085	1.93 (0.55 - 6.70)	0.299
Residence				
Urban	1.45 (0.83 - 2.55)	0.187	1.45 (0.83 - 2.55)	0.187
Rural (Ref.)	1.00		1.00	
Clinical factors				
Viral load detection				
Detected	1.15 (0.62 - 2.12)	0.645	1.15 (0.62 - 2.12)	0.645
Not detected (Ref.)	1.00		1.00	
Viral load counts				
< 100 (Ref.)	1.00		1.00	
101 - 500	0.68 (0.18 - 2.47)	0.562	2.80 (0.25 - 30.81)	0.398
501 - 1000	1.11 (0.14 - 8.74)	0.916	4.28 (0.23 - 77.21)	0.324
>1000	0.24 (0.28 - 2.13)	0.203	4.37 (0.49 - 38.70)	0.184
Adherence to ARTs				
Adherent (Ref.)	1.00		1.00	
Non- adherent	0.48 (0.26 - 0.88)	0.019*	2.07 (1.12 - 3.80)	0.019*

*statistically significant (p<0.05)

CHAPTER FIVE

DISCUSSION

5.0 Introduction

The chapter is organized into four (4) main sections. The prevalence of HIV comorbidities among children and adolescents is presented in the first section. In the next section, 5.2, discussions on clinical and socio-demographic factors associated with HIV comorbidities among children and adolescents are presented. The clinical and socio-demographic factors associated treatment outcomes of HIV comorbidities among children and adolescents are presented in the third section. The final section, 5.4 provides a summary of the chapter.

5.1 Prevalence of HIV Comorbidities among Children and Adolescents

This study recorded 48 HIV comorbidities among 474 patients presenting with HIV infection at the Eastern Regional Hospital, Koforidua. The prevalence of HIV comorbidities among children and adolescents was 33.0%. The study grouped comorbidities guided by the ICD version 11 classifications. These were Respiratory, Circulatory, Neurologic, Skin, Blood, Ear, Visual, Infectious, Digestive, Genitourinary, Endocrine/Metabolic/Nutritional and Neoplasms.

Findings of this study showed Respiratory diseases had the highest prevalence of 14.1% among the study population. Respiratory diseases reported in the study were Bronchopneumonia, Pleural Effusion, Airway Obstruction, Pulmonary Tuberculosis, Pneumocystis Pneumonia, Lung Abscess, Asthmatic Attack, and Upper Respiratory Tract Infection, with Bronchopneumonia as the most frequent comorbidity among the study population.

McHugh et al., (2020) reported that several studies in sub-Saharan Africa had reported high prevalence of respiratory diseases among children and adolescents living with HIV. The study reported prevalence of respiratory diseases of 25% - 37.5%. A study in Zimbabwe by Desai et al.,

2018 reported a prevalence of respiratory diseases as 25% among children and adolescents with HIV infection on ART and receiving co-trimoxazole prophylaxis. The findings of the present study support both studies by McHugh et al., 2020 and Desai et al., 2018.

Findings of this present study shows that Bronchopneumonia (22.4%, 106) was the most frequent comorbidity among children and adolescents. A study by Becker et al., (2015), reported pneumonia as the commonest cause of hospitalization in African HIV infected children and adolescents. In another study conducted by Moreira-Silva et al., (2013), other forms of pneumonia such as *Pneumocystis jirovecii* pneumonia (PJP) were recorded among their study population. However, the study reported anemia as the most prevalent comorbidity in all age groups but more frequent in children less than a year old. In another study, Kukoyi et al., (2016) reported that anemia was common among children. Anemia, a blood disease, was the eighth most frequent comorbidity (37 cases) among the 48 comorbidities recorded in this present study, with a prevalence of 2.6%.

Results of this study showed that infectious diseases were the second most prevalent comorbidities, with prevalence of 11.8%. The infectious diseases were Sepsis, Oral Candidiasis, Tonsillitis, Dysentery, Hepatitis B and Tetanus with frequencies as 46, 41, 37, 15, 4 and 1 respectively. (Kukoyi et al., 2016). A study in Tanzania by Ngasala et al., (2016) reported frequency of oral candidiasis as 132/314 among children and adolescents. The study further stated that oral candidiasis remains the most frequently HIV-associated oral lesion in Tanzania. Another study on infectious diseases by Ford et al., (2015.) reported a prevalence of 13% in the eastern Mediterranean region among adolescents living with HIV. The study reported that 177 children, between the ages of 6 to 15 years living with the HIV infection were admitted in a hospital, due to infectious comorbidities.

Findings of this study showed prevalence of circulatory diseases as 2.5%. The circulatory diseases were deep vein thrombosis (DVT) and congenital heart disease (CHD) with 6 and 9 as frequencies respectively. A study conducted by Okoromah et al., (2012) which looked at only circulatory diseases among African children and adolescents with HIV reported that prevalence of cardiac abnormalities in HIV-infected children was 75.9%. The study further reported prevalence dilated cardiomyopathy (33.7%) and increased left ventricular mass (20.5%) and pericardial effusion (14.5%). The present study supports the findings of Okoromah et al., (2012) that cardiovascular comorbidities are seen among children and adolescents with the HIV infection. However, there is a huge difference in the prevalence of the cardiovascular comorbidities between the two studies. Considering the time between the Okoromah et al., (2012) study and this present study, interventions put in place to curb HIV among children and adolescents may have been adapted, hence reduction in the prevalence since both studies were conducted in Africa. Similarities between this present study and other studies on the prevalence of HIV comorbidities among children and adolescents may be poor due to differences in geographical locations and standard of living of the settings.

5.2 Clinical and Socio-demographic Risk Factors associated with HIV Comorbidities

5.2.1 Clinical Risk Factors

Results of the study showed that more than half of the study population (782, 54.4%) had undetected viral loads. Four hundred and forty-nine (31.3%) had their viral loads detected. A study conducted by Lokpo et al., (2020) in Ho, Volta Region of Ghana, showed that 80 (31.3%) of 284 HIV positive children and adolescents were not able to detect level of their viral load. This present study concurs with the Lokpo et al., (2020) study on viral loads detection.

A study by (Opoku et al., 2022) on viral load suppression and rebound among HIV patients defined viral load suppression as “a recording, at least one viral load less than 50 copies/mL after commencement of treatment”. Another study conducted in Ghana by Ansah et al., (2021) reported 76.4% of viral suppression among their study population. Comparing this present study to the studies of Lokpo et al., (2020) and Ansah et al., (2021), the implication is that there might be variations in the proportion of HIV-infected people achieving undetectable viral load and suppression in different parts of the country. The study’s results of viral load detection is below the WHO 95% target by the year 2030.

Findings of this study showed that 602 (41.9%) of the study population adhered to anti-retroviral therapy (ARTs) and 450 (31.3%) were non-adherents. One hundred and eighty-one (38.2%) adherents and 197 (41.6%) non-adherents were with HIV comorbidities. A study by Aderemi-Williams et al., 2021) reported that out of 34 participants involved in the study, 20 (58.8%) were adhering to treatment, even though 22 (64.7%) knew what adherence means and 26 (76.5%) knew that not adhering will affect their immune system which would make their health worse (Aderemi-Williams et al., 2021). Comparing this present study and the study conducted by (Aderemi-Williams et al., 2021), it can be deduced that adherence to ART among HIV patients is low. This implies poor counselling after testing positive to HIV infection in the health facilities.

5.2.2 Association between Socio-demographic, Clinical Factors and HIV Comorbidities.

Results of this study showed that age ($p=0.014$) was significantly associated with HIV comorbidities. This study further showed that children aged 5 – 9 years old are 30% (OR = 0.70; 95% CI: 0.52 – 0.93, $p= 0.017$) less likely to have a comorbidity than children under 5 years old and this was statistically significant. After adjusting for all other factors, children aged 5 - 9 and 15 - 19 years old are 36% (aOR = 0.64; 0.40 - 0.89, ($p= 0.008$)) and 25% (aOR = 0.75; 0.56 - 0.99,

$p = 0.047$) less likely to have a comorbidity. These were statistically significant. However, sex ($p = 0.63$) was not significantly associated with HIV comorbidities. A study on sociodemographic risk factors and HIV comorbidities conducted by (Yang et al., 2020) reported that out of 402 participants, among children and adolescents, age was ($p = 0.01$) significantly associated with HIV comorbidities. In the study, sex ($p = 0.08$) was not significantly associated with the comorbidities. The differences in this present study and that of (Yang et al., 2020) could be as a result of the total study population in each study. Age and gender are important factors that determine HIV comorbidities among age groups. For example, most adolescents are likely to be exposed to a number comorbidity because they undergo significant changes during this period; physically, emotional and psychologically as compared to other age groups.

Findings from this study showed that educational status ($p = 0.005$) was significantly associated with HIV comorbidities. However, that level of education of parents or guardians ($p = 0.484$) was not significantly associated with HIV comorbidities. A study conducted by (Ibrahim et al., 2019) reported that a hospital-based study in India on socio-demographic factors associated with HIV showed that level educational attainment was associated with HIV comorbidities. Another study conducted in some countries of Africa by (Mee et al., 2018) reported a strong evidence that attaining some level of education was associated with a reduced odds of being HIV positive and getting other comorbidities in Lesotho (aOR: 0.37; 95%CI: 0.17±0.79), Swaziland (aOR: 0.32; 95%CI: 0.17±0.59), and Uganda (aOR: 0.48; 95%CI: 0.29±0.80). There was no statistical significant evidence for this in Kenya, Malawi, Mozambique, Tanzania, Zambia or Zimbabwe.

Results from this study showed that viral load detection ($p = 0.308$) was not significantly associated with HIV comorbidities. Results further showed that the odds of having a comorbidity was 1.13 (cOR; 95% CI = 0.88 - 1.45; $p = 0.309$) higher among children and adolescents whose viral loads

were detected than those whose viral loads were undetected. A study conducted by (George et al., 2019) reported that the association between viral load detection and HIV comorbidities in Western Cape, South Africa found no association between a detectable HIV viral load and HIV comorbidity ($p = 0.92$). This present study supports the study conducted by (George et al., 2019) on viral load detection and HIV comorbidities.

Adherence to ARTs ($p=0.000$) was significantly associated with HIV comorbidities in this study. Results of this study showed that the odds of having a comorbidity was 45% less likely (OR = 0.55; 95% CI = 0.42 - 0.71; $p= 0.000$) among children and adolescents who were not adherent to ARTs than those who were adherent to ARTs. This was statistically significant ($p=0.000$). After adjusting for all other factors, at 95% confidence interval, children and adolescents who were not adherent to ARTs were 45% OR = 0.55; 95% CI = 0.42 - 0.71; $p= 0.000$) less among children and adolescents who were adherent to ARTs than those who were adherent to ARTs and this was statistically significant ($p = 0.000$). This observation concurs with a study done on adherence to ARTs by (Molla et al., 2018) which reported that the overall rate of adherence to ART was 88.2% (95% CI = 85.2 - 91.1) and was statistically significant.

5.3 Treatment Outcomes of HIV Comorbidities among Children and Adolescents

Results of this study showed that out of the 474 study population who were either admitted or seen as OPD cases, more than half (421, 88.8%) were either discharged home after treatment or referred to Teaching Hospitals for further management. Fifty-three (11.2%) died. A study conducted by Heller et al., (2022) reported that among 3,340 patients admitted, 11.7% died and 9.0% were discharged home. The patients who died were more than patients who were discharged. Both

studies show that HIV-infected patients on admission either could face mortality or be discharged home. Responses to treatment among patients may differ.

5.3.1 Socio-demographic and Clinical Factors associated with Treatment Outcomes of HIV Comorbidities

Findings from this study showed that socio-demographic factors, age ($p=0.269$), and sex ($p=0.615$) were not significantly associated with the treatment outcome of comorbidities experienced by the children and adolescents. This supports a study on treatment outcomes conducted by (Kwara et al., 2010.), which reported that age ($p=0.938$), gender ($p=0.841$) were not significantly associated with treatment outcomes.

Findings from this study also showed no significant association between educational status ($p=0.594$), level of education of parents or guardian ($p=0.121$), residence ($p=0.185$) and treatment outcomes of HIV comorbidities. A study conducted by (Hargreaves & Glynn, 2002) reported that in SSA, educational attainment is often associated with a greater risk of HIV infection and its comorbidities. The study further reported that in Thailand, those with more schooling remain at lower risk of HIV infection. Higher education may increase awareness and access to HIV treatment and therapy.

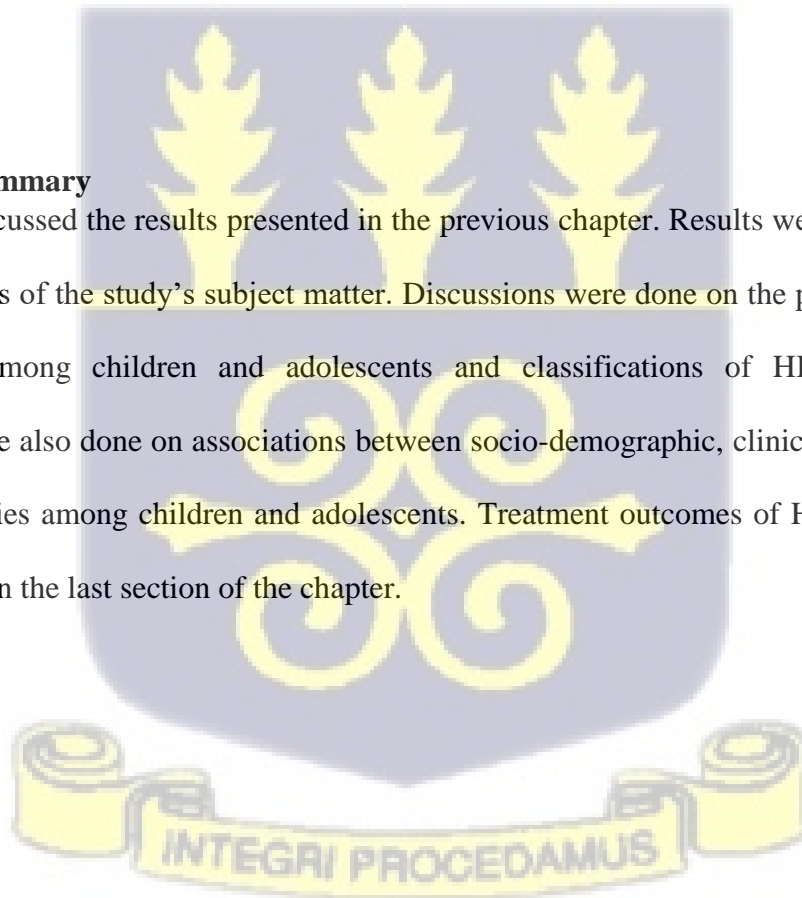
Results of viral load ($p=0.624$) in this study was also not significantly associated with the treatment outcome of comorbidities experienced by the study population. This study's results are different from a study conducted by Okomo et al., (2012) on the association between viral load and treatment outcomes of HIV comorbidities. Results of the Okomo et al., (2012) study showed that

children and adolescents who died had significantly higher viral loads ($p = 0.004$). This may be due to differences in the comorbidities recorded among study populations.

Results from this study showed that there was no significant association between adherence to ARTs ($p=0.259$) and treatment outcomes. A study in Ghana also reported that out of 102 admissions among 76 children, ART adherence ($p= 0.685$) was not significantly associated with treatment outcomes. This study was conducted by (Kwara et al., 2010.). It could be that knowledge on HIV/AIDS and adherence to ARTs has not been thoroughly done across Ghana, since both this present study and the study by (Kwara et al., 2010.) showed that adherence to ARTs is insignificant.

5.4 Chapter Summary

This chapter discussed the results presented in the previous chapter. Results were compared with literature reviews of the study's subject matter. Discussions were done on the prevalence of HIV comorbidities among children and adolescents and classifications of HIV comorbidities. Discussions were also done on associations between socio-demographic, clinical (viral load) and HIV comorbidities among children and adolescents. Treatment outcomes of HIV comorbidities were discussed in the last section of the chapter.



CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.0 Introduction

This chapter is presented in five sections. A summary of the study objectives, methods, and findings are shown in the first section. The next section concludes the study based on reviewed literatures on the subject matter. This is followed by recommendations for policy decisions, study limitations, and an area for future research in the last three sections respectively.

6.1 Summary of Study

The purpose of the study was to determine the prevalence and risk factors associated with HIV comorbidities and treatment outcomes among children and adolescents. This was a hospital-based cross-sectional study, which used a clinical record review to obtain retrospective data at the Eastern Regional Hospital, Koforidua. Clinical records of children and adolescents infected with HIV and registered at the hospital from January 2018 to January 2021 were assessed using a specially designed tool to extract the data from the clinical records.

A study population of 1,437 were used in this study. Bivariate analysis using Pearson Chi-square tests and logistic regression to determine Socio-demographic and Clinical Factors associated with HIV comorbidities and treatment outcomes among children and adolescents was conducted. Cross tabulations of the variables were presented.

Results showed that bronchopneumonia, a respiratory disorder was the comorbidity with the highest frequency while tetanus was the least common comorbidity among children and adolescents. The frequent number of comorbidities experienced by an individual was two. Comorbidities were grouped using ICD version 11 classifications for diseases.

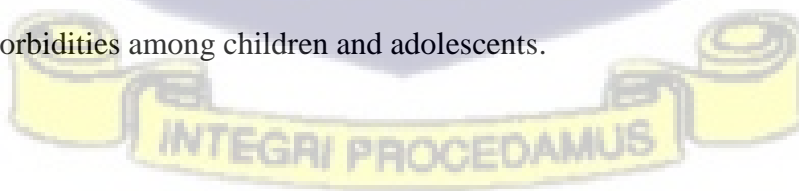
6.2 Conclusions

Children and adolescents living with HIV suffer from several other illnesses independent of HIV and face many medical problems that significantly contribute to the global burden of HIV. There is a high prevalence of Respiratory comorbidities among children and adolescents with HIV infection. Children and adolescent patients also experience a higher risk of Bronchopneumonia, Pulmonary TB, and Pneumocystis pneumonia. Clinical and Socio-demographic risk factors contribute to the presence of HIV comorbidities and affect their treatment outcomes. To decrease the prevalence of HIV comorbidities among children and adolescents, education and counselling on HIV comorbidities and adherence to ARTs should be effective and consistent.

Every child has the right to live, enjoy and benefit from economic and social policies. This will aid them to continue into adulthood. Whether HIV positive or not, children and adolescents have the right to quality of life.

6.2.1 Contribution to knowledge

1. The study contributes to the knowledge on comorbidities among children and adolescents living with HIV.
2. Findings from the study showed that children and adolescents experience more respiratory HIV comorbidities than other classifications of diseases.
3. Findings from the study will aid public health surveillance to improve efforts in managing HIV comorbidities among children and adolescents.



6.3 Recommendations

To the management of the Eastern Regional Hospital, Koforidua:

1. The hospital should provide a system that will effectively monitor the comorbidities and health conditions of children and adolescent patients living with HIV, whether on admission or not.
2. The hospital should develop an effective system for counselling children and adolescents as well as their parents and guardians on adhering to ARTs.

To the Ministry of Health (MOH) and Ghana AIDS Commission (GAC):

1. The Ministry of Health and Ghana AIDS Commission should expand routine monitoring of pediatric HIV clinics and ensure that children and adolescents adhere to ART from infancy into adolescence and beyond.

6.4 Study Limitations

The study looked at risk factors associated with HIV comorbidities among children and adolescents and their treatment outcomes. The risk factors were categorized into clinical, socio-demographic, and psychological factors. Results on psychological factors associated with HIV comorbidities among the study population were excluded because the study used a retrospective record, which did not include data on psychological factors.

For clinical factors, the study looked at viral load detection, viral load counts and adherence to ARTs. Other clinical factors such as results of Cluster of Differentiation 4 (CD4), antibodies, and antigens were not available.

6.5 Future Research

Future studies should conduct a prospective cohort study on risk factors associated with HIV comorbidities and treatment outcomes among pediatrics and adolescents.



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APPENDICES

Appendix A: Data Collection Tool

A. PATIENT DETAILS

Patient's Initials

Folder Number

Sex Male Female

Age

Religion

Residence

Date of Registration at ARV Clinic

Adherence to ARVs Yes No

Adherence to Review dates Yes No

B. PARENT/ GUARDIAN DETAILS

Parent/Guardian Occupation

Parent/Guardian Level of Education

C. PATIENT INVESTIGATIONS

CD4 Counts

HIV RNA plasma (viral load)

Antigen and Antibody tests

Other Clinical Investigations

D. TREATMENT

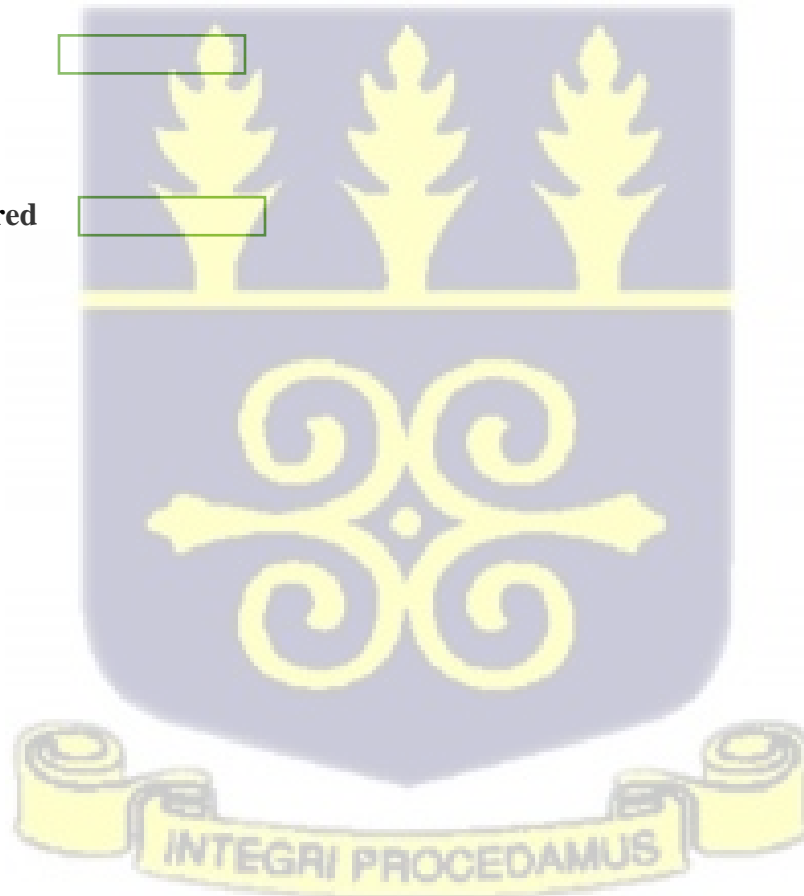
Date of Admission	<input type="text"/>
No of days on Admission	<input type="text"/>
Diagnoses of Commodities	<input type="text"/>

D. TREATMENT OUTCOME

a. Discharge

b. Died

c. Referred



Appendix B: Ethical Clearance

GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE

In case of reply the number and date of this Letter should be quoted.



Research & Development Division
Ghana Health Service
P. O. Box MB 190
Accra
Digital Address: GA-050-3303
Mob: +233-50-3539896
Tel: +233-302-681109
Fax + 233-302-685424
Email: ethics.research@ghsmail.org
10th December, 2021

My Ref. GHS/RDD/ERC/Admin/App 121/542
Your Ref. No.

Phyllis Otubea Otu
School Of Public Health
P. O. Box LG 13,
University Of Ghana, Legon – Greater Accra

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

GHS-ERC Number	GHS-ERC: 023/10/21
Study Title	Prevalence and Factors associated with HIV Comorbidities among Pediatric Patients at the Eastern Regional Hospital, Koforidua
Approval Date	10 th December, 2021
Expiry Date	9 th December, 2022
GHS-ERC Decision	Approved

This approval requires the following from the Principal Investigator

- Submission of a yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report after completion of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.

You are kindly advised to adhere to the national guidelines or protocols on the prevention of COVID -19

Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....

 Dr. James Akazili
 (Head, Ethics & Research Management Department)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra