NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF CLINICAL MICROBIOLOGY

PREVALANCE OF MALARIA AS A CO - INFECTION AMONG HIV SERO-POSITIVE INDIVIDUALS: A CASE STUDY OF INDIVIDUALS ATTENDING ANTI-RETROVIRAL TREATMENT (ART) CLINIC AT HOLY FAMILY HOSPITAL-TECHIMAN IN GHANA

BY

APPIAH ANTHONY MENSAH

APRIL 2013

PREVALANCE OF MALARIA AS A CO - INFECTION AMONG HIV SERO-POSITIVE INDIVIDUALS: A CASE STUDY OF INDIVIDUALS ATTENDING ANTI-RETROVIRAL TREATMENT (ART) CLINIC AT HOLY FAMILY HOSPITAL-TECHIMAN IN GHANA

BY

APPIAH ANTHONY MENSAH

SUPERVISOR

DR S.C.K TAY

A DISSERTATION SUBMITTED TO THE SCHOOL OF POSTGRADUATE STUDIES THROUGH THE DEPARTMENT OF CLINICAL MICROBIOLOGY, SCHOOL OF MEDICAL SCIENCES,

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI,

IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF

MASTER OF PHILOSOPHY (M. Phil) DEGREE

IN CLINICAL MICROBIOLOGY

DECLARATION

I, the undersigned, declare that this is my original work and has never been presented in this or any other institution and that all the source materials used for this thesis have been duly acknowledged;

APPIAH ANTHONY MENSAH …… ……

(Student) Signature Date

DR S.C.K. TAY …… ……...

(Supervisor) Signature Date

PROF. E. H. FRIMPONG …… ……

(Head of Department) Signature Date

DEDICATION

This study is dedicated to my beloved wife Hagar Oduro and my beautiful daughter Chantel Appiah Kwaa.

ACKNOWLEGEMENT

The first and most special acknowledgement is to my parents, Mr. & Mrs. John Mensah, whose belief in education has brought me this far and without whose love, support and encouragement I may not have succeeded.

I am much grateful to my supervisor, Dr S.C.K. Tay for his invaluable support and words of encouragement, for painstakingly reading through every part of this thesis over and over again. My sincere thanks go to the entire staff of Holy Family Hospital – Techiman with special mention of the staff of the Anti-Retroviral Treatment (ART) Clinic. I am also grateful to Mr. Christopher Nkrumah (Methodist Hospital – Wenchi) for his help and support.To my dear wife, Hagar Oduro and my beautiful daughter, Chantel Kwaa Appiah, there are no words which would express my heartfelt gratitude. The love, care and support they have given me in my education will never be forgotten.

To all parties whose names I have not mentioned, I wish to express my thanks in the words of Albert Einstein: (1879 – 1955) "The most important method of education always has consisted of that in which the pupil was urge to actual performance" an education which would not have been completed without their help and concern.

It was under the guidance of Almighty God and with his blessings that this study was undertaken

TABLE OF CONTENT

CHAPTER THREE

CHAPTER FOUR

CHAPTER FIVE

LIST OF TABLES AND FIGURES

Tables

Abstract

Malaria and HIV are two of the most common infections in sub-Saharan Africa and, to a lesser extent, in other developing countries. The determination of malaria and HIV co-infection rate is important because there are hypotheses and even study reports on the possible association between the two infections. This study was therefore carried out at Holy Family Hospital – Techiman between November 2011 and January 2012 with the main objective of determine the prevalence of malaria among HIV sero-positive patients attending anti-retroviral treatment clinic of the hospital. The study design was cross sectional, restricted to randomly selected HIV sero-positive patients attending anti-retroviral treatment clinic of the hospital. All participants were sampled using participant leaflet and consent forms. A total of 400 HIV sero-positive patients between aged1year 8months and 73 years were included in the study. Of these 292 (73%) were females and the rest 108 (27%) were males. A questionnaire was administered and 2mls of venous blood sample was drown for detection of malaria parasite, estimation of CD4 count and haemoglobin level. The study revealed that 47 (11.75%) patients were slide positive for malaria parasite. There was no statistically significant difference in the prevalence rate for females (12.1%) and males (10.2%), P = 0.6047. Using the World Health Organization (WHO) definition for anemia as hemoglobin levels less than 13.0g/dl in adult men and hemoglobin levels less than 12.0g/dl in adult women, an overall prevalence of 67% (268 out of 400) anemia was observed in this study. The prevalence of anemia among the study participants who had malaria was 93.6% (44 out of 47). All patients studied had a CD4 cell count ranging from 3 – 1604 Cells/µl. The mean CD4 cell count of the patients was 386.2 (±274.3) Cells/µl. All patients with

malaria infection had CD4 cell count ranging from 3 Cells/µl to 512 Cells/µl with mean CD4 cell count of 186.33 (±133.49) Cells/µl. Out of the study participants, 377 (participants above15years) were interviewed on knowledge on malaria transmission and prevention in which 328 (87.0%) out of 377 of the participants claimed they had knowledge about malaria infection. Only 32 (8.5%) of the interviewed 377 of the participants interviewed used bed net for the prevention of malaria. Due to high mortality rates associated with malaria infection in an endemic area, it may be necessary that routine malaria screening be adopted as part of the management policy to check HIV and malaria co-infection since only tuberculosis (TB) and hepatitis B virus are presently screen for.

CHAPTER ONE

1.1.0 INTRODUCTION

Infection by malaria parasite and Human immunodeficiency virus (HIV) represent major public health problems in many parts of the world (Huff, 2009). Both infections kill millions of people each year and both infections are scourges in developing nations in Africa, India, Southeast Asia and South America (Huff, 2009). Although these two infections are of major public health and clinical importance in developing nations, their interaction is little understood (Huff, 2009).

Malaria is one of the world most common and serious infectious diseases, causing approximately 500 million clinical cases and 1 million deaths each year (3000 deaths per day), and 90% of them occur in sub-Saharan Africa (Snow et al., 2005). It is estimated that 40% of the world's population lives in malaria endemic areas (Amman et al., 2007).

Children under the age five are the group most heavily affected by malaria because of their low level of immunity (Amman et al., 2007). Malaria infection accounts for approximately 35% preventable cases of low birth weight and for 5-10% of infant mortality in sub-Saharan Africa (Guyatt et al., 2001). In fact, malaria is the leading cause of death worldwide among children in this age group (Amman et al., 2007). Pregnant women are also vulnerable to malaria (Amman et al., 2007). Malaria is a major cause of maternal anemia, which in turn is a risk factor for maternal mortality

(Guyatt et al., 2001). The cost of malaria prophylaxis, the need for repeated treatment, and the loss productive laborers constitute a significant impact on the economies of countries in which malaria remain highly endemic (Barat et al., 2004). Malaria infection is estimated to cost sub-Saharan Africa approximately US$2 billion annually (Barat et al., 2004).

Because there is a great deal of geographic overlap between high-prevalence areas for malaria and HIV infection, there is growing concern among health care professionals, researchers, and policy makers that the two may reinforce each other synergistically, fueling incidence of both and complicating treatment efforts (Amman et al., 2007). In recent years, it has been hypothesized that a possible deleterious interaction between the two infections exists (Yaffe, 2001). The presented hypothesis suggested that chronic latent malaria infection prepares the niche where otherwise feeble HIV infection can thrive and cause acquired immuno deficiency syndrome (AIDS) (Yaffe, 2001). However, an earlier critical review from numerous available reports on this subject showed that there was hardly evidence to support this hypothesis (Chandramhan et al., 1998). Depending on the perspective it is viewed, malaria has either a lot or very little in common with HIV.

As with HIV, malaria has been difficult to control because of emerging drugs resistance, poor availability of low cost prophylactic drugs, inadequate health care infrastructure, and lack of vaccine for prevention (Greenwood et al., 2005). However whereas antiretroviral drugs were developed relatively rapid after the emergence of

HIV, the development of anti-malaria drugs powerful enough to treat resistant strain has been slow (Greenwoon et al., 2005). As the number of malaria and HIV co-infection has increased, it has become apparent that anti-retroviral drugs interact with both new and established anti-malaria drugs, complicating treatment efforts for both infections (Bretlinger et al., 2006). Malaria and HIV co-infection also result in interactions that adversely affect the outcome of both conditions. This is especially true for pregnant women and infants born to HIV infected mothers (Kamya et al., 2006). Understanding the pathogenesis of HIV and malaria, therefore, is important for determining approaches to treatment and prevention.

1.2.0 PROBLEM STATEMENT

Malaria and HIV are among the two most important global health problems of our time. The association between the two infections has important implications. According to WHO report (2010), about 3.3 billion people – half of the world's population – are at risk of malaria. People living in the poorest countries are the most vulnerable. Africa accounts for the majority of estimated malaria cases (78%) and deaths (91%), but only 12 – 13% of the world's population.

An estimated 33.3 million people worldwide are infected with HIV/AIDS. In 2009, 1.8million people died due to HIV/AIDS, and another 2.6 million were newly infected (Amman et al., 2007). Approximately 22.5 million people living with HIV are in sub-Saharan Africa. This represents 68 percent of global total HIV infection (Amman et al., 2007).

Therefore, any interaction between these infections will have a significant public health effect, even if the statistical effect is modest. On a population basis, an increased prevalence of malaria and increased parasite density in HIV-infected individuals could lead to increased malaria transmission affecting both HIV-positive and HIV -negative individuals (Snow et al., 2005). The increased risk of clinical malaria in HIV-positive subjects could increase the burden on clinical services in areas where HIV is prevalent.

1.3.0 AIM

To study malaria infection and it prevalence among HIV sero-positive individuals

1.4.0 OBJECTIVES

- To determine the prevalence of malaria infection among HIV sero-positive patients at the study site
- To study the prevalence of anemia among HIV sero-positive patients
- To study the CD4 count of HIV sero-positive patients infected with malaria
- To assess knowledge of HIV sero-positive patients on malaria infection
- To determine predisposing factors to malaria infection among HIV sero-positive patients
- To suggest preventative measures for malaria infection among HIV sero-positive individuals.

1.5.0 JUSTIFICATION

Tropical Africa is the most endemic area for malaria and HIV infection. Therefore, the outcome of this study will help raise public awareness on malaria and HIV co-infection and also having determined the prevalence of malaria among HIV sero-positive individuals and the predisposing factors, recommendations be made to reduce malaria infection among HIV sero-positive individuals.

1.6.0 BASIC ASSUMPTIONS

The following assumptions were made in this study:

- That the respondents clearly understood all the questions.
- That respondents gave truthful answers
- That respondents were all HIV positive

1.7.0 LIMITATIONS

- The study was conducted in the dry season which has low rate of malaria infection
- There was no follow up for patients found to be malaria positive

CHAPTER TWO

2.0.0 LITERATURE REVIEW

2.1.0 MALARIA INFECTION

Malaria is caused by parasites transmitted to humans by mosquitoes (Greenwood, 2005). It is a disease that can be treated in just 48hours, yet it can cause fatal complications if diagnosis and treatment are delayed. Malaria is the fifth cause of death from infectious diseases worldwide (after respiratory infections, HIV/AIDS, diarrheal disease, and tuberculosis) and the second in Africa, after HIV/AIDS (WHO, 2010). Malaria is the number one priority tropical disease of the World Health Organization (WHO, 2010)

According to WHO report in 2010, about 3.3 billion people – half of the world's population – are at risk of malaria. Every year, this leads to about 250 million malaria cases and nearly one million deaths. People living in the poorest countries are the most vulnerable. Africa accounts for the majority of estimated malaria cases (78%) and deaths (91%), though Africa represents 12 – 13% of the world's population (WHO, 2010).

2.2.0 EPIDEMIOLOGY OF MALARIA

Malaria is widely distributed in the tropical and sub-tropical zones being endemic throughout South and South-East Asia, Africa, areas of the Middle East and South and Central America (Cowan et al., 1993). The four species of human malaria parasite differ in their geographical distributions:

- *Plasmodium falciparum* is most common in Sub-Saharan Africa and Melanesia (Papua New Guinea and the Solomon Islands);
- *Plasmodium vivax* is found mainly in Central and South America, North Africa, the middle East and within the Indian subcontinent;
- *Plasmodium ovale* is found almost exclusively in West Africa; and
- *Plasmodium malariae* occurs worldwide, although most cases occur in Africa (Cowan et al., 1993).

In recent years, some human cases of malaria have also occurred with *Plasmodium knowlesi* – monkey malaria that occurs in certain forested areas of South-East Asia (McCutchan et al., 2008).

With modern air travel, individuals with malaria parasites can be rapidly transported within hours to any part of the world that makes malaria the single most common imported infection (Tatem et al., 2006).

2.3.0 TRANSMISSION AND LIFE CYCLE OF MALARIA PARASITE

Human malaria parasites share a common life cycle. They require two hosts:

- The mosquito for the sexual reproductive stages (sporogony) and
- Humans for the asexual reproductive stages (schizogony) (Brian et al ,2008)

The life cycle begins when a female anopheles mosquito feeding on a patient with malaria parasites, ingests blood-containing male gametocytes (microgametocytes) and female gametocytes (macrogametocytes). The gametocytes undergo sexual development (sporogony) within the mosquito's stomach. While in the mosquito's

stomach, the microgametes penetrate the macrogametes generating zygotes. The zygotes in turn become motile and elongated (ookinetes) and invade the midgut wall of the mosquito where they develop into oocysts. The oocysts grow, rupture, and release sporozoites, which make their way to the mosquito's salivary glands. The mosquito is now infective at this stage the next time it bites (Brian et al., 2008)

As the mosquito feeds on man it injects the sporozoites into his blood. The sporozoites migrate to the liver cells where they multiply asexually (exoerythrocytic phase) (Brian et al., 2008). Some of the sporozoites of *P. vivax* and *P. ovale* delay their development after invading the liver cells (Cheesbrough 1998). They become dormant (hypnozoites) and become active and multiply asexually at a later date causing relapse infections months to years after initial clinical disease (Cheesbrough 1998)

After a period of maturation ranging from days to months, merozoites are released from the liver cells into the blood and invade the red blood cells (erythrocytic phase) initiating the clinical cause of disease (Cheesbrough 1998). All four parasites multiply asexually in the red blood cell to produce new generations of merozoites. The red blood cells rupture and new generations of merozoites are released. In some red blood cells, gametocytes are formed. These cannot self – replicate and they die unless ingested by the female anopheles mosquito for completion of their sexual cycle (Brian et al., 2008)

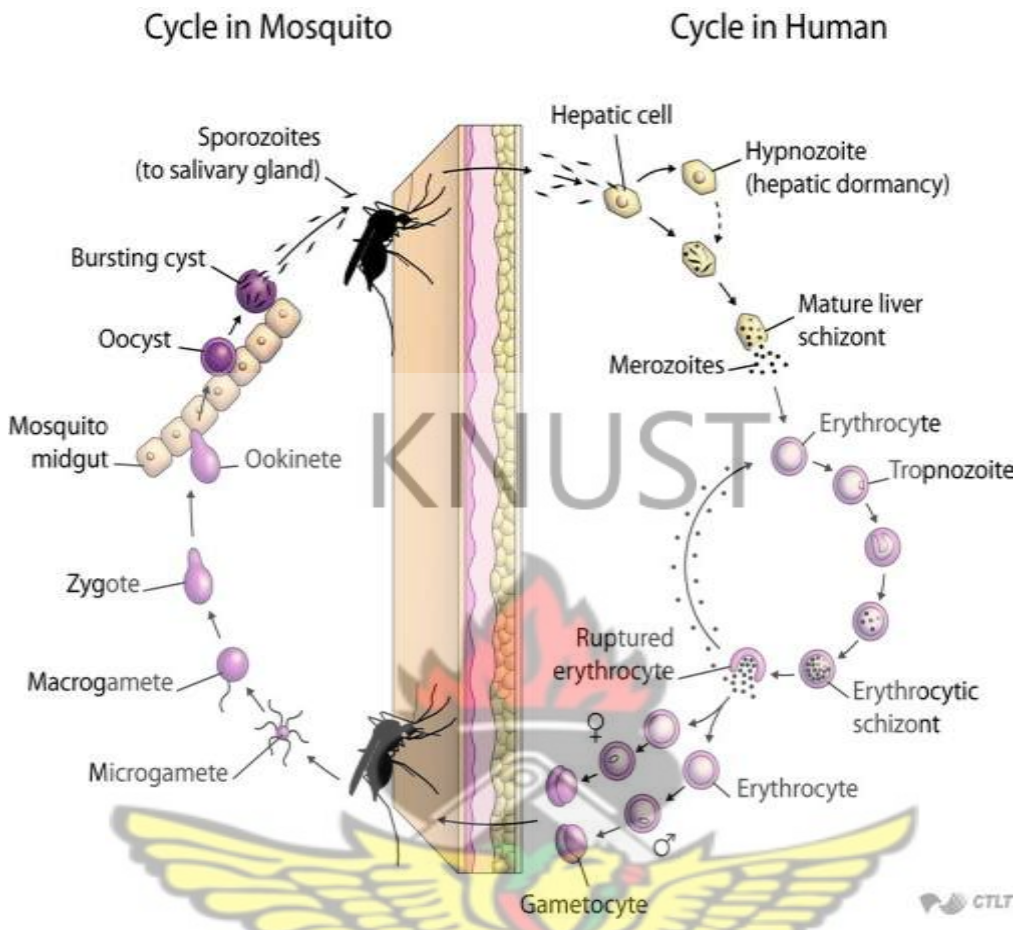


Figure 1: Life cycle of malaria parasite [source: http://ocw.jhsph.edu/]

2.3.1 TRANSMISSION OF MALARIA PARASITE OTHER THAN BY MOSQUITOES

Malaria can be transmitted by the inoculation of blood from an infected person to a healthy person. There are three main means by which such transmission is effected:

- Transfusion of infected blood from a donor.
- Mechanically through the use of needles and syringes contaminated with infected blood.
- Transplacentally (Frean et al., 2008).

Under these circumstances, asexual forms of Plasmodium are directly inoculated into the blood and pre-erythrocytic development of the parasite in the liver does not occur. Therefore, this type of malaria has a shorter incubation period and relapses due to persisting exoerythrocytic forms do not occur (Kakkilaya, 2011).

2.4.0 PATHOGENESIS OF MALARIA

All the manifestation of malarial illness is caused by the infection of the red blood cells by the asexual forms of the malaria parasite. The involvement of the red cells makes malaria a potentially multisystem disease, as every organ of the body is reached by the blood (Brian et al., 2008).

All types of malaria manifest with, common symptoms such as fever. Some patients may have severe forms of malaria. Although the severe malaria is more often seen in cases of *P. falciparum* infection, complications and even deaths have been reported in non-falciparum malaria as well (Brian et al., 2008)

Malaria fever occurs at the time of rupture of red blood cells upon release of merozioites. If this process becomes synchronized, episodes of fever occur on every second day (tertian fever) as in *P. vivax* and *P. ovale* infection, or on every third day (quartan fever) as with *P. malariae*. In *P. falciparum* disease, multiplication and invasion occur so rapidly that no synchronous pattern develops and the fever persists (Warren et al, 1992). Fever in malaria results from the release of endogenous cytokines (e.g. interleukin 1(IL-1), tumour necrosis factor (TNF) in reaction to parasite antigens,

which help to protect the patient from further invasion by enhancing the immune response and inhibiting multiplication of the parasite but which in severe infection may potentiate damage to vital organs (Cowan., 1993).

The degree of parasitemia produced by the different species of plasmodia varies considerably. *P. vivax* and *P. ovale* develop most readily in the reticulocytes (early red cell forms). *P. malariae* tends to invade the older red blood cells. *P. falciparum* invade red cells of any age (Nicholas et al., 2009). In *P. vivax, P. ovale* and *P. malariae* infections, it is rare for more than 1% of circulating red blood cells to be parasitized Duerden., 1993).

The pathogenesis of severe and complicated malaria, which is always due to *P. falciparum*, has been intensively studied in recent years (Schull, 1999). In the 1960s the theory of increased capillary permeability as the cause of pathology prevailed. Considerable studies have since been advanced to show that microvascular obstruction by parasitized red blood cells explains many of the disease process (Duerden, 1993, Schull, 1999). It has long been known that *P. falciparum* schizont rarely appear in peripheral blood; it is now clear that red cells containing them are sequestered in deep capillary beds throughout the body, most crucially in the brain and kidneys, and importantly in bone marrow, liver and the placenta in pregnancy (Chen et al., 2000). Sequestration allows the malaria parasites to avoid destruction in the spleen. This results from increased adherence by parasitized red cells to capillary endothelium (Cowan, 1993). The resulting capillary stasis in vital organs produces metabolic arrest,

without causing total vascular occlusion. In cerebral malaria, brain cells in particular are unable to perform aerobic glycolysis to obtain energy and so depend on inefficient anaerobic glycolysis; these results in lactic acidosis and total brain dysfunction leading to coma and death (Schull, 1999). Hypoglycemia, acute renal failure and anaemia are important complications of P. falciparum. Hypoglycemia may result from:

- Increased utilization of glucose (anaerobic glycolysis) by malaria parasites
- Reduced liver gluconeogenesis, due to microvascular obstruction.
- Insulin released from pancreatic islets by quinine or quinidine used in treatment (Schull, 1999).

Acute renal failure is an important contribution to the mortality of severe malaria and may be caused by:

- Hypovolaemia due to sweating, vomiting and diarrhea.
- Microvascular obstruction in glomeruli and tubules.
- Malaria pigment and haemoglobin nephropathy due to haemolysis.

Progressive anaemia results from haemolysis of parasitized red blood cells and hyperspenic destruction of normal red cells and from ischaemia of bone marrow (Cowan 1993, Mackintosh 2004).

2.5.0 CLINICAL FINDINGS OF MALARIA

The patient may report malaria's prodromal signs and symptoms such as chills, fever, headache, fatigue and myalgia interspersed with periods of well-being after an incubation period of 12-30 days (Mackintosh, 2004). Acute attacks (paroxysms) occur when red blood cells rupture. These attacks have three stages:

- Cold stage, lasting for 1 to 2 hours ranging from chills to extreme shaking (Mackintosh, 2004)
- Hot stage, lasting for three to four hours characterized by high fever (up to 41.7°C) accompanied by cough, headache, backache, abdominal pain, nausea, vomiting and delirium (Mackintosh, 2004).
- Wet stage, lasting for 4 hours characterized by profuse sweating (Mackintosh, 2004).

Between paroxysms, the patient typically experiences a period of well-being, except in *P. falciparum* (Brian et al., 2008, C Mackintosh, 2004).

2.6.0 DIAGNOSIS OF MALARIA

The diagnosis of malaria depends on the microscopic demonstration of stained parasites in the red cells of thick and thin peripheral smears stained with Giemsa, Leishman or Field methods (Cheesbrough, 1998). Peripheral smear examination for malaria parasite is the gold-standard in confirming the diagnosis of malaria (Cheesbrough, 1998). Although the peripheral blood smear examination has been the gold – standard for malaria diagnosis, immunochromatographic tests (Rapid Malaria Test (RDT) for the detection of malaria antigens, have opened a new and exciting avenue in malaria diagnosis. However, their role in the management and control of malaria appears to be limited at present (Endeshaw et al., 2008).Immunochromatographic tests are based on the capture of the parasite antigens from the peripheral blood using either monoclonal or polyclonal antibodies against the parasite antigen targets (Endeshaw et al., 2008).

Currently, immunochromatographic tests can target the histidine-rich protein 2 of *P. falciparum*, a pan-malarial *Plasmodium* aldolase, and the parasite specific lactate dehydrogenase. These RDTs do not require a laboratory, electricity, or any special equipment (Bisoffi, 2009).

Other serological methods are also available for the diagnosis of malaria parasite in blood, but none are useful for diagnosing acute infection. They are mostly used for epidemiological surveys. Immunofluorescence (IF), Radioimmunoassay (RIA) and Enzyme-Linked Immunoassay (ELISA) methods are the most commonly used. Polymerase chain reaction (PCR) is useful for making an accurate species diagnosis detecting low levels of parasitemia but is expensive (Bisoffi, 2009).

2.7.0 TREATMENT OF MALARIA

The effectiveness of antimalarial drugs differs with different species of the parasite and with different stages of the parasite life cycle. Anti-malarial drugs include chloroquine, melfloquine, quinine, artemether-lumefantrine, primaquine, pyrimethamine-sulfadoxine (fansider), doxycycline and artesunate (WHO 2001).

Some Plasmodium has developed resistance to certain medication. Multidrug resistance has been reported from most parts of the world and as a result, monotherapy or some of the available combination chemotherapies for malaria are either ineffective or less effective. New antimalarial regimens are, therefore, urgently needed and antimalarial combination chemotherapy is widely advocated. Antimalarial combinations can

increase efficacy, shorten duration of treatment (and hence increase compliance), and decrease the risk of resistant parasites arising through mutation therapy (WHO 2010)

The current WHO recommendations for treatment of malaria are:

- Uncomplicated *P. falciparum* malaria should be treated with an artemisinin-based combination therapy (ACT).
- *P. vivax* malaria should be treated with chloroquine in areas where it is effective, or an appropriate ACT in areas where *P. vivax* resistance to chloroquine has been documented
- Severe malaria should be treated with a parenteral artemisinin derivative or quinine, and followed by a complete course of an effective ACT as soon as the patient can take oral medications (WHO. 2010).

The five ACTs currently recommended for use are artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, artesunate plus sulfadoxine-pyrimethamine (SP), and dihydroartemisinin plus piperaquine. The choice of the ACT should be based on the efficacy of the combination in the country or area of intended use (WHO, 2010).

2.8.0 PREVENTION AND CONTROL OF MALARIA

Prevention and control of malaria have had as their main objective reduction of *Anopheles* below the transmission level since there is no effective vaccine as yet (Beaver et al., 1985). As a complementary line of action, transmission of plasmodia

from man to mosquito could be prevented by treating infected people, providing chemoprophylaxis, and protecting infected as well as uninfected populations from anopheline vectors (Mark, 1998).

This is embodied in the measures below:

1. Protection of human population from exposure to bites of Anopheles (Mark, 1998). This is provided through individual precautions such as :
    - Covering the exposed skin in the evenings since the anopheline vectors are night biters.
    - Use of insecticide repellent creams containing dimethylphthalate, dibutylphthalate or diethyltocamide.
    - The use of efficient mosquito netting over the bed preferably impregnated with a synthetic pyrethroid such as permethrin or deltamethrin (Mark, 1998).
2. Public health services could assist communities in the development of measures directed at destroying arthropod vectors such as mass spraying, or ensuring that every household has adequate mosquito-proof netting, or carrying out programmes to prevent breeding of Anopheles mosquitoes, such as larviciding and draining breeding sites for mosquito. This breaks the life cycle of the parasite and thus reduces the hazards of individual and group exposure (Mark. 1998)
3. Treatment of human infections with antimalarial drugs wherever practicable. At times mass chemotherapy may be effective in preventing insects from acquiring and transmitting the parasite in endemic areas (Macintyre et al., 2003)

4. Provision of chemoprophylaxis to people traveling to endemic areas, establishment of malaria surveillance programmes and institution of programmes to dispense practical advice to the public on prevention measures (Macintyre et al., 2003;WHO 2000)

2.9.0 AIDS/HIV INFECTION

Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) date back to 1981, when homosexual men with symptoms of a disease that now are considered typical of AIDS were first described in Los Angeles and New York (UNAIDS 2010).

An estimated 33.3 million people worldwide are infected with HIV/AIDS. In 2009, 1.8 million people died due to HIV/AIDS, and another 2.6 million were newly infected. Approximately 22.5 million people living with HIV are in sub-Saharan Africa. This represents 68 percent of global total HIV infection (UNAIDS , 2010).

In Ghana the first case of HIV was reported in 1986. The disease spread slowly but steadily until 2003, when prevalence peaked at 3.1 percent (UNAIDS, 2010).

Human Immunodeficiency Virus (HIV) is the virus that causes AIDS in humans. Two strains of HIV have been identified: HIV-1 AND HIV-2. Although these two strains of HIV have almost the same modes of transmission and result in identical clinical manifestations, there are some differences in transmission and disease progression rates.

It is also possible to be infected with both strains of HIV simultaneously. HIV-1 is the most common (or prevalent) strain, with transmission occurring globally. HIV-2 is most commonly found in West Africa (NACP 2005).

2.10.0 MODE OF TRANSMISSION OF HIV/AIDS

HIV is found in bodily fluids, including blood, semen, vaginal fluids and breast milk and can be transmitted from infected individuals by three main modes:

- Sexual transmission
- Transmission through infected blood
- Mother to child transmission (Palella et al., 1998).

2.10.1 SEXUAL TRANSMISSION OF HIV/AIDS

HIV is spread most commonly by sexual contact with an infected partner. The virus can enter the body through the lining of the vagina, vulva, penis, rectum or mouth (NACP 2005).

2.10.2 TRANSMISSION THROUGH INFECTED BLOOD

HIV is also spread through contact with infected blood (Palella et al., 1998). Transmission occurs through the transfusion of contaminated blood or blood products, contaminated injecting equipment, the exchange and re-use of needles contaminated syringes and surgical operation where equipment previously used with an HIV – positive patient and which have not been sterilized (Palella et al., 1998). Organ transplant from infected donors (e.g. kidney and liver) can also transmit the infection

(NACP, 2005). HIV can be transmitted through direct contact with materials that have been contaminated with infected blood during rituals such as circumcision and tattooing (NACP, 2005).

2.10.3 MOTHER TO CHILD TRANSMISSION OF HIV/AIDS

Many children are infected through mother to child transmission (Arthur et al., 2007). They receive the infection from their mothers during pregnancy at the time of birth or through breast feeding (Arthur et al., 2007). About 30 to 40 percent of infants born to infected mother will themselves be infected (NACP, 2001). The other 60 to 70 percent will not become infected, but are at risk of becoming orphan when their parents die from AIDS. Mother to child transmission of HIV account for approximately 15 percent of all HIV transmissions (NACP, 2001).

2.11.0 CD4 T-CELL COUNT IN HIV PATIENTS

HIV can infect and kill many different types of cells in the body, but the primary targets are immune cells called CD4 T-cells. The CD4 T-cells are a type of T-lymphocyte (white blood cells) that helps coordinate the immune system's response to infection and disease. These cells express a molecule called CD4 on their surfaces, which allow them to detect foreign substances, including viruses that enter the body. HIV binds to the receptors on CD4 cells and enters the white blood cell. Once inside the cell, HIV begins replicating (Natural Standard, 2011).

The first stage of HIV, known as the primary or acute infection, is the most infectious stage of the disease, and it typically lasts several weeks. During this phase, the virus replicates rapidly, which leads to an abundance of the virus in the bloodstream and a drastic decline in the number of CD4 T-cells. The CD8 T-cells (cells that kill abnormal or infected body cells) are then activated to destroy HIV-infected body cells and antibodies are produced. An estimated 80-90% of HIV patients experience flu-like symptoms during this stage (Natural Standard, 2011).

The next stage, called clinical latency, may last anywhere from two weeks to 20 years. During this phase, HIV is active in the lymph nodes, where large amounts of the virus become trapped. The surrounding tissues, which contain high levels of CD4 T-cells, may also become infected. The virus accumulates in infected cells and in the blood as free virus (Natural Standard, 2011).

HIV infection progresses to AIDS when CD4 cell counts drop below 200 cells per microliter of blood. Healthy individuals have a CD4 cell count between 600 and 1,200 cells per microliter of blood. Individuals with a CD4 cell lower than 200 cells per microliter of blood have the greatest risk of developing opportunistic infections (Natural Standard, 2011).

Several different CD4 tests are used along with a viral load test to evaluate HIV/AIDS patients' medical conditions and monitor their responses to treatment. CD4 blood tests measure the amount of CD4 T-cells that are circulating in the blood, while viral load tests determine how many viral particles are present in the blood (NACP, 2005).

HIV patients who are otherwise healthy and symptom-free should have their CD4 cell count and viral load tested about two to four times a year. However, symptomatic patients should be tested more frequently to evaluate both the risk of opportunistic infections and the response to HIV drug treatments (Natural Standard, 2011).

2.12.0 SIGNS AND SYMPTOMS OF HIV INFECTION

Some people experience signs and symptoms of HIV as soon as they become infected while others do not. When they occur, early signs and symptoms are often mistaken for the flu or a mild viral infection. Initial signs and symptoms of HIV include (Arthur et al., 2007):

- Fever
- Headache
- Tiredness
- Nausea
- Diarrhea
- Enlarged lymph nodes in the neck, armpits or groin

An infected person may not experience severe symptoms for eight (8) to ten (10) years or more. This period – called asymptomatic period- varies in length for each person. Some people may have symptoms within a few months and others may be symptom free for years (NACP, 2010).

Late stage HIV infection is known as AIDS infection. Left untreated, HIV weakens the immune system so much that the body develops serious life – threatening condition. Possible symptoms of a serious infection caused by a damaged immune system include:

- Fever and sweats
- Herpes infection that cause severe mouth, genital or anal sores
- Lack of energy (persistent tiredness)
- Pelvic inflammatory disease in women who do not respond to treatment
- Persistent skin rashes or flaky skin
- Shingles
- Short – term memory loss
- Weight loss

AIDS agravating illnesses, such as tuberculosis, pneumonia, and some cancers may appear. Many of these, though serious, can be treated to some extent and some are likely to improve if treatment is started and Cluster of Differentiation 4 (CD4) count increases (NACP, 2010).

2.13.0 LABORATORY DIAGNOSIS

Clinical diagnosis of HIV infection is most often based on serological testing (blood test), with an indirect diagnostic method designed to reveal the presence of HIV antibodies in the patient's serum (WHO, 2007). There are two main types of HIV antibody tests. These are the enzyme linked immunosorbent assay (ELISA) which includes the rapid HIV test and the Western Blot Antibody Test which is more expensive but gives more accurate results (NACP, 2010).

Rapid HIV test usually produce test results in five to 30 minutes. Some of these tests do not require a blood sample from client. HIV test based on saliva is an alternative to blood based tests. Under special circumstances such as in recently infected individuals, a more direct diagnostic method may be used. The virologic test determines HIV infection by detecting the virus itself. There are three virologic tests (NACP, 2010). These are:

- Viral antigen detection test (also known as the p24 antigen test)
- Nucleic acid-based test (specialized test that look for genetic information on HIV polymerase chain reaction or PCR)
- Virus culture, which isolates the virus

Virologic test are rarely used to diagnose HIV in developing countries since they require sophisticated laboratories. They may however be used to monitor progress of infection or response to therapy (e.g. by measuring the viral load) (NACP, 2010)

2.14.0 TREATMENT

There is currently no cure for HIV infection. Treatment consists of Highly Active Antiretroviral Therapy or HAART (NACP 2001). This has been highly beneficial to many HIV infected individuals since its introduction in 1996, when the protease inhibitor-based HAART initially became available (Palella et al., 1998).

Current HAART regimens are a combinations consisting of at least three drugs belonging to at least two classes of antiretroviral drugs. These classes are two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) plus either a Protease Inhibitors (PIs) or a Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) (NACP, 2010).

New classes of drugs such as entry inhibitors provide treatment options for patients infected with viruses already resistant to common therapies, although they are not widely available and not typically accessible in resource limited settings. These drugs are very expensive and the patient needs to take for life (Department of Health 2005). As a result of HAART, mortality from HIV has declined continuously. However, the long term outlook remains uncertain (NACP 2010).

2.15.0 AREAS OF POTENTIAL OVERLAP BETWEEN HIV AND MALARIA INFECTIONS

With what we know of HIV infection, it is only natural that one expects a far poorer outcome for malaria infection in HIV patients. But on the contrary, the reports available indicate either no effect or even a protective effect of HIV infection against death from complications of *P. falciparum* malaria (Xiao et al., 1998).

Studies showed that although high level of malaria parasitemia has been observed in African children with symptomatic HIV infection, these children have been found to be 'protected' against cerebral malaria. This has been attributed to lower levels of Tumor necrosis factors (TNF) in HIV infected children. TNF is reported to have a potentiating effect on the endothelial adherence and clogging of microcirculation by parasitized red cells (Xiao et al., 1998). In an animal study using mice, murine AIDS was found to confer protection against the severity of neurological manifestations of experimental cerebral malaria and this protection was higher with longer duration of immunodeficiency. IL-10 from splenic cells was shown to play a crucial role in this protection (Kakkilaya et al., 2004).

In Africa, human immunodeficiency virus type-1 (HIV-1) infection is a serious emerging infectious disease, and *P. falciparum* malaria infection is the most prevalent infectious diseases. Studies to date have not demonstrated a direct, biologic association between HIV infection and *P. falciparum*; that is, malaria has not appeared as an opportunistic infection, nor does it accelerate progression of HIV related diseases. However, altered cell mediated immunity in HIV infected person could influence the frequency and course of malaria infection. Inadequate sample sizes and the cross sectional nature of previous studies might have limited their ability to adequately assess any interaction between the two infections. The one confirmed area of overlap reported was the increased risk of HIV transmitted through blood transfusion to persons with severe malarial anemia (Nahlen et al., 1996).

There are also evidence that T-cell function is impaired during acute episodes of malaria. Proliferate responses to a variety of antigens are depressed during acute episodes of malaria when assessed by tests carried out on peripheral blood mononuclear cells. It is possible, however, that this anergy is due in part to sequestration rather than depletion of competent cells. Of particular importance here is the observation that T-cell control over EB virus infection is lost transiently in children with acute falciparum malaria. Thus, one might expect malaria infection to have an adverse effect on HIV infection both by stimulating T-cell turn over and by impairing T-cell cytotoxic function. Malaria infection may damage the placenta in such a way as to facilitate transmission of HIV in-utero. There could as well be several other areas of interest to be assessed for potential overlap between these two illnesses.

- Safety and efficacy of anti-malarials: the high incidence of febrile episodes among HIV infected persons may result in greater exposure to anti-malarial drugs and thus a higher risk of adverse drug reactions, particularly to sulfonamides.
- Chloroquine as a cofactor for HIV replication: data from invitro studies indicate that chloroquine may be a cofactor for increased viral replication
- Malaria as a cofactor for HIV progression: malarial parasitemia and the released antigens may be a cofactor for increased viral load and subsequent progression of HIV related disease.
- HIV as a confounder in studies of malaria related mortality: the impacts of malaria control efforts on reduction of severe morbidity and mortality may be less than expected in areas where HIV prevalence is high.
- Malaria and HIV during pregnancy: recent studies indicate that HIV infected pregnant women are at increased risk of peripheral, placental, and cord blood parasitemia which may be a cofactor for mother to infant transmission of HIV and for earlier progression of HIV related disease, and that HIV impairs the efficacy of sulfadoxine-pyremethamine for control of placental parasitemia (Nahlen et al., 1996).

2.16.0 THE ASSOCIATION BETWEEN HIV AND MALARIA

A review of clinical studies in 1998 concluded that the numerous studies published to that date had failed to show any convincing and consistent link between HIV and malaria, with the exception of an increased rate of placental malaria in HIV-infected pregnant women. This

review included several cross-sectional, retrospective, and longitudinal studies conducted in urban hospitals or clinics in African children and adults, but many of these studies had potential bias or had small sample sizes .In addition, they did not take into account the wide variation in immunosuppression found at different stages of HIV-1 infection (Chandramhan, 1998).

Infection with HIV-1 causes progressive cellular immunosuppression, and any resulting impairment in the immune response to malaria might be associated with failure to prevent infection or to suppress parasitemia and clinical disease (Good, 1999).

On the other hand, *P falciparum* has been shown to stimulate HIV-1 replication through the production of cytokines (interleukin-6 and tumor necrosis factor-alpha) by activated lymphocytes (Migot 1996, Moore 2000).*P falciparum* also increases the potential reservoir for HIV in the placenta by increasing the number of $CCR5^{+}$ macrophages (Moore 2000). An important study from Malawi showed that HIV-1 plasma viral loads were significantly higher in patients with malaria infection than in those without, and these levels remained higher for up to 10 weeks after treatment. The increases in viral load were greatest in those with clinical malaria, high levels of parasitemia, and relatively low CD4 counts (Kublin et al., 2005). This study suggests that malaria may speed the progression of HIV disease, and this is supported by a study from Uganda showing increased CD4 cell decline associated with episodes of malaria despite prompt treatment. However, the true clinical impact of malaria on HIV progression remains to be determined (Mermin et al., 2006).

Clear evidence indicates an interaction between HIV-1 and malaria in pregnancy, causing

more peripheral and placental parasitemia, higher parasite densities, more clinical malaria, more anemia, and increased risks of adverse birth outcomes (Mwapasa et al., 2004). HIV-infected women remain susceptible to the effects of malaria whether or not they are pregnant. Placental HIV-1 viral load is increased in women with placental malaria, especially those with high parasite densities (Mwapasa et al., 2004).

The effect of malaria on mother-to-child transmission of HIV is unclear because published studies to date have given conflicting findings. It has been suggested that the discrepancy might be due to variations in maternal immunocompetence. That is, immunocompromised mothers have deranged chemokine and cytokine profiles, less protective immune responses, and consequently higher parasite densities and viral loads, leading to an increased risk of mother-to-child transmission of HIV (Ned, 2005).

Studies in men and nonpregnant women show that the underlying epidemiology and intensity of malaria transmission seem to be critical for determining the consequences of coinfection. In areas of stable malaria, transmission is intense and continuous, although seasonal variations may occur. Immunity develops early in life, and young children and pregnant women are at greatest risk of morbidity and mortality from malaria. In malaria endermic areas, HIV-related immunosuppression may increase rates of malaria infection and clinical malaria disease, but does not increase the rates of severe or complicated malaria (French 2001, Francesconi 2001).

The odds of parasitemia and risk of malarial fever increase with decreasing CD4 count and increasing viral load. These findings suggest that HIV infection not only may interfere with parasite control, but also, perhaps more important, may cause the loss of antitoxic immunity,

which protects persons with parasitemia from clinical disease (Cohen, 2005). In regions of unstable malaria, transmission is intermittent and less predictable, and epidemics may occur. The disease burden is similar in all age groups because preexisting antimalarial immunity is limited. As a result, malarial fever rates are a direct function of parasite transmission rates. Thus, HIV coinfection has its impact on disease presentation, with an increased risk of complicated and severe malaria and death (Greenberg, 1991).

A study in rural Kwazulu-Natal, an area of unstable malaria, reported that HIV-infected children were more likely to experience severe disease, coma, and death (Grimwade, 2003).More data are required to document any significant malaria and HIV interactions in children.

2.17.0 RESPONSE TO TREATMENT AND DRUG INTERACTIONS

Antimalarial therapy is most effective in individuals who have acquired some immunity to malaria. One would predict, therefore, that the response to therapy would be decreased in immunocompromised HIV-infected individuals living in regions of stable transmission. Early study in the Democratic Republic of Congo (formerly Zaire) found no difference in responses to antimalarial treatment in HIV-infected children compared with uninfected children (Greenberg, 1991).

More recent studies suggested that treatment with artemisinin, sulfadoxine-pyrimethamine (SP), and artemether-lumefantrine was less effective in HIV-infected than in uninfected men and nonpregnant women (Shah et al., 2004, Van et al., 2004). However, investigators in

Uganda used molecular genotyping of malaria parasites to demonstrate that the increased clinical treatment failure rate for malaria seen in HIV-infected adults is due to a higher frequency of new infections rather than recrudescence of existing infections (Kamya et al 2006).

No information is available on the most effective antimalarial therapy for HIV-infected individuals, although case reports of travelers suggest that the effectiveness of chemoprophylaxis may be reduced in this group (Nathoo et al., 2003). Interactions between antimalarial drugs and antiretroviral drug therapy (ART) mostly involve protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs) .Most ART guidelines do not consider PIs as part of first-line regimens, but they are included in second-line therapy. The antimalarial drugs halofantrine, artemether, and lumefantrine should not be given to patients receiving PIs (or the NNRTI delavirdine) because of excessive risk of toxicity (Skinner-Adams et al., 2000). For patients receiving other NNRTIs (nevirapine or efavirenz), drug-drug interactions may reduce the concentrations of lumefantrine and artemether, thereby increasing the risk of treatment failure (Skinner-Adams et al., 2000). An interaction may also occur between quinine and NNRTI or PI drugs. However, the magnitude and clinical significance of these potential interactions need further research (Khoo, 2005).

CHAPTER THREE

3.0.0 SUBJECTS AND METHODS

3.1.0 STUDY DESIGN

The study was cross sectional. HIV sero-positive patients who attend ART Clinic of the Holy Family Hospital- Techiman were randomly selected to participate in the study.

3.2.0 STUDY AREA AND PERIOD

The study was conducted in Techiman municipality, between November 2011 and January 2012. The study area, Techiman, is a strategically situated junction town in Brong Ahafo region linking not only to most of Ghana's major commercial centres, but also to the republics of Togo, Burkina Faso and Cote D'Ivoire. It has an estimated total land area of about 669.7 square kilometers.

The municipality shares local boundaries with Wenchi municipality to the west, Sunyani West and Offinso North Districts to the south, Kintampo South District to the north and Nkoranza South District to the east.

According to the 2000 population and housing census, the population of the municipality was estimated to be 202,409 by December 2005, with an average growth rate of 3.0% per annum. The major economic activities in the municipality are agriculture and related trade. Over half of the economically active population is engaged in this activity. The major crops grown are food crops such as yam, maize,

cassava, cocoyam, plantain, and vegetables like tomatoes, garden eggs, onions and okro as well as cash crops like cocoa, cashew and mango. This has made the municipality of its Techiman market, the largest food crop market in Ghana and a major commercial centre in the Brong Ahafo region.

The municipality has twenty four (24) health care facilities; including two (2) mission hospitals at Techiman, that is Holy Family Hospital and Ahamadiya Hospital, nine (9) government health centers, four (4) private maternity clinics and (3) private clinics.

3.3.0 SOURCE AND STUDY POPULATION

The study was conducted in Holy Family Hospital since it is the only hospital in the municipality that provides ART services to HIV patients. The hospital has bed capacity of 167 beds and is owned by the Catholic Diocese of Techiman and is part of the National Catholic Health Services (NCHS). The hospital is also a member of the Christian Health Association of Ghana (CHAG).Patients diagnosed to have HIV/AIDS infection and who sought treatment at ART clinic at the Holy Family Hospital were the source population for the study.

3.4.0 ETHICAL CONSIDERATIONS

The study was conducted after a proposal was approved by the Committee on Human Research Publication and Ethics from Kwame Nkrumah University of Science Technology. Before conducting the survey, written permission was obtained from Holy Family Hospital - Techiman. All the study participants were briefed on the purpose and

benefit of the study and permission was orally obtained in advance from each patient. They were assured that any information concerning them would never be used by any individual or institution in any way identifying their personal identity. To keep anonymity, every participant was given a unique identifier code number and only this code numbers were attached to the questionnaires and test tubes. During data entry and analysis, only these codes which were used to draw associations and conclusions about the study population. Refusal of a patient to participate in the study did not interfere with the routine care at the hospital. Those who refused to be involved in the study were managed according to the routine procedures in the hospital.

3.5.0 SAMPLE SIZE

A total of 400 HIV sero-positive individuals were involved in the study. The sample size was determined by using the formula from U.S. Department of Health and Human Services. (http://bphc.hrsa.gov/policiesregulations/performancemeasures/patientsurvey/calculating.html):

Sample size = n/ [1+ (n/population)] in which $n=Z^2$ [P (1-P)/D^2]

Z=confidence level at 95% (standard value of 1.96)

P=expected frequency value. If no information is available P should be assumed to be 0.5.

D=margin of error of 5% (standard value of 0.05)

Therefore, $n=1.96^2[0.5(1-0.5)/0.05^2] = 384.16$

By substituting n=384.16 in the sample size equation in which population has been recorded to be 1419 (number of registered HIV/AIDS patients attending ART clinic as at December 2010) Sample size = 384.16/ [1+ (384.16/1419)]=302.32. This represents the minimum study participants. However to achieve an even distribution results for the study a total of 400 participants were involved in the study. All HIV patients who sought care at the ART unit of the hospital and were willing to participate in the study were included until the required sample size was attained.

3.6.0 STRUCTURED QUESTIONNAIRE

A questionnaire, in both English and the local language (Twi) which included the basic socio- demographic of the study subjects as well as their knowledge and prevention towards malaria was used (Annex Two). No personal identifiers were included and individuals were given a unique code number attached on the questionnaire and their laboratory specimens (test tubes).

3.7.0 LABORATORY TEST

Malaria parasite: laboratory investigation was done by using Giemsa stained thick blood film method. A drop of blood, 3-5mm in diameter was put on a slide and spread with the corner of another slide to form a thick blood smear. The smear was thoroughly allowed to dry and stained with Giemsa stain for 10-15 minutes. The stained smear was washed with running tap water, allowed to air dry and was examined microscopically for detection of malaria parasite.

Test to determine HIV infection:

HIV test was done using First Response HIV Card Test 1-2.0 manufactured by Premier Medical Corporation Limited and Oraquick Rapid HIV – ½ Antibody Test manufactured by OraSure Technologies, Inc. Both test kits are immunochromatographic (rapid) test for the qualitative detection of antibodies specific to HIV in human serum, plasma or whole blood. However oralquick Rapid HIV – ½ Antibody test kit can detect HIV antibodies in mucosal fluid. The First Response HIV Card Test 1-2.0 was used as the first line test. Reactive blood samples were then confirmed with the Oraquick Rapid HIV – ½ Antibody Test.

CD4 count test and Haemoglobin concentration

The CD4 count and haemoglobin concentration of the study population was estimated by *Becton, Dickinson (*BD) FASCount machine manufactured by BD Biosciences and sysmex xt – 2000i haematology analyzer manufactured by Sysmex Corporation respectively.

CHAPTER FOUR

4.0.0 RESULTS

4.1.0 SOCIODEMOGRAPHIC CHARACTERISTICS

A total of 400 HIV sero-positive patients between 1year 8months – 73 years were included in the study. Of these 292 (73%) were females and the rest 108 (27%) were males. The female to male ratio was 1:0.40. Twenty percent of the respondents were 30-34 years old. The mean (SD) age of the patients was 34.5 (12.2) years with a median age of 34 years. Most patients were married (38%) followed by the bachelors and spinsters (35 %). The rest 27% were either widowed or divorced. (Table1).

One hundred and ninety eight (49.5%) of the patients were unemployed and 123 (30.75%) were farmers. The employed patients were traders 49 (12.25%); skilled workers (carpenters, fitters, hairdressers, seamstresses) 18 (4.5%). The rest 12 (3.0%) were laborers, merchants and government employees and drivers. About 37.8% (151) of the patients had no formal education. Whereas 62.2 % (249) had various levels of formal education either primary school (24.5%), junior high school / O-level (25.8%) senior high school/ A-level (9.0%) and above (3.0%) (Table1).

Table 1: Socio-demographic characteristics of patients

Variable	Frequency (NO.)	Percentage (%)
Sex		
Male	108	(27)
Female	292	(73)
Age (years)		
0-4	12	(3.00)
5-9	2	(0.50)
10-14	9	(2.25)
15-19	5	(1.25)
20-24	32	(8.00)
25-29	66	(16.50)
30-34	81	(20.25)
35-39	78	(19.50)
40-44	40	(10.00)
45-49	43	(10.75)
50-54	21	(5.25)
55-59	6	(1.50)
Above 60	5	(1.25)
Marital Status		

Married	152	(38)
Single	140	(35)
Divorced/Widowed	108	(27)
Literacy Status		
No formal education	151	(37.8)
Primary education	98	(24.5)
JHS/O-Level	103	(25.8)
SHS/A-Level	36	(9.0)
Tertiary	12	(3.0)
Occupation		
Unemployed	198	(49.50)
Farmers	123	(30.75)
Traders	49	(12.25)
Skilled	18	(4.50)
Others	12	(3.00)

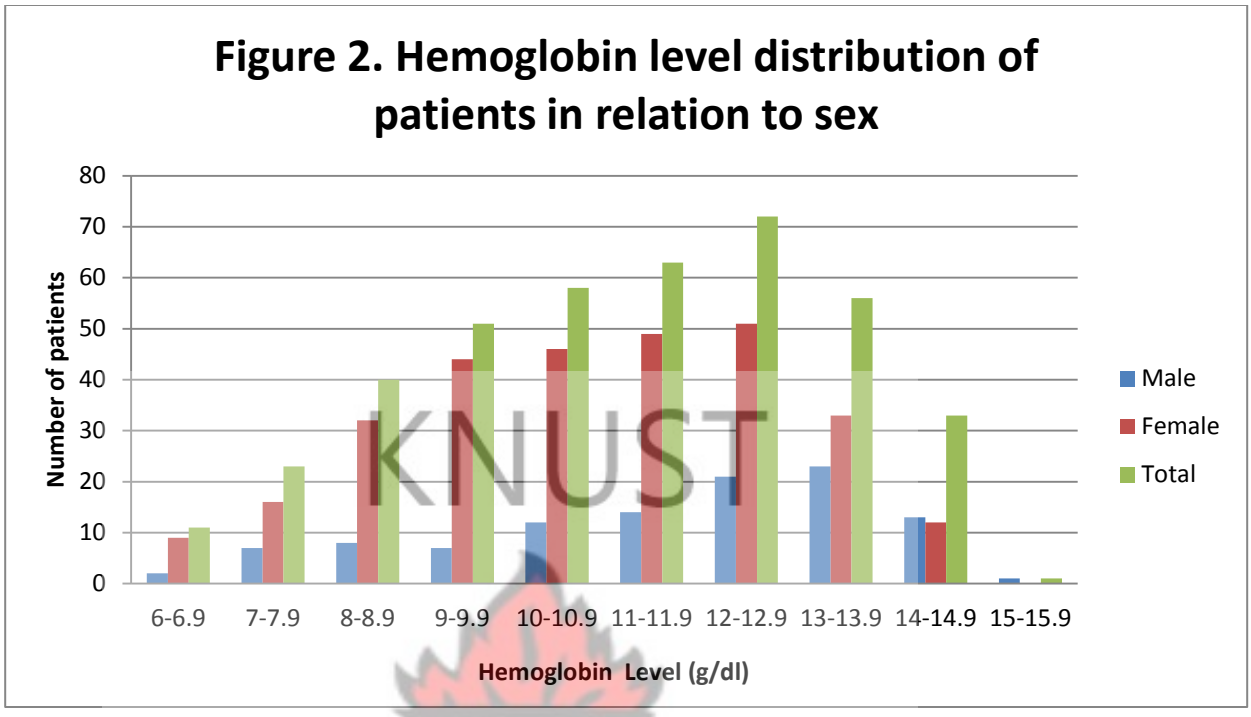
4.2.0 HEMOGLOBIN LEVEL OF PATIENTS

Hemoglobin (Hb) concentration levels of the patients were between 6.4 and 15.4 g/dl with majority (18.0%) of patients having Hb levels in the range of 12-12.9g/dl. The mean (SD) Hb level of the patients was 10.8g/dl (2.26) with mean (SD) for male and female as 11.5g/dl (2.26) and 10.56 g/dl (2.22) respectively (Table 2).

Using the World Health Organization (WHO) definition for anemia as hemoglobin levels less than 13.0g/dl in adult men and hemoglobin levels less than 12.0g/dl in adult women, an overall prevalence of 67% (268 out of 400) anemia was observed in this study. Majority of patients had mild to moderate anemia. Mild to moderate anemia was detected in 64% of patients while severe anemia was observed in 2.8% of patients. There was no significant difference in prevalence of anemia among males and females. Prevalence of anemia in males and females were 66.7% (72 out of 108) and 67.1% (196 out of 292) P=1.000.

Table 2: Hemoglobin level of patients in relation to sex

HAEMOGLOBIN (g/dl)	Male	Female	Total
	Frequency (%)	frequency (%)	frequency (%)
6-6.9	2 (1.9)	9 (3.1)	11 (2.75)
7-7.9	7 (6.5)	16 (5.4)	23 (5.75)
8-8.9	8 (7.4)	32 (11.0)	40 (10.0)
9-9.9	7 (6.5)	44 (15.1)	51 (12.75)
10-10.9	12 (11.1)	46 (15.8)	58 (14.50)
11-11.9	14 (13.0)	49 (16.8)	63 (15.75)
12-12.9	21 (19.4)	51 (17.4)	72 (18.00)
13-13.9	23 (21.3)	33 (11.3)	56 (14.00)
14-14.9	13 (12.0)	12 (4.1)	25 (6.25)
15-15.9	1 (0.9)	0 (0.00)	1 (0.25)

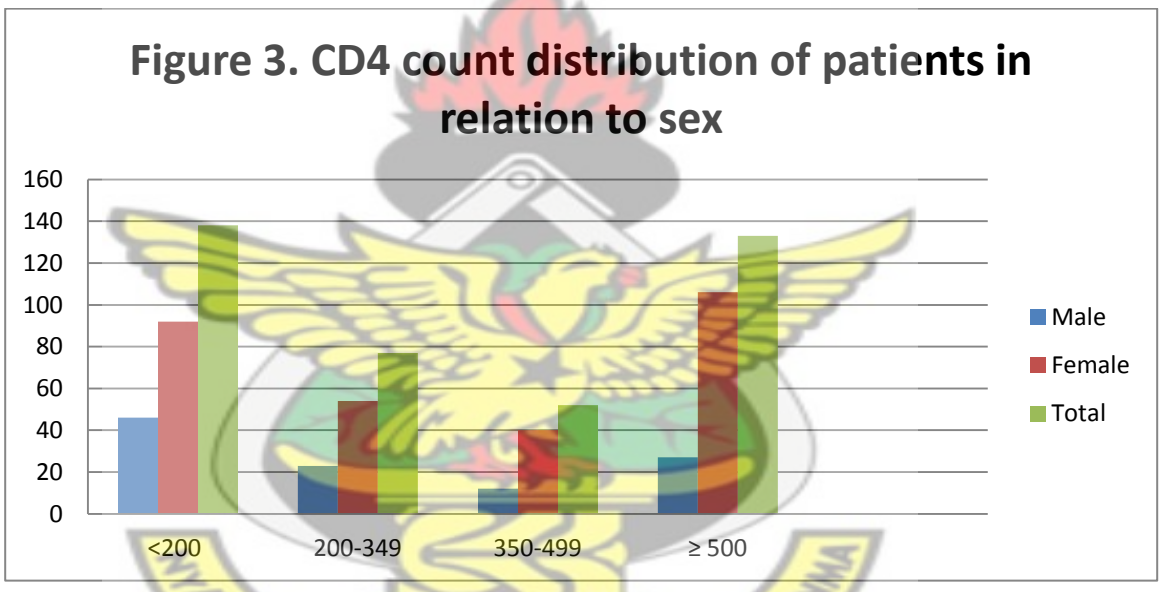


4.3.0 CD4 COUNT OF PATIENTS

All patients studied had a CD4 cell count ranging from 3 – 1604 cells/µl. The mean (SD) CD4 cell count of the patients was 386.2 (274.3) cells/µl. Males and females had CD4 count mean (SD) of 345.7 (270.1) cells/µl and 386.1(276.0) cells/µl respectively. CD4 cell count of less than 200 cells/µl (signifying the terminal stage of HIV infection (AIDS) was observed in 34.5% (138 out of 400) patients. Out of the 400 patients, 77 of them (19.25%) had CD4 cell count between 200-349 cells/µl and 13.00% (52 out of 400) patients had CD4 cell count between 350 – 499 cells/µl. The rest 33.25% (133 out of 400) patient had CD4 count greater than500 cells/µl (Table 3).

Table 3: CD4 count distribution of patients in relation to sex

CD4 COUNT	Male Frequency (%)	Female Frequency (%)	Total Frequency (%
<200	46 (42.6)	92 (31.5)	138 (34.50)
200-349	23 (21.3)	54 (18.5)	77 (19.25)
350-499	12 (11.1)	40 (13.7)	52 (13.00)
≥ 500	27 (25.0)	106 (36.3)	133 (33.25)



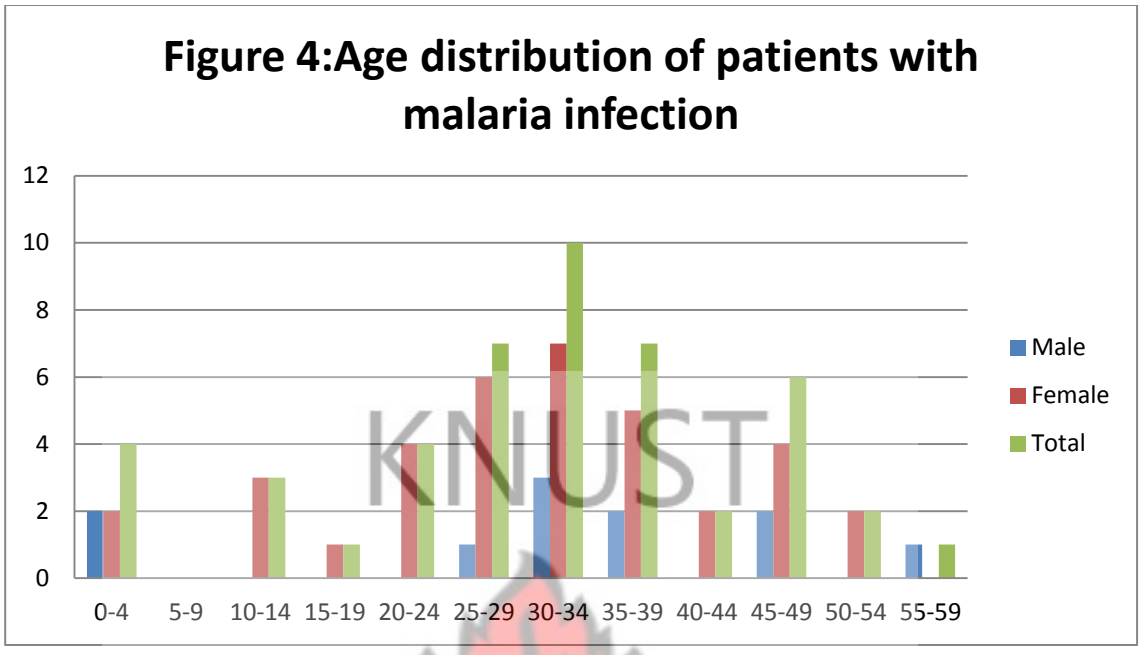
4.4.0 PREVALENCE OF MALARIA

Among the 400 patient screened for malaria parasites, 47 (11.75%) patient were found to be slide positive for malaria parasite with ages ranging from 2 years to 56 years. Malaria positivity was mostly within the age range of 30-34 years, followed by those in the age ranges of 25-29 years and 35-39 years. The least infected malaria patients were within the age ranges of 15-19years and 55-59 years (Table 4).

On the basis of sex, females had the highest prevalence of malaria compared with their male counterparts. However there was no statistically significant difference in the prevalence rate for female (12.1%) and males (10.2%), P = 0.6047.

Table 4: Age distribution of patients with malaria infection

Age (%)	Male Frequency (%)	Female Frequency (%)	Total Frequency
0-4	2 (18.2)	2 (5.6)	4 (8.5)
5-9	0 (0.0)	0 (0.0)	0 (0.0)
10-14	0 (0.0)	3 (8.3)	3 (6.4)
15-19	0 (0.0)	1 (2.8)	1 (2.1)
20-24	0 (0.0)	4 (11.1)	4 (8.5)
25- 29	1 (9.1)	6(16.7)	7 (14.9)
30-34	3 (27.3)	7 (19.4)	10 (21.3)
35-39	2 (18.2)	5 (13.9)	7 (14.9)
40 – 44	0 (0.0)	2 (5.6)	2 (4.2)
45- 49	2 (18.2)	4 (11.1)	6 (12.8)
50-54	0 (0.0)	2 (5.6)	2 (4.2)
55-59	1 (9.1)	0 (0.0)	1 (2.1)
TOTAL	11 (23.4)	36 (76.6)	47



4.5.0 MALARIA INFECTION AND HEMOGLOBIN LEVEL

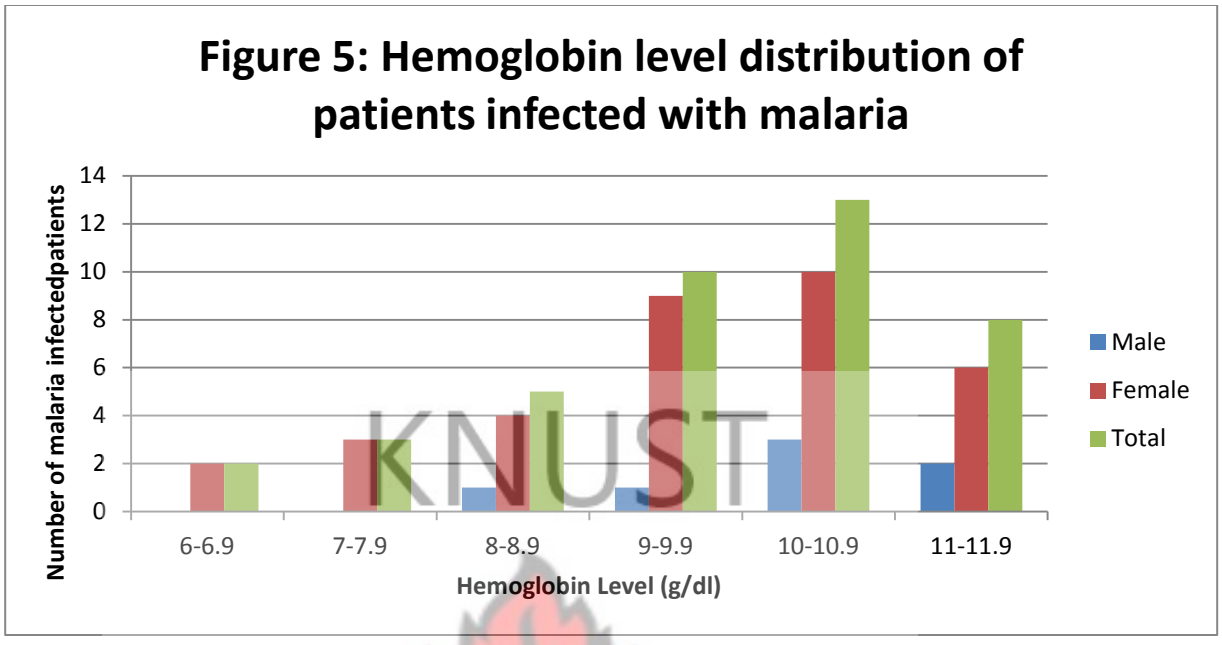
The overall mean (SD) hemoglobin level of the study participants who had malaria infection was 9.9g/dl (1.613) .The hemoglobin level range was from 6.2g/dl to 13.2g/dl. Most of the study participants with malaria infection (13 out of 47) had hemoglobin level between the ranges of 10.0g/dl-10.9g/dl. Ten out of 47 the participants with malaria infection had hemoglobin level between 9.0g/dl-9.9g/dl and 8 out of 47 had hemoglobin level between 11.0g/dl -11.9g/dl. Only one participant with malaria infection had hemoglobin level of 13.2g/dl (Table 5).

Almost all the study participants with malaria infection were anemic. The prevalence of anemia among them was 93.6% (44 out of 47). There was no significant difference in prevalence of anemia with respect to sex. The prevalence of anemia with respect to sex was 90.9% and 94.4% for males and females respectively. Majority of the subjects with

malaria infection 45 (89.4%) had mild to moderate anemia with only 4.3% (2 out 47) having severe anemia. Severe anemia was observed in only females.

Table 5: Haemoglobin level distribution of patients infected with malaria

Hemoglobin	Frequency	Male	Female	P-value
6-6.9	2	0	2	0.4667
7-7.9	3	0	3	0.4643
8-8.9	5	1	4	0.5804
9-9.9	10	1	9	0.0485
10-10.9	13	3	10	0.1693
11-11.9	8	2	6	0.3875
12-12.9	5	3	2	1.0000
13-13.9	1	1	0	1.0000
Total	47	11	36	



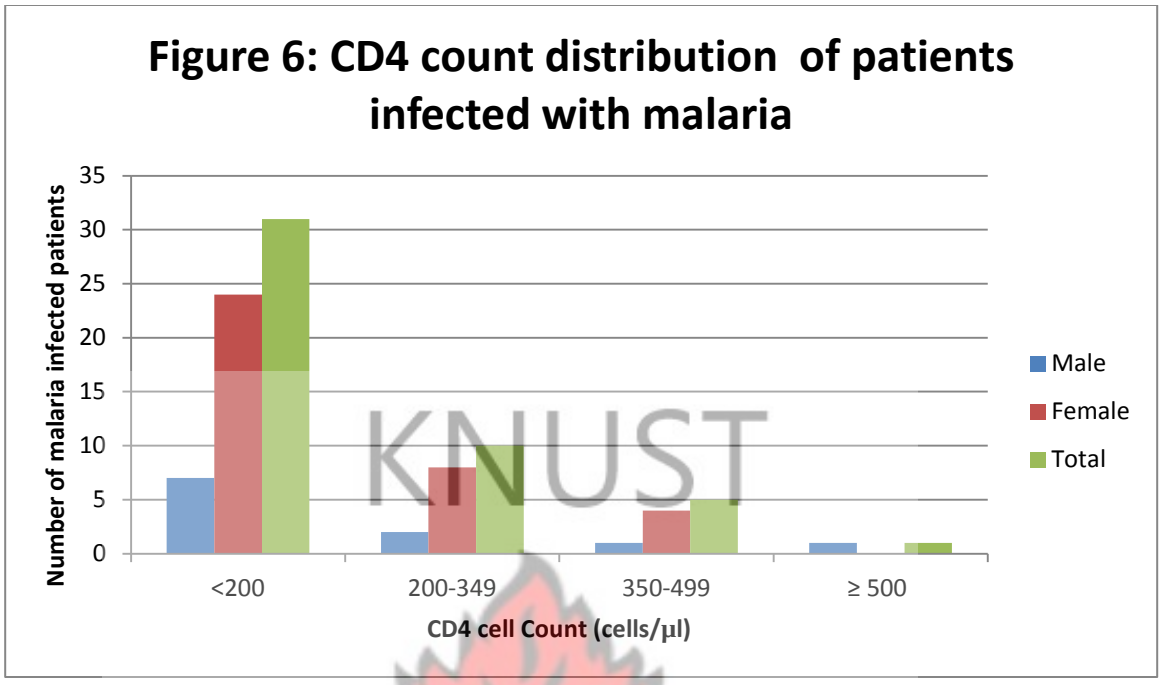
4.6.0 Malaria infection and CD4 count

All patients with malaria infection had CD4 cell count ranging from 3 cells/µl to 512 cells/µl with mean (SD) CD4 cell count of 186.3 (133.5) cell/ul. Males and females with malaria infection had CD4 count mean (SD) of 209 (198.4) cells/µl and 178.7 (110.8) cells/µl respectively. CD4 cell count less than 200 cells/µl was observed in 66.0% (31 out of 47) of patients infected with malaria. With respect to sex, 63.6% (7 out of 11) males infected with malaria infection and 66.7% (24 out of 36) females infected with malaria infection had CD4 cell count less than 200 cells/µl. 21.3% (10 out 47) patients with malaria infection had CD4count in the range of 200 cells/µl – 349 cells/µl. CD4 count in the range of 200 cells/µl – 349 cells/µl was observed for 18.2% (2 out of 11) and 22.2% (8 out 36) males and females with malaria infection had. Further 10.6% (5 out of 47) patients with malaria infection had CD4count in the range of 350 cells/µl –499 cells/µl. 9.1% (1 out of 11) males and 11.1% (4 out 36) females

patients infected with malaria had CD4 cell count in the range of 350 cells/µl –499 cells/µl. 2.1% (1 out of 47) patient with malaria infection had CD4 cell count greater than or equal to 500 cells/µl and was observed in only males (Table 6).

Table 6: CD4 cell count distribution of patients infected with malaria

CD4 COUNT	Frequency (%)	Male Frequency (%)	Female Frequency (%)	P-value
<200	31 (66.0)	7 (63.6)	24 (66.7)	0.0140
200-349	10 (21.3)	2 (18.2)	8 (22.2)	0.2353
350-499	5 (10.6)	1 (9.1)	4 (11.1)	0.5804
≥ 500	1 (2.1)	1 (9.1)	0 (0.0)	1.0000
Total	47	11	36	



4.7.0 KNOWLEDGE OF MALARIA TRANSMISSION AND PREVENTION

Three hundred and seventy seven of the study participants (participants above15years) were interviewed on malaria transmission and prevention. Three hundred and twenty eight (87.0%) out of 377 of the participants claimed they have knowledge about malaria infection. Out of the 328 respondents that claimed to have knowledge about malaria, 216 (65.9%) claimed that malaria could be transmitted from an infected person to a healthy person and the rest 112 (34.1%) claimed that either malaria cannot be transmitted from person to person or they had no idea at all. Among those who claimed that malaria is transmissible (n=216), 197(91.2%) reported mosquito bite as a means of transmission followed by respiratory route 24(11.1%), and bodily contact 13(3.4%).The remaining 28 (13.0%) reported that malaria can be transmitted through various ways like flies, and dirty water (Table 7).

About 92.7% (304) of study participant who claimed to have knowledge about malaria reported that malaria is preventable. The most frequently mentioned method of prevention was environmental sanitation 286 (94.1%) followed by taking antimalarial tablets 238(78.3%), bed nets 231(76.0%) and mosquito repellent 196 (64.5%). The remaining 87(28.6%) reported various other methods like traditional cotton clothes, smoke and good diet. With usage of bed net, only 32 (8.5%) participants out of 377 of the participants interviewed on knowledge on malaria use bed net (Table 7).

Table 7: Knowledge of Malaria Transmission and Prevention

Variable	Frequency (%)
Knowledge about malaria (n =377)	
Yes	328 (87.0)
No	49 (13.0)
Malaria transmissible? (n=328)	
Yes	216 (65.9)
No	112(34.1)
Means of malaria transmission (n =216)	
Mosquito bite	197 (91.2)
Body contact	13 (3.4)
Respiratory route	24 (11.1)
Others	28 (13.0)
Malaria is preventable (n = 328)	

yes		304 (92.7)
no		24 (7.3)
Preventive methods	(n =304)	
Antimalarial tablets		238 (78.3)
Bed nets		231 (76.0)
Mosquito repellents		196 (64.5)
Environmental sanitation		286 (94.1)
Others		87 (28.6)
Use of bed nets	(n = 377)	
Yes		32 (8.5)
No		345 (91.5)

CHAPTER FIVE

5.0.0 DISCUSSION

The determination of malaria HIV co-infection rate is important because there are hypotheses and even study reports on the possible association between the two infections (Chandramhan et al 1998, Nahlen et al 1996). If this is the case, knowing the magnitude of the problem will have many practical implications especially in countries where both diseases are leading causes of morbidity and mortality. For example, the decision to integrate or not to integrate resources against HIV and malaria, as was for TB and HIV, will depend on sound evidence. Assessment of the knowledge and attitude and practice of patients towards malaria and HIV related risk factors also will help in planning intervention activities for the prevention of these problems in the community. The study also serves comparative data for similar future studies.

In this study, the prevalence of malaria infection among HIV sero-positve patients was 11.75% which is higher than previous studies in South Africa and Mozambique (Cohen et al 2005, Aase et al 2008).This prevalence is relatively same as a study done in Southeastern part of Nigeria in which the prevalence of malaria as a co-infection amongst asymptomatic HIV sero positive patients was 11.8% (Onyenekwea 2007).The prevalence of malaria in this, and other studies, points to an important interaction between HIV and malaria; especially in our setting where a large population of severely immunodeficiency patients and endemic malaria coexist. Malaria is known to cause an increase in transitory viral load while HIV causes more clinical malaria, higher

parasitemia and higher rates of treatment failure in co-infected patients (Kamya et al 2006).

Females had the highest prevalence of malaria infection (12.1%), compared with their male counterparts who had prevalence of 10.2%. The high prevalence of malaria infection in females could be attributed to their social behavior such as dressing code, which in most cases involves sleeveless blouse and short skirt, thereby exposing parts of their body to mosquito attack. Females often stay out late during mosquito biting hours carrying out domestic activities. The finding agrees with that of Warren et al 1992, who observed that females are at higher risk of malaria infection compared to their male counterparts.

Also, among the various age groups, it was revealed that the age 30-34 years had more of malaria parasitic infection than the other age groups and this was also confirmed with the high cumulative density index. However, prevalence of malaria infection was high in children within the age group of 0-4 years in which out of 12 patients, 4 patients representing 33.3% had malaria infection. This strongly agrees with study by Onifade et al 2007 in which prevalence of malaria infection in HIV children was high. However Kwaku P. Asante et al 2011 reported different figure of 22.8% prevalence of malaria among non HIV children under five years in the Ahafo area of Ghana.

The susceptibility of children to malaria infection could be attributed to their low immune statuesque, which in this context might be due to HIV infection, which has

degenerative effect on the immune system (Moormann 2009). It can also be attributed to the non-challant altitude of their parent toward them, which may be direct consequence of poverty or inadequate knowledge about the mode of transmission. This is supported by Asante et al., 2011.

The mean (SD) CD4 cell count of the patients was 386.2 (274.3). Males and females had CD4 count mean (SD) of 345.7(270.1) cells/µl and 386.1(276.0) cells/µl respectively. The difference in the mean CD4 count is due to the fact that HIV infection is detected earlier in females than their male counterparts. With the introduction of Prevention of Mother -To- Child Transmission of HIV (PMTCT) programme, women of child bearing age are screened for HIV infection during antenatal care or at obstetrics and gynecology clinics. Those who test positive are then incorporated into ART clinics while there is no similar program for males for the early detection of HIV.

CD4 cell count less than 200 cells/µl (signifying the terminal stage of HIV infection (AIDS) was seen in 34.5% patients. Obviously the major reason for this high proportion of AIDS is because of late presentation, largely due to the fact that we are yet to imbibe the culture of voluntary screening for early detection and treatment. Fear of stigmatization, lack of awareness and inadequate trained counseling personnel are some of the factors militating against voluntary screening. Many patients only seek medical attention and are diagnosed when HIV infection becomes complicated by AIDS defining illnesses.

Majority of the patients (66.0%) with malaria infection had CD4 cells count less than 200 cells/µl. This can be attributed to the well establishment that CD4+ T lymphocyte cells <200 cells/µl is associated with a higher risk of opportunistic infection and poor disease progression (Cohen et al 2005).

Anemia is a frequent complication of infection with the human immunodeficiency virus, and could be clinically important. Multifactorial origin of anemia complicates determining its original cause and/or its proper treatment **(**Asante et al., 2011**).**

Using hemoglobin level of less than 13.0g/dl and 12.0g/dl as the cutoff point for anemia in males and females respectively, the overall prevalence of anemia among the patients was 67%. The prevalence of anemia in this study is comparable with other studies (approximately 70%) (Patrick et al 1998, Frontiera et al 1987) .The incidence of anemia was strongly and consistently associated with the progression of HIV disease as measured by diagnosis of an AIDS-defining opportunistic illness and measurement of a CD4 count of 200 cells/µl. This association is most likely explained by the increasing viral burden as HIV disease progresses, which could cause anemia by increased cytokine mediated myelosuppression which impair erythropoiesis. Also several opportunistic organisms like *Mycobacterium tuberculosis*, *Histoplasma*, *Cryptococcus*, *Coccidiodes*, *Pneumocystis carinii*, and *Leishmania* have been shown to infiltrate the bone marrow and disrupt erythropoiesis (Hambleton 1996). Alternativly anemia may be a surrogate marker for some aspect of disease progression not captured by controlling for CD4 count and clinical AIDS diagnosis. Several drugs used to combat HIV and its

complications may contribute to the anemia that is seen in HIV infection. The administration of Zidovudine is recognized to cause anemia because of myelosuppression (Patrick et al 1998).

Males and females did not show significant difference in the prevalence of anemia. Different studies have reported increase prevalence of anemia in females than males which were largely attributed to menstrual blood loss and to the drains on iron stores that occur with pregnancy and delivery (Meidani et al 2012). However in this study, it was revealed that most males report to the ART clinic late by which HIV infection without antiretroviral therapy in the vast majority of infected males has progressively destroyed the immune system leading to opportunistic diseases and other condition that lead to anaemia in HIV infection has advanced.

Majority of the HIV patients with anemia were mild to moderate anemia with few patients (2.75%) with severe anemia. This is in agreement with studies by Meidani, et al 2012 and Patrick et al 1998 where mild to moderate anemia was observed in majority of HIV patients with anemia in their studies. It was revealed that almost all the patients with malaria infection were anemic. This could be as a result of the clearance and/or destruction of infected RBCs, the clearance of uninfected RBCs, erythropoietic suppression and dyserythropoiesis as reported by Lamikanra et al 2007.

About 87 % of the patients who responded to the questionnaire using English and the local language (Twi) reported that either they knew or had heard of the occurrence of malaria in their area of residence. This is an indication that the area selected for the study is malarious and known to have malaria transmission. More than half (65.9 %) of the respondents who claimed to know or have heard of malaria, reported malaria to be transmissible. The rest (34.1%) reported that malaria cannot be transmitted from infected person to healthy ones or they have no idea about it at all. Among those who knew that malaria is transmitted, 91.2 % reported mosquito bite as a means of transmission. These findings are consistent with the findings of Matta et al 2004.

These are encouraging results and show the presence of a better knowledge in the method of malaria transmission however despite good knowledge about malaria transmission, this study also revealed evidence of knowledge gaps about malaria by some respondents misconception that that malaria is transmitted through drinking contaminated/unboiled water, eating contaminated food, staying in the sun and working in rain.

Over 92.0% of the patients in this study reported that malaria is preventable. Over 75% of the patients who reported malaria is preventable stated taking tablets and use of bednets as methods of malaria prevention however only 8.5% use bednets. This is in conformity with study by Matta et al 2004, in which of 51 respondents who were aware of mosquito net as preventive measure for malaria, only 10.5% were using mosquito nets. Discomfort, primarily due to heat, and perceived (low) mosquito density were the

most widely identified reason for non-use of mosquito net. There were concerns by respondents about higher prices of mosquito nets to the extent of not being affordable by some respondents.

CONCLUSION

From the above results and discussion, it could be concluded that:

- Prevalence of malaria infection among HIV positive patients was 11.75%. This points to an important interaction exist between HIV and malaria
- Females had the highest prevalence of malaria (12.1%) compared to their male counterparts(10.2%) however there was no significant difference in the prevalence of malaria with respect to sex P = 0.6047.
- Children were most venerable to malaria infection
- Malaria infection was high in HIV positive patients with CD4 count less than 200 cells/µl.
- Mild to moderate anemia was frequent in HIV positive patients but severe anemia was not prevalent in the study population
- Almost all study participants with malaria were found to be anemic. This confirms the association between malaria and anemia

RECOMMENDATIONS

- Due to high mortality rates associated with malaria infection in an endemic area, it may be necessary that routine malaria screening be adopted as part of the management policy to check the co-infection since similar screening is currently being carried out for TB and hepatitis B virus in HIV patients.
- Strategies to reduce malaria morbidity and mortality must reinforce the development of effective programs for malaria chemoprophylaxis.
- Appropriate health education on malaria transmission and prevention methods including ITN promotion should be provided.
- This study underscores the continuing importance of monitoring for anemia and maintaining normal hemoglobin levels as a treatment goal in HIV patients as component of ART.
- The findings from this study have provided additional baseline information on the burden of malaria and HIV co infection in Ghana. Further studies should be done in the area with a relatively improved study designs and methodologies, which employ follow up for outcomes of treatment

REFERENCE

Aase B**,** Sam P**,** Nina L and Bjorn B. (2008). **'**Falciparum malaria and HIV-1 in hospitalized adults in Maputo, Mozambique: does HIV-infection obscure the malaria diagnosis?' *Malaria Journal* 7**:**252.

Amman A and Burrowes S. (2007). 'Malaria and HIV: The impact on pregnant woman and infant's'. *Women's UN Report Network*. Available at: http://www.womenchildrenhiv.org/wchiv?page=tp-02-05 (Accessed: 20 November 2011).

Anonymous. (2000). WHO Expert Committee on Malaria. World Health Organisation Technical Report series; 892:1-5.

Asante P K, Zandoh C, Dery D B, Brown C, Adjei G, Antwi-Dadzie Y, Adjuik M, Tchum K, Dosoo D, Amenga-Etego S, Mensah C, Owusu-Sekyere K B, Anderson C, Krieger G and Owusu-Agyei S. (2011) 'Malaria epidemiology in the Ahafo area of Ghana'. *Malaria Journal*, 10:211.

Barat LM, Palmer N, Basu S, Worrall E, Hanson K, Mills A.. (2004) 'Do malaria control interventions reach the poor? A view through the equity lens'. *Am J Trop Med Hyg* . ; 71(2supply): 174-8. Review

Beaver PC, Jung RC. (1985) Animal agents and vector of human disease, 5th Edition Philadelphia Lea & Febiger.

Bisoffi Z, Gobbi F, Angheben A, Van den Ende J**.** (2009). 'The Role of Rapid Diagnostic Tests in Managing Malaria'**.** *PLoS Med*;6(4)

Bretlinger PE, Behren CB, Micek MA. (2006). 'Challenges in the concurrent management of malarial and HIV in pregnancy in sub-Saharan Africa'. *Lancet Infect Dis*. 6(2):100-11.

Brian M. Greenwood, David A. Fidock, Dennis E. Kyle, Stefan H.I. Kappe, Pedro L. Alonso, Frank H. Collins, Patrick E. Duffy. (2008). 'Malaria: progress, perils, and prospects for eradication'. *J. Clin. Invest.*; 118:1266–1276.

Chandramhan D, Geenwood B M. (1998). 'Is there and interaction between HIV and Plasmodium falciparum?' Int J Epidemiol; 27:296-301.

Chauhan V, Negi R C, Verma B, Thakur S. (2009). 'Transfusion Transmitted Malaria in a Non-Endemic Area'. *JAPI;* 57: 653-654.

Cheesbrough Monica. (1998) 'Examination of blood for malaria parasites'. District Laboratory Practice in Tropical Countries (Part 1). Cambrigde University Press 5.7: 239-258

Chen Q, Schlichtherle M, Wahlgren M. (2000). ' Molecular Aspects of Severe Malaria' . Clinical Microbiology Reviews; 13(3); 439-450.

Cohen C, Karstaedt A, Frean J, Thomas J, Govender N, Prentice E, Dini L, Galpin J, Crewe-Brown H.(2005). ' Increased prevalence of severe malaria in HIV-infected adults in South Africa' . *Clin Infect Dis*; 41:1631-7.

Cowan G O, Heap B J. (1993). Clinical Tropical Medicine; 1: 3-18

Department of Health and Human Services. (2005) Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children. "Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection"

Duerden B I, Reid T M S, Jewsbury J M, Turk D C. (1993). Microbial and Parasitic Infection;17:236-254

Endeshaw T, Gebre T, Ngondi J,Graves P M, Shargie E B, Ejgsemahu Y, Ayele B. Yohannes G, Teferi T, Messeke A, Zurihun M, Genet A, Mosher A W, Emerson P M, Richards F O. (2008). 'Evaluation of light microscopy and rapid diagnostic test for the detection of malaria under operational field conditions: a household survey in Ethiopia'. *Malaria Journal;* 7:118.

Francesconi P, Fabiani M, Dente MG, Lukwiya M, Okwey R, Ouma J, Ochakachon R, Cian F, Declich S.(2001). 'HIV, malaria parasites, and acute febrile episodes in Ugandan adults: a case-control study'. *Aids*; 15:2445-50.

Frean J A, Blumberg L. (2008) ' Odyssean and Non-Mosquito Transmitted Forms of Malaria'. Travelers Malaria. Hamilton Ontario, BC Decker 2nd edition. 21:347-349

French N, Nakiyingi J, Lugada E, Watera C, Whitworth J A, Gilks CF. (2001). 'Increasing rates of malarial fever with deteriorating immune status in HIV-1-infected Ugandan adult's'. *Aids*; 15:899-906.

Frontiera M, Myers A M. (1987). 'Peripheral blood and bone marrow abnormalities in the acquired immunodeficiency syndrome'. *West J Med;* **147:157**.

Global Report: UNAIDS Report on the Global AIDS Epidemic**. (**2010) Joint United Nations Programme on HIV/AIDS.

Good M F, Doolan D L. (1999). 'Immune effector mechanisms in malaria'. *Curr Opin Immunol*; 11:412-9.2

Greenberg AE, Nsa W, Ryder RW, Medi M, Nzeza M, Kitadi N, Baangi M, Malanda N, Davachi F, Hassig SE. (1991). 'Plasmodium Falciparum malaria and perinatally acquired human immunodeficiency virus type 1 infection in Kinshasa, Zaire. A prospective, longitudinal cohort study of 587 children'. *N Engl J Med*; 325:105-9.

Greenwood BM, Bojang K, Whitty CJ, Targett G A. (2005). Lancet 23-2; 365(9469)1487-98.

Grimwade K, French N, Mbatha DD, Zungu DD, Dedicoat M, Gilks CF. (2003). 'Childhood malaria in a region of unstable transmission and high human immunodeficiency virus prevalence'. *Pediatr Infect Dis J*; 22:1057-63.

Guyatt HL, Snow RW. (2001).'Malaria in pregnancy as an indirect cause of infant mortality in sub-Saharan Africa'.*Trans R Soc Trop Med Hyg*. 95(6):569-76.

Hambleton, J. (1996). 'Hematologic complications of HIV infection'.*Oncology*, *10*, 671-680

http://bphc.hrsa.gov/policiesregulations/performancemeasures/patientsurvey/calculating.html (no date)

Huff B. (2000). 'HIV and malaria: Two intertwining epidemics'. *Am Found Aids Res*; 6:1-5.

Kakkilaya B S. (2011) Malaria Web Site. Available at: http://www.malariasite.com/malaria/transmission.html, April 3rd 2011

.

Kakkilaya BS. Malaria and AIDS. Kakkiala's Malaria Web Site. *Malaria site.com.* 2002-2004.

Kamya MR, Gasasira AF, Yeka A, Bakyaita N, Nsobya SL, Francis D, Rosenthal PJ, Dorsey G, Havlir D.(2006). 'Effect of HIV-1 infection on antimalarial treatment outcomes in Uganda: a population-based study'. *J Infect Dis*; 193:9-15.

Khoo S, Back D, Winstanley P. (2005). 'The potential for interactions between antimalarial and antiretroviral drugs'. *Aids*; 19:995-1005.

Kublin JG, Patnaik P, Jere CS, Miller WC, Hoffman IF, Chimbiya N, Pendame R, Taylor TE, Molyneux ME.(2005). 'Effect of Plasmodium falciparum malaria on concentration of HIV-1-RNA in the blood'. *Lancet*; 365(9455):233.

Lamikanra Abigail A, Brown Douglas, Potocnik Alexandre, Casals-Pascual Climent, Langhorne Jean, and Roberts David J. (2007)1 'Malarial anemia: of mice and men'. *Blood*. 110: 18-28

Macintyre K, Sosler S, Letipila F et al. (2003). 'A new tool for malaria prevention?: Results of a trial of permethrin-impregnated bedsheets (shukas) in an area of unstable transmission'. *International Journal of Epidemiology*;32 (1):157-160.

Mackintosh C L, Beeson J G, Marsh K. (2004). 'Clinical features and pathogenesis of severe malaria'. *Trends in Parasitology* ;20(12):597-603 \

Mark S. Fradin. (1998). 'Mosquitoes and Mosquito Repellents: A Clinician's Guide'. *Ann Int Med*; 128(11):931-940.

Matta S, Khokhar A and Sachdev T R. (2004). 'Assessment of knowledge about malaria among patients reported with fever : a hospital-based study'. J Vect Borne Dis 41, pp 27–31

McCutchan TF, Piper RC, Makler MT, 2008. 'Use of Malaria Rapid Diagnostic Test to Identify Plasmodium knowlesi Infection'. Emerging Infectious Diseases 14:11.

Meidani M, Rezaei F, Maracy MR, Avijgan M, Tayeri K. (2012). 'Prevalence, severity, and related factors of anemia in HIV/AIDS patients'. *J Res Med Sci*; 17(2): 138-42.

Mermin J, Lule JR, Ekwaru JP. (2006). 'Association between malaria and CD4 cell count decline among persons with HIV'. *J Acquir Immune Defic Syndr*; 41:129-30.10

Migot F, Ouedraogo JB, Diallo J, Zampan H, Dubois B, Scott-Finnigan T, Sanou PT, Deloron P. (1996). 'Selected P. falciparum specific immune responses are maintained in AIDS adults in Burkina Faso'. *Parasite Immunol*; 18:333-9.

Moore JM, Ayisi J, Nahlen BL, Misore A, Lal AA, Udhayakumar V. (2000). 'Immunity to placental malaria. II. Placental antigen-specific cytokine responses are impaired in human immunodeficiency virus-infected women'. *J Infect Dis*; 182:960-4.

Moormann A M. (2009) Parasite Immunol. ; 31(9): 547–559

Mwapasa V, Rogerson SJ, Molyneux ME, Abrams ET, Kamwendo DD, Lema VM, Tadesse E, Chaluluka E, Wilson PE, Meshnick SR. (2004). 'The effect of Plasmodium falciparum malaria on peripheral and placental HIV-1 RNA concentrations in pregnant Malawian women'. *Aids*; 18:1051-9.

NACP (National AIDS/STD Control Programme), Ministry of Health. (2001) AIDS in Ghana:Background, Projections, Impacts, Interventions. Third Edition, Accra, Ministry of Health.

NACP (National AIDS/STD Control Programme) . (2005) Republic of Ghana. National HIV Counseling and Testing Training Manual.

Nahlen B. (1996). 'Areas of potential overlap between HIV and malaria in Africa'. *Journal of Parasitic Diseases.*; 20 (1): 63-64

Nathoo S, Serghides L, Kain KC. (2003). ' Effect of HIV-1 antiretroviral drugs on cytoadherence and phagocytic clearance of Plasmodium falciparum-parasitised erythrocytes'. *Lancet;* 362:1039-41.

Natural Standard, 2011.Available at:http//www.naturalstandard.com (Accessed 2nd June 2011).

Ned RM, Moore JM, Chaisavaneeyakorn S, Udhayakumar V. (2005).' Modulation of immune responses during HIV-malaria co-infection in pregnancy'. *Trends Parasitol*; 21:284-91.

Nicholas M. Anstey, Bruce Russell, Tsin W. Yeo, Ric N. Price. (2009). 'The pathophysiology of vivax malaria'. *Trends in Parasitology*; 25(5):220-227.

Onifade A K, Akanni EO and Mewoyeka OO. (2007). 'Incidence of malaria infection among Human Immunodificiency Virus in patients in Ondo State, Nigeria'. *Middle-East Journal of Scientific Research*; 2 (2): 48-52.

Onyenekwea C.C, Ukibea N, Meludub S.C, Ilikac A, Abohb N, Ofiaelid N, Ezaenie M& Onochief A. (2007). 'Prevalence of malaria as co-infection in HIV-infected individuals in a malaria endemic area of southeastern Nigeria'. *J Vector Borne Dis* 44, pp. 250–254

Palella F J, Delaney K M, Moorman A C, Loveless M O, Fuhrer J, Satten G A, Aschman D J and Holmberg S D. (1998). "Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection". *N. Engl. J. Med.* **338** (13): 853–860.

Schull. (1999). 'Malaria'. *Common Medical Problems in the Tropics*;13:55-74

Shah, S, Smith E, Obonyo C, Bloland P, Slutsker L, Hamel M. (2004) 'The effect of HIV-infection on antimalarial treatment response: preliminary results of a 28-day drug efficacy trial in HIV-infected and HIV-uninfected adults in Siaya, Kenya. Abstracts of the 53rd Annual Meeting of the American Society of Tropical Medicine and Hygiene Florida 2004'. *American Journal of Tropical Medicine and Hygiene*;71(4):318

Skinner-Adams TS, McCarthy JS, Gardiner DL, Hilton PM, Andrews KT. (2004) 'Antiretrovirals as antimalarial agents'. *J Infect Dis*; 190:1998-2000.

Snow EW, Guerra CA, Noor AM, Myint H Y and Has S I. (2005). 'The global distribution of clinical episodes of Plasmodium falciparum malaria'. *Nature*; 434(7030):214-7

Sullivan P S, Hanson D L, Chu S Y, Jones J L, Ward J W. (1998). 'Epidemiology of Anemia in Human Immunodeficiency Virus (HIV)-Infected persons: result from the Multistate Adult and Adolesscent Spectrum of HIV Disease Surveillance Project' .*Blood* 91: 301-308.

Tatem A J, Rogers D J, Hay S I. (2006). 'Global Transport Networks and Infectious Disease Spread'. *Adv Parasitol*. 2006; 62: 293–343.

Tkachuk AN, Moormann AM, Poore JA, Rochford RA, Chensue SW, Mwapasa V, Meshnick SR. (2001) 'Malaria enhances expression of CC chemokine receptor 5 on placental macrophages'. *J Infect Dis*; 183:967-78

UNAIDS (2010) Report on the Global AIDS Epidemic. Joint United Nations Programme on HIV/AIDS.

Van geertruyden JP, Mwananyanda L, Chalwe V, Moerman F, Chilengi R, Kestens L, D'Alessandro U. (2004) 'Higher risk of antimalarial treatment failure in HIV positive than in HIV negative individuals with clinical malaria. Abstracts of the 53rd Annual Meeting of the American Society of Tropical Medicine and Hygiene Florida 2004'. *American Journal of Tropical Medicine and Hygiene*;71(4):315

Warren E Levinson, Ernest Jawetz. (1992) Medical Microbiology and Immunology; 52:245-253

WHO (2001). Antimalarial Drug Combination Therapy, Report of a WHO Technical Consultation. Geneva.

World Health Organization. (2007)WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva: pp. 6–16.

World Health Organization. (2010)World Malaria Report.

World Health Organiztion. (2001) Antimalarial Drug Combination Therapy: Report of a WHO Technical Consultation. 4-5 April 2001.

Xiao L, Owen SM, Rudolph DL, Lal RB, Lal AA. (1998) 'Plasmodium falciparum antigen-induced human immunodeficiency virus type 1 replication is mediated through induction of tumor necrosis factor-alpha'. *J Infect Dis*; 177:437-45

Yaffe I. (2001). 'AIDS possibly caused by HIV and latent malaria coinfection'. *Hypothesis*; 57:419-22.

ANNEXES

ANNEX ONE

DEFINITIONS

- HIV infection: presence of HIV-1 antibodies in the blood
- HIV- sero positive**:** a positive test result for HIV with the first response test kit.
- HIV- sero negative**:** a negative test result for HIV with the first response test kit
- Malaria and HIV co-infection: presence of both malaria parasites and HIV infection in an individual at the same time
- Malaria infection**:** presence of malaria parasites in the peripheral blood film as is detected by blood microscopy.
- Anemia: a clinical condition associated with decrease in hemoglobin concentration of the blood as compared with that of a normal person
- Hemoglobin : the respiratory pigment which occurs in the red blood cells and is responsible for the transport of oxygen in the blood
- CD4 (cluster of differentiation 4): is a glycoprotein expressed on the surface of T helper cells, monocytes, macrophages, and dendritic cells
- Antiretroviral**:** Refers to an agent or effect that counters or acts against a retrovirus, usually understood to be HIV
- Antiretroviral clinic: it is specific clinic that takes care of health needs of HIV patients

ANNEX TWO.

QUESTIONNAIRE FOR PREVALANCE OF MALARIA AS A CO - INFECTION AMONG HIV SERO-POSITIVE INDIVIDUALS: A CASE STUDY OF INDIVIDUALS ATTENDING ANTI-RETROVIRAL TREATMENT (ART) CLINIC AT HOLY FAMILY HOSPITAL-TECHIMAN IN GHANA

CODE NO……

Age…… Sex……

Occupation……

Marital status:

[ ] Married

[ ] Divorced

[ ] Not married before

Level of education:

[ ] Illiterate [ ] Primary education

[ ] JHS/JSS/O – Level [ ] SHS/SSS/ A- Level

[ ] Tertiary education [ ] Non – formal education

KNOWLEDGE AND ASSESSMENT OF ANTI-MALARIA PROGRAMME

Have you ever heard about malaria before?

[ ] Yes [ ] No

Do you have any knowledge on malaria?

[ ] Yes [ ] No

If YES, how does one get malaria?

[ ] Through mosquito bite [ ] Through bodily contact with patients

[ ] Via respiratory route [ ] By flies

[ ] I do not know [ ] Others

(specify)……

How does one prevent himself/herself from malaria infection?

[ ] Take tablets [ ] Use mosquito repellent

[ ] Use mosquito nets (bednet) [ ] I do not know

[ ] Others (specify)……

Do you use any anti - malaria drug?

[ ] Yes [ ] No

Do you use mosquito repellent?

[ ] Yes [ ] No

If YES, which type do you use?

[ ] insecticide spray [ ] mosquito coil

[ ] mosquito repellent cream [ ] Others

(specify)……

Do you use bed net?

[ ] Yes [ ] No

If NO, why do you not use bed net? .....

If YES which type do you use?

[ ] insecticide treated bed net [ ] Non insecticide treated bed net

Are you given any education on malaria infection and prevention in any of your visits to the ART clinic?

[ ] Yes [ ] No

Do you follow the malaria infection prevention method being given at the ART clinic?

[ ] Yes [ ] No

If NO, why?

……

……

If YES, which type do you use?

.....

LABORATORY RESULTS

Malaria Status…… CD4 Count……..

Hemoglobin (Hb) level……..