PREVALENCE OF HIV AND MALARIA COINFECTION AMONG HIV AND AIDS PATIENTS ADMITTED TO MEDICAL WARDS AT AMANA MUNICIPAL HOSPITAL, ILALA DISTRICT, DAR ES SALAAM

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CERTIFICATION

The undersigned certifies that he has read and hereby recommends for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation titled: **"Prevalence of HIV and Malaria co-infection among HIV patients admitted to medical wards at Amana municipal hospital, Ilala District, Dar es salaam"** in partial fulfillment of the requirement for the degree of Master of Medicine (Internal Medicine), of the Muhimbili University of Health and Allied Sciences.

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ABBREVIATIONS

ACT	-	Artemisinin-based combination therapy
GFATM	-	Global Fund to fight AIDS, Tuberculosis and Malaria
HRP2	-	Histidine-rich protein
RDT	-	Rapid diagnostic test
AIDS	-	Acquired Immunodefienciency Syndrome
CDC	-	Centers for Disease Control and Prevention
HIV	-	Human immunodeficiency virus
STD	-	Sexually transmitted disease
UNAIDS	-	United Nations Programme on HIV/AIDS
HAART	-	Highly Active Antiretroviral Therapy
WHO	-	World Health Organization

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ABSTRACT

Background:

HIV and AIDS pandemic has been superimposed on the long standing malaria pandemic, where *P. falciparum* malaria is consistently one of the major causes of death. The high prevalence of both HIV and malaria infection in Tanzania means that even small interactions between the two could have substantial effects on populations.

Objective:

To determine the prevalence of HIV and Malaria co-infection among HIV and AIDS patients admitted to medical wards at Amana, Municipal hospital, Ilala, Dar es salaam.

Study design and setting:

A cross-sectional study conducted at Amana hospital, Ilala, in Dar es salaam, between August 2009 and December 2009.

Methodology:

A standard data collecting forms were used to collect demographic and examination findings from the patients. Laboratory findings were entered into the laboratory data collecting sheet.

Results:

A total of 180 HIV and AIDS patients, 68% females and 32% males were recruited into the study. The prevalence of HIV and malaria co-infection was found to be 25.6%.The majority of the patients were in the sexually active age group (15 - 49) years. Prevalence of HIV and malaria co-infection was high among patients with lower CD4+ T-cell counts.

Among patients with HIV and malaria co-infection 53% of females and 20% of males were married. More than 80% of patients with HIV and malaria co-infection had malaria parasite density between 1 and 500 per 200wbcs.
No significant difference was seen in Anaemia by WHO grading classification between the two group of HIV without malaria infection and HIV with malaria co-infection.

On duration of hospital stay, 46% of HIV and malaria co –infection stayed longer in the hospital than the 25% of HIV without malaria infection. p= 0.001.

Among HIV patients with malaria co-infection, those with higher mean CD4+ T- cell counts of 372 cells/ul stayed in the hospital less than 5 days compared to those with low mean CD4+ T- cell counts of 207cells/ul. Similarly, to those with low mean malarial parasites of 190 per 200wbcs had a shorter hospital stay (less than 5 days) while those with high mean malarial parasites of 246 stayed in the hospital for more than 5 days.

Conclusion and Recommendation:
HIV and malaria co-infection is common and occurs mostly in HIV and AIDS patients with low CD4+- T cell counts. Fever was a common symptom. (It was associated with long hospital stay and death). There is a need for collaboration between malaria and HIV programmes to spear head for the HIV patients to be screened for malaria infection.

CHAPTER ONE

1: INTRODUCTION AND LITERATURE REVIEW

1.1. HIV AND AIDS PANDEMIC

AIDS was first recognized in the United States in 1981, when the U.S. Centers for Disease Control and Prevention (CDC) reported the unexplained occurrence of *Pneumocystis jiroveci* (formerly P. carinii) pneumonia in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma (KS) with or without *P. jiroveci* pneumonia in 26 previously healthy homosexual men in New York and Los Angeles.[1]

The disease became recognized in male and female injection drug users and soon thereafter in recipients of blood transfusions and in hemophiliacs.[1]

As the epidemiologic pattern of the disease unfolded, it became clear that an infectious agent transmissible by sexual contact and blood or blood products was the most likely etiologic cause of the epidemic.[1, 2]

In 1983, human immunodeficiency virus (HIV) was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated clearly to be the causative agent of AIDS.

In 1985, a sensitive enzyme-linked immunosorbent assay (ELISA) was developed, which led to an appreciation of the scope and evolution of the HIV epidemic at first in the United States and other developed nations and ultimately among developing nations throughout the world.[3]

The etiologic agent of AIDS is HIV, which belongs to the family of human retroviruses (Retroviridae) and the subfamily of lenti viruses. The most common cause of HIV disease

throughout the world is HIV-1, which comprises several subtypes with different geographic distributions.

HIV-2 was first identified in 1986 in West African patients and was originally confined to West Africa. However, a number of cases that can be traced to West Africa or to sexual contacts with West Africans have been identified throughout the world.[3]

The Pan troglodytes' troglodytes species of chimpanzees has been established as the natural reservoir of HIV-1 and the most likely source of original human infection.[4]

1.2 HIV GENOME

HIV-1 has genes that encode the structural proteins of the virus: gag encodes the proteins that form the core of the virion (including p24 antigen); pol encodes the enzymes responsible for protease processing of viral proteins, reverse transcription, and integration; and env encodes the envelope glycoproteins. However, HIV-1 is more complex than other retroviruses, particularly those of the non primate group, in that it also contains at least six other genes (tat, rev, nef, vif, vpr, and vpu), which code for proteins involved in the modification of the host cell to enhance virus growth and the regulation of viral gene expression.[5]

Several of these proteins are thought to play a role in the pathogenesis of HIV disease. Flanking these genes are the long terminal repeats (LTRs), which contain regulatory elements involved in gene expression. The major difference between the genomes of HIV-1 and HIV-2 is the fact that HIV-2 lacks the vpu gene and has a vpx gene not contained in HIV-1.[5]

1.3 TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS

HIV is transmitted by both homosexual and heterosexual contact, by blood and blood products; and by infected mothers to infants either intrapartum, perinatally, or via breast milk.

After more than 25 years of scrutiny, there is no evidence that HIV is transmitted by casual contact or that the virus can be spread by insects, such as mosquitoes. HIV infection is predominantly a sexually transmitted disease (STD) and worldwide the most common mode of infection particularly in developing countries, is clearly heterosexual transmission. In Tanzania heterosexual transmission accounts for more than 90% of the HIV and AIDS cases diagnosed among adults and adolescents.[6]

1.4 PATHOPHYSIOLOGY OF HIV

The hallmark of HIV disease is a profound immunodeficiency resulting primarily from a progressive quantitative and qualitative deficiency of the subset of T lymphocytes referred to as helper T cells. This subset of T cells is defined phenotypically by the presence on its surface of the CD4 molecule, which serves as the primary cellular receptor for HIV. [7]

A co-receptor must also be present together with CD4 for efficient fusion and entry of HIV-1 into its target cells. HIV uses two major co-receptors for fusion and entry; these co-receptors are also the primary receptors for certain chemo attractive cytokines termed chemokines and belong to the seven-transmembrane-domain G protein–coupled family of receptors. CCR5 and CXCR4 are the major co-receptors used by HIV.[7]

A number of mechanisms responsible for cellular depletion and/or immune dysfunction of CD4+ T cells have been demonstrated in vitro. These include direct infection and destruction of these cells by HIV and immune clearance of infected cells, as well as indirect effects such as immune exhaustion due to aberrant cellular activation and activation-induced cell death. [7]

Patients with CD4+ T cell levels below certain thresholds are at high risk of developing a variety of opportunistic diseases, particularly the infections and neoplasms that are AIDS-defining illnesses. Some features of AIDS, such as Kaposi's sarcoma and neurological

abnormalities, cannot be explained completely by the immunodeficiency caused by HIV infection, since these complications may occur prior to the development of severe immunologic impairment.[7, 8, and 9]

The combination of viral pathogenic and immunopathogenic events that occurs during the course of HIV disease from the moment of initial (primary) infection through the development of advanced-stage disease is complex and varied. It is important to appreciate that the pathogenic mechanisms of HIV disease are multifactorial and multiphasic and are different at different stages of the disease. Therefore, it is essential to consider the typical clinical course of an untreated HIV-infected individual in order to more fully appreciate this pathogenic events.[8, 9]

1.5 EPIDEMIOLOGY OF HIV AND AIDS

In 2008, an estimated 1.9 million [1.6 million–2.2 million] people living in sub-Saharan Africa became newly infected with HIV, bringing the total number of people living with HIV to 22.4 million [20.8 million–24.1 million]. While the rate of new HIV infections in sub-Saharan Africa has slowly declined—with the number of new infections in 2008 approximately 25% lower than at the epidemic's peak in the region in 1995—the number of people living with HIV in sub-Saharan Africa slightly increased in 2008, in part due to increased longevity stemming from improved access to HIV treatment. Adult (15–49) HIV prevalence declined from 5.8% [5.5–6.0%] in 2001 to 5.2% [4.9–5.4%] in 2008.
In 2008, an estimated 1.4 million [1.1 million–1.7 million] AIDS-related deaths occurred in sub-Saharan Africa. This number represents an 18% decline in annual HIV-related mortality in the region since 2004.[10, 11]
UNAIDS estimated, that global HIV prevalence has been at the same level since 2001. HIV incidence likely peaked in the late 1990s at more than 3 million new infections per year. Recent reductions in global HIV incidence likely reflect natural trends in the pandemic as well as the results of intervention programs resulting in behavior change.

1.6 CURRENT STATUS OF HIV AND AIDS IN SUB SAHARAN AFRICA

Sub-Saharan Africa has been particularly devastated by the epidemic. More than two-thirds of all people with HIV infection (about 22.5 million) live in this region, even though sub-Saharan Africa is home to just 10–11% of the world's population. Within the region, southern Africa is worst affected.[10, 11]

1.7. CURRENT STATUS OF HIV AND AIDS IN TANZANIA

In Tanzania the first cases of HIV and AIDS were reported in1983, although for sub-Saharan Africa as a whole the problem began to surface in the late 1970s.The epidemic has evolved from being rare and new disease to a common household problem, which has affected most Tanzanian families.[12]

According to the data from Tanzania HIV and AIDS Indicator Survey, the national prevalence among the sexually active populations (between 15 and 49 years of age) is reported to be 5.7 %.[13] The data shows that more women (6.6 %) are infected than men (4.6%) and the estimated number of people living with HIV and AIDS is 1.3 million.

The overall national figures show stabilizing figures and some slight decrease in prevalence rate for last five years.

HIV infection is unevenly distributed across geographic areas, gender, age groups and social economic classes in the country. The percentage of the population infected by HIV ranges from less than three percent across most of the country to more than 44.4 percent in certain sub populations. The epidemic has struck more the most economically active group of adults; those aged 15-45 years.[13]

During the last eighteen years, Tanzania has undertaken many different approaches in attempting to slow the spread of HIV infection and minimize its impact on individuals, families and the society in general. Since 1983, when the first 3 AIDS cases in Tanzania were reported, the HIV epidemic has progressed differently in various population groups while national response has developed itself into phases of program activities led by the National AIDS Control Programme since 1985.

Situation analysis of HIV and AIDS in Tanzania was performed in 1997 and has shown a worsening epidemiological situation whereby the epidemic has rapidly spread into rural

areas thereby increasing the previously low rural prevalence to more than 10% in some areas. Mother-to-child transmission appears to be on the increase, as more and more women continue to become infected and pregnant.[13]

The youth and the women have been the most affected groups because of economic, social-cultural, biological and anatomical reasons. Hence, poverty, which reflects the country's economy, is an important determinant. Mobile population groups have also been categorized as vulnerable to HIV infection as their occupation forces them into high-risk sexual behavior. The mobile population groups include commercial sex workers, petty traders, migrant workers, military personnel and long distance truck drivers. Determinants of the epidemic have been identified and grouped into societal, behavioral and biological ones.

The HIV and AIDS epidemic has had a serious impact on the country's economy. It has affected agricultural and industrial production as well as affected socio-demographic parameters such as life expectancy.

AIDS orphans have been increasing in number while families, communities and the Government cannot cope with the needed resources to cater for their needs.[13]As regards the country's response to the epidemic there have been various national efforts to control the spread of HIV. While the initial efforts were mainly implemented by the Tanzania ministry of health, over time, there has been gradual involvement of other public sectors, Non governmental organizations and community-based organizations.

This multi-sectoral response to the HIV and AIDS problem has involved, among others, IEC activities for the prevention of HIV transmission, care for AIDS patients in hospitals and at home, family life education, Government budgetary allocation for AIDS activities, condom procurement and distribution and STD management activities. Encompassing all the above responses is the development of a National Policy on HIV and AIDS to widen and strengthen the national response against the epidemic[14].

2. LABORATORY TESTING FOR INITIAL ASSESSMENT OF HIV

The following laboratory tests are recommended as initial assessment for each new patient during initial patient visits, HIV antibody testing ,CD4+ T-cell count ,Plasma

HIV RNA, Complete blood count, chemistry profile, transaminase levels, BUN and creatinine, urinalysis, RPR or VDRL for syphilis, *Toxoplasma gondii* IgG, Hepatitis A, B and C serology, and PAP smear in women.[15]

The fasting blood glucose and serum lipids if considered at risk for cardiovascular disease and for baseline evaluation prior to initiation of combination antiretroviral therapy. For patients with pretreatment HIV RNA more than 1,000 Copies/mL, genotypic resistance testing is recommended when the patients enter into care, regardless of whether therapy will be initiated immediately. However HIV RNA genotype testing for resistance is not routinely done in Tanzania due to limited number of equipments.

2.1. CD4 T-CELL COUNT

The CD4+ T-cell count (or CD4 count) serves as the major clinical indicator of immunocompetence in patients with HIV infection. It is usually the most important consideration in decisions to initiate antiretroviral therapy [15]

The most recent CD4+ T-cell count is the strongest predictor of subsequent disease progression and survival, according to clinical trials and cohort studies data on patients receiving antiretroviral therapy. In general, CD4+ T- count should be determined every 3 to 6 months to:

1. Determine when to start antiretroviral therapy in patients who do not meet the criteria for initiation.
2. Assess immunologic response to antiretroviral therapy.
3. Assess the need for initiating chemoprophylaxis for opportunistic infections.

2.2. VIRAL LOAD TESTING

Plasma HIV RNA (viral load) may be a consideration in the decision to initiate therapy. In addition, viral load is critical for evaluating response to therapy. Three HIV viral load assays have been approved for clinical use:

1. HIV-1 reverse transcriptase polymerase chain reaction (PCR) assay (Amplicor HIV-1 Monitor Test, version 1.5, Roche Diagnostic)
2. Nucleic acid amplification test for HIV RNA (NucliSens HIV-1 QT, bioMerieux).

3. Signal amplification nucleic acid probe assay (VERSANT HIV-1RNA 3.0 assay, Bayer).

Analysis of 18 trials including more than 5,000 participants with viral load monitoring showed a significant association between decreases in plasma viremia and improved clinical outcome.

Thus, viral load testing serves as a surrogate marker for treatment response and may be useful in predicting clinical progression. The minimal change in viral load considered to be statistically significant (2 standard deviations) is a threefold or a 0.5 log10 copies/Ml change.

One key goal of therapy is a viral load below the limits of detection (at <50 copies/mL for the Amplicor assay, <75 copies/mL for the VERSANT assay, and <80 copies/mL for the NucliSens assay). This goal should be achieved by 16–24 weeks of treatment by proper antiretroviral drugs, adherence and compliance from the patient.[15]

3. TREATMENT OF HIV AND AIDS

Antiretroviral therapy (ART) for treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection has improved steadily since the advent of combination therapy in 1996. More recently, new drugs have been approved that offer new mechanisms of action, added potency, dosing convenience, and improved safety profiles, whereas some previously popular drugs are being used less often as their drawbacks become better defined.[15]

Eradication of HIV infection cannot be achieved with available antiretroviral regimens. This is chiefly because the pool of latently infected CD4 T-cells is established during the earliest stages of acute HIV Infection[16] and persists with a long half-life, even with prolonged suppression of plasma viremia[16-21].

The primary goals driving the decision to initiate antiretroviral therapy therefore are to:

- Reduce HIV-related morbidity and prolong survival,
- Improve quality of life,
- Restore and preserve immunologic function,
- Maximally and durably suppress viral load, and
- Prevent vertical HIV transmission.

- Several preferred and alternative antiretroviral regimens are recommended for use. They vary in efficacy, pill burden, and potential side effects. A regimen tailored to the patient may be more successful in fully suppressing the virus by allowing more complete medication adherence. Individual tailoring is based on such considerations as expected side effects, convenience, co morbidities, interactions with other required medications, and results of pretreatment genotypic drug resistance testing.

3.1 TYPES OF ANTIRETROVIRAL

There are six classes of antiretroviral which includc the nucleoside/nucleotide reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), protease inhibitors (PI), fusion inhibitors, CCR5 antagonists, and integrase inhibitors.

3.2 RECOMMENDED ANTIRETROVIRAL DRUGS IN TANZANIA

The use of monotherapy in the treatment of HIV infection is not recommended in Tanzania. Antiretroviral therapy both in naïve patients and those who have received treatment before involves the use of a combination of drugs, triple therapy consisting of 2NRTI + 1NNRTI or 2NRTI+1PI or 3NRTI's is recommended but the regimens should be recommended on the basis of a patient's clinical condition, lifestyle, and ability to tolerate the regimen.

3.2.1 First Line Antiretroviral drugs Combination Regimen for Adults and Adolescent Antiretroviral drugs Naïve Patients

The Ministry of health and Social welfare of Tanzania recommends the following drugs for first line treatment; Zidovudine (AZT), Stavudine (d4T), Lamivudine (3TC),Emtricitabine(FTC),Tenofovir(TDF), Nevirapine(NVP) and Efavirenz(EFV), and the following drug combination can be made out of these drugs for adults and adolescents, and should be used according to indications that govern the use of

Antiretroviral to minimize side effects and drug- drug interactions: AZT + 3TC +NVP, AZT +3TC +EFV, d4T +3TC +NVP, d4T + 3TC + EFV, TDF + FTC +EFV, TDF +FTC +NVP, TDF +3TC + EFV and TDF+3TC +NVP.

The following drugs may appear in fixed drugs combinations (FDC);

- AZT +3TC, e.g. Combivir or Duovir
- AZT +3TC+NVP, e.g. Duovir N
- d4T + 3TC+NVP, e.g.Triomune
- TDF +FTC +EFV, e.g. Atripla
- TDF +FTC, e.g. Truvada

The default first line regimen in Tanzania is; Zidovudine (AZT) 300mg/ Lamivudine (3TC) 150mg twice daily and Efavirenz (EFV) 600mg once daily at night. For women in the child bearing age, Nevirapine (NVP) 200mg twice a day is given instead of Efavirenz

4.0. MALARIA

Malaria is caused by infection of the red blood cells with protozoan parasites of the genus *Plasmodium* which is transmitted by the most wide spread malaria vector in Africa, Anopheles gambiae complex and due to its inherent characteristics it is the most difficult vector to control [22] The four *Plasmodium* species that infect humans are *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*.

Plasmodium falciparum, is the most virulent of the four human malaria parasites species and is the main species found in sub Saharan Africa. Almost all deaths are caused by falciparum malaria.

Human infection begins when a female anopheline mosquito inoculates plasmodial *sporozoites* from its salivary gland during a blood meal. These microscopic motile forms of the malarial parasite are carried rapidly via the bloodstream to the liver, where they invade hepatic parenchymal cells and begin a period of asexual reproduction.

By this amplification process (known as *intrahepatic* or *preerythrocytic schizogony* or *merogony*), a single sporozoite eventually may produce from 10,000 to more than 30,000 daughter merozoites.[23]

The swollen infected liver cell eventually bursts, discharging motile *merozoites* into the bloodstream. These then invade the red blood cells (RBCs) and multiply six- to twenty fold every 48–72 h. When the parasites reach densities of about 50/μL of blood, the symptomatic stage of the infection begins.[23, 24]

4.1. EPIDEMIOLOGY

Malaria occurs throughout most of the tropical regions of the world. *P. falciparum* predominates in Africa, New Guinea, and Haiti; *P. vivax* is more common in Central America.

The prevalence of these two species is approximately equal in South America, the Indian subcontinent, Eastern Asia, and Oceania. *P. malariae* is found in most endemic areas, especially throughout sub-Saharan Africa, but is much less common. *P. ovale* is relatively unusual outside of Africa and, where it is found, comprises less than 1% of isolate.

Its prevalence worldwide is estimated to be in the order of 300 – 500million clinical cases each year [25].

4.2. HOST RESPONSE

The host responds to plasmodial infection by activating nonspecific defense mechanisms. Splenic immunologic and filtrative clearance functions are augmented in malaria, and the removal of both parasitized and uninfected erythrocytes is accelerated.

The parasitized cells escaping splenic removal are destroyed when the schizont ruptures. The material released induces the activation of macrophages and the release of pro inflammatory mononuclear cell–derived cytokines, which cause fever and exert other pathologic effects. Temperatures of 40°C damage mature parasites; in untreated infections, the effect of such temperatures is to further synchronize the parasitic cycle, with eventual production of the regular fever spikes and rigors that originally served to characterize the different malarias.

These regular fever patterns (tertian, every 2 days; quartan, every 3 days) are seldom seen today in patients who receive prompt and effective antimalarial treatment. Nonspecific host defense mechanisms stop the infection's expansion, and the subsequent specific immune response controls the infection. Eventually, exposure to sufficient strains confers protection from high-level parasitemia and disease but not from infection. As a result of this state of infection without illness (*premunition*), asymptomatic parasitemia is common among adults and older children living in regions with stable and intense transmission.

Immunity is mainly specific for both the species and the strain of infecting malarial parasite. Both humoral immunity and cellular immunity are necessary for protection, but the mechanisms of each are incompletely understood.

Immune individuals have a polyclonal increase in serum levels of IgM, IgG, and IgA, although much of this antibody is unrelated to protection. Antibodies to a variety of parasitic antigens presumably act in concert to limit in vivo replication of the parasite. In the case of falciparum malaria, the most important of these antigens is the surface adhesin—the variant protein PfEMP1.

Several factors retard the development of cellular immunity to malaria. These factors include the absence of major histocompatibility antigens on the surface of infected RBCs, which precludes direct T cell recognition; malaria antigen–specific immune unresponsiveness; and the enormous strain diversity of malarial parasites, along with the ability of the parasites to express variant immunodominant antigens on the erythrocyte surface that changes during the period of infection. Parasites may persist in the blood for months (or, in the case of *P. malariae*, for many years) if treatment is not given. The complexity of the immune response in malaria, the sophistication of the parasites' evasion mechanisms, and the lack of a good in vitro correlate with clinical immunity have all slowed progress toward an effective vaccine.

4. 3. CLINICAL FEATURES OF MALARIA

The first symptoms of malaria are nonspecific and similar to the symptoms of a minor systemic viral illness. They comprise: headache, lassitude, fatigue, abdominal discomfort and muscle and joint aches, followed by fever, chills, perspiration, anorexia, vomiting and worsening malaise. This is the typical picture of uncomplicated malaria.

Residents of endemic areas such as Dar es salaam, Tanzania are often familiar with this combination of symptoms, and frequently self-diagnose.

A patient may progress from having minor symptoms to having severe disease within a few hours if not treated properly. This usually manifests with one or more of the following: coma (cerebral malaria), metabolic acidosis, severe anaemia, hypoglycaemia and, in adults, acute renal failure or acute pulmonary oedema. By this stage, mortality in people receiving treatment has risen to 15 to 20%. If untreated, severe malaria is almost always fatal.

4.4. BURDEN OF MALARIA

The worldwide mortality due to malaria is estimated to be over one million deaths each year, about 90% of all malaria death occurs in sub Saharan Africa[26, 27].

This is because the majority of infections in Africa are caused by Plasmodium falciparum, the most dangerous of the four human malaria parasites. It is also because the most effective malaria vector - the mosquito Anopheles gambiae - is the most widespread in Africa and the most difficult to control.

In all malaria –endemic countries in Africa, 25 to 40% (average 30%) of all outpatient clinic visits are for malaria (with most diagnosis made clinically) [27].

In these same countries, between 20% and 50% of all hospital admissions are a consequence of malaria[27]. With high case-fatality rates due to late presentation, inadequate management, and unavailability or stock-outs of effective drugs, malaria is also a major contributor to deaths among hospital inpatients.

High burden may in fact be partly a result of misdiagnoses, since many facilities lack laboratory capacity and it is often difficult clinically to distinguish malaria from other infectious diseases. Nonetheless, malaria is responsible for a high proportion of public health expenditure on curative treatment, and substantial reductions in malaria incidence would free up available health resources and facilities and health workers' time, to tackle other health problems.

Both direct and indirect costs associated with a malaria episode represent a substantial burden on the poorer households. A study in northern Ghana found that, while the cost of

malaria care was just 1% of the income of the rich, it was 34% of the income of poor households [28].

In Tanzania, an estimated 16-18 million cases of malaria occur each year, resulting in more than 100,000 deaths. Malaria accounts for some 30% of the national disease burden, 35 % of hospitalizations and 37% of deaths for children under five. Among pregnant women, malaria and anemia are responsible for 25% of maternal deaths[29].

Poor people are at increased risk both of becoming infected with malaria and of becoming infected more frequently. Child mortality rates are known to be higher in poorer households and malaria is responsible for a substantial proportion of these deaths.

In a demographic surveillance system in rural areas of the United Republic of Tanzania, under-5 mortality following acute fever (much of which would be expected to be due to malaria) was 39% higher in the poorest socioeconomic group than in the richest[30].

4.5 DIAGNOSIS OF MALARIA

The diagnosis of malaria is based on clinical criteria (clinical diagnosis) supplemented by the detection of parasites in the blood (parasitological or confirmatory diagnosis). Clinical diagnosis alone has very low specificity and in many areas parasitological diagnosis is not currently available. The signs and symptoms of malaria are nonspecific. Malaria is clinically diagnosed mostly on the basis of fever or history of fever .[31]

In settings where the risk of malaria is low, clinical diagnosis of uncomplicated malaria should be based on the degree of exposure to malaria and a history of fever in the previous 3 days with no features of other severe diseases.

In settings where the risk of malaria is high, clinical diagnosis should be based on a history of fever in the previous 24 h and/or the presence of anemia.

Although rates of clinical malaria increase in HIV-infected adults, the much increased rates of fever as a consequence of HIV infection[32,33,34,35,36], and its associated complications, mean that the proportion of fever that is attributable to malaria decreases as immunosuppression progresses. This reduces further the specificity of a diagnosis of malaria based on febrile symptoms alone.

Two methods used for parasitological diagnosis are light microscopy and rapid diagnostic tests (RDTs).

4.4.1 Malaria Rapid Diagnostic Test (RDTs)

Malaria rapid diagnostic tests, sometimes called "dipsticks" or malaria rapid diagnostic devices (MRDDs), assist in the diagnosis of malaria by providing evidence of the presence of malaria parasites in human blood. RDTs are an alternative to diagnosis based on clinical grounds or microscopy, particularly where good quality microscopy services cannot be readily provided. Variations occur between malaria RDT products, though the principles of the tests are similar.

Malaria RDTs detect specific antigens (proteins) produced by malaria parasites, that are present in the blood of infected or recently infected individuals. Some RDTs can detect only one species (Plasmodium falciparum), some also detect other species of the parasite (P. vivax, P. malariae and P. ovale). Blood for the test is commonly obtained from a finger-prick.

4.4.1.1. The Mechanism of action, sensitivity and specificity of malaria rapid diagnostic tests.

Rapid diagnostic tests are lateral flow 'immuno-chromatographic' antigen-detection tests, which rely on the capture of dye-labeled antibodies to produce a visible band on a strip of nitro-cellulose. With malaria rapid diagnostic test, the dye-labeled antibody first binds to a parasite antigen, and the resultant complex is captured on the strip by a band of bound antibody, forming a visible line (test line). A control line gives information on the integrity of the antibody-dye conjugate, but does not confirm the ability to detect parasite antigen.

The first step of the test procedure involves mixing the patient's blood with a lysing agent in a test strip or well. This raptures the red blood cells, releasing more parasite protein. Labeled antibody, either in the well or on the strip, may then bind with the target protein (antigen).

The resulting mixture of blood products and antigen-labeled antibody complex then passes along the nitro-cellulose strip. This is facilitated partly by capillary action through

the fiber-mesh of the strip, and partly by flushing with a fluid buffer placed behind the blood. It passes over the test and control bands.

The free, labeled antibody will capture the parasite antigen if present which will in turn be captured by the test-band antibody. The accumulation of microscopic dye particles on the thin band produces a visible line if sufficient antigen-labeled antibody complex is present.

The control band will become visible as sufficient labeled antibody accumulates on the line. Antibodies (or antigen) bounds to the strip captures labeled antibodies which failed to bond to antigen from the patient's blood. A visible control line indicates that labeled antibody has traversed the full length of the strip, past the test line, and that at least some free antibody remains conjugated to the dye and that some of the capturing properties of the antibodies remain intact.

The intensity of the test band will vary with the amount of antigen present, at least at low parasite densities (antigen concentration), as this will determine the amount of dye particles which will accumulate on the line. The control band intensity may decrease at higher parasite densities, as much of the labeled antibody will have been captured by the test band before reaching the control.

The sensitivity of a malaria RDT means that it will produce a True Positive result when used in a population infected with malaria as compared to the reference malaria test gold standard of microscopy. In other words, it measures how often the test is positive when malaria is present.

The sensitivity of an RDT for detecting malaria parasitaemia (or recent parasitaemia) depends on the concentration of circulating antigens in the patient's blood, and the ability of the labelled antibody on the RDT to bind the antigen and accumulate to form a visible line. In good conditions, some products can achieve sensitivity similar to that commonly achieved by microscopy (~100 parasites /µl). Sensitivity can vary between products.

The specificity of a malaria RDT means that it will produce a True Negative result when used in a population not infected with malaria as to the reference malaria test gold standard of microscopy. In other words, it measures how often the test is negative when malaria is absent.

Both sensitivity and specificity are influenced by product storage and use conditions. In general, it is recommended that at least 95 per cent of *P. falciparum* infections should be detected at 100 parasites per microlitre, and at higher parasite densities, which is probably similar to good field microscopy.

4.4.2 PREPARING BLOOD SMEARS FOR MICROSCOPY EXAMINATION

Microscopic examination remains the gold standard for the laboratory confirmation of malaria. The preparation of the blood smear for microscopy examination using venous blood, should be done as soon as possible after collection of blood (delay can result in changes in parasite morphology and staining characteristics).

4.4.2.1 Thick smears

Thick smears consist of a thick layer of dehemoglobinized (lysed) red blood cells (RBCs). The blood elements (including parasites, if any) are more concentrated (app. 30×) than in an equal area of a thin smear. Thus, thick smears allow a more efficient detection of parasites (increased sensitivity). However, they do not permit an optimal review of parasite morphology. For example, they are often not adequate for species identification of malaria parasites: if the thick smear is positive for malaria parasites, the thin smear should be used for species identification.

Two thick blood smears should be prepared for each patient for microscopic examination.

1. Place a small drop of blood in the center of the pre-cleaned, labeled slide.
2. Using the corner of another slide or an applicator stick spread the drop in a circular pattern until it is the size of a dime (1.5 cm^2).
3. A thick smear of proper density is one which, if placed (wet) over newsprint, allows you to barely read the words.
4. Lay the slides flat and allow the smears to dry thoroughly (protect from dust and insects!). Insufficiently dried smears (and/or smears that are too thick) can detach from the slides during staining. The risk is increased in smears made with anticoagulated blood. At room temperature, drying can take several hours; 30

minutes is the minimum; in the latter case, handle the smear very delicately during staining. Protect thick smears from hot environments to prevent heat-fixing the smear.

5. Do not fix thick smears with methanol or heat. If there will be a delay in staining smears, dip the thick smear briefly in water to hemolyse the RBCs.

6. Then staining done with Giemsa stain reagent is washed off after 30minutes and is examined with a 100x oil immersion objective for detection and quantification of malaria parasites.

4.4.2.2 Thin smears

Thin smears consist of blood spread in a layer such that the thickness decreases progressively toward the feathered edge. In the feathered edge, the cells should be in a monolayer, not touching one another.

Prepare at least 2 smears per patient!

1. Place a small drop of blood on the pre-cleaned, labeled slide, near its frosted end.
2. Bring another slide at a 30-45° angle up to the drop, allowing the drop to spread along the contact line of the 2 slides.
3. Quickly push the upper (spreader) slide toward the unfrosted end of the lower slide.
4. Make sure that the smears have a good feathered edge. This is achieved by using the correct amount of blood and spreading technique.
5. Allow the thin smears to dry. (They dry much faster than the thick smears, and are less subject to detachment because they will be fixed.)
6. Fix the smears by dipping them in absolute methanol.

4.5 TREATMENT OF UNCOMPLICATED P. FALCIPARUM MALARIA IN TANZANIA

Uncomplicated malaria is defined as symptomatic malaria without signs of severity or evidence of vital organ dysfunction. In acute falciparum malaria there is a continuum from mild to severe malaria. Young children and non-immune adults with malaria may deteriorate rapidly. [37]

To counter the threat of resistance of *P.falciparum* to monotherapies, and to improve treatment outcome, combinations of antimalarials are now recommended by World Health Organization for the treatment of falciparum malaria.

Antimalarial combination therapy is the simultaneous use of two or more blood schizontocidal drugs with independent modes of action and thus unrelated biochemical targets in the parasite[37].

The concept is based on the potential of two or more simultaneously administered schizontocidal drugs with independent modes of action to improve therapeutic efficacy and also to delay the development of resistance to the individual components of the combination.

The rationale for combining antimalarials with different modes of action is twofold: (1) the combination is often more effective; and (2) in the rare event that a mutant parasite that is resistant to one of the drugs arises de novo during the course of the infection, the parasite will be killed by the other drug. This mutual protection is thought to prevent or delay the emergence of resistance.[37]

To realize the two advantages, the partner drugs in a combination must be independently effective. The possible disadvantages of combination treatments are the potential for increased risk of adverse effects and the increased cost.

The following Artemisinin Based Combination Therapies (ACTs) are currently recommended in Tanzania:

- Artemether- lumefantrine,
- Artesunate + amodiaquine,
- Artesunate + mefloquine,

- Artesunate + sulfadoxine–pyrimethamine.

Note: amodiaquine + sulfadoxine–pyrimethamine may be considered as an interim option where ACTs cannot be made available, provided that efficacy of both is high.

4.6 TREATMENT OF SEVERE FALCIPARUM MALARIA

In a patient with *P. falciparum* asexual parasitaemia and no other obvious cause of their symptoms, the presence of one or more of the following clinical or laboratory features classifies the patient as suffering from severe malaria:

Clinical feature:

- Prostration
- Impaired consciousness
- Respiratory distress (acidotic breathing)
- Multiple convulsions
- Circulatory collapse
- Pulmonary oedema (radiological)
- Abnormal bleeding
- Jaundice
- Haemoglobinuria

Laboratory test:

- Severe anaemia
- Hypoglycemia
- Acidosis
- Renal impairment
- Hyperlactataemia
- Hyperparasitaemia

4.6.1 TREATMENT OBJECTIVES OF SEVERE MALARIA

The main objective is to prevent the patient from dying; secondary objectives are prevention of recrudescence, transmission or emergence of resistance and prevention of disabilities.

The mortality of untreated severe malaria is thought to approach 100%. With antimalarial treatment the mortality falls to 15–20% overall, although within the broad definition are syndromes associated with mortality rates that are lower (e.g. severe anaemia) and higher (metabolic acidosis). Death from severe malaria often occurs within hours of admission to hospital or clinic, and so it is essential that therapeutic concentrations of antimalarial are achieved as soon as possible.

Management of severe malaria comprises four main areas: clinical assessment of the patient, specific antimalarial treatment, adjunctive therapy and supportive care.

4.6.1.1Clinical assessment of severe malaria

Severe malaria is a medical emergency. The airway should be secured in unconscious patients and breathing and circulation assessed. The patient should be weighed or body weight estimated so that drugs, including antimalarials and fluids can be given on a body weight basis.

An intravenous cannula should be inserted and immediate measurements of blood glucose (stick test), haematocrit/haemoglobin, and parasitaemia and, in adults, renal function should be taken. A detailed clinical examination should be conducted, with particular note of the level of consciousness and record of the coma score.

Unconscious patients should have a lumbar puncture for cerebrospinal fluid analysis to exclude bacterial meningitis.

The degree of acidosis is an important determinant of outcome; the plasma bicarbonate or venous lactate level should therefore be measured if possible.

If facilities are available, arterial or capillary blood pH and gases should be measured in patients who are unconscious, hyperventilating or in shock.

Blood should be taken for cross-match, and (if possible) full blood count, platelet count, clotting studies, blood culture and full biochemistry should be conducted.

The assessment of fluid balance is critical in severe malaria.

Respiratory distress, in particular with acidotic breathing in severely anemic children, often indicates hypovolaemia and requires prompt rehydration and, where indicated, blood transfusion.

4.6.2 Specific antimalarial treatment

It is essential that antimalarial treatment in full doses is given as soon as possible in severe malaria. Two classes of drugs are currently available for the parenteral treatment of severe malaria: the cinchona alkaloids (quinine and quinidine) and the artemisinin derivatives (artesunate, artemether and artemotil).

4.6.2.1 Quinine

Quinine treatment for severe malaria was established before modern trial methods were developed. Several salts of quinine have been formulated for

parenteral use, but the dihydrochloride is the most widely used. Peak concentrations following intramuscular quinine in severe malaria are similar to those following intravenous infusion. Pharmacokinetic modeling studies suggest that a loading dose of quinine of twice the maintenance dose (i.e. 20 mg salt/kg body weight) reduces the time to reach therapeutic plasma concentrations. After the first day of treatment, the total daily maintenance dose of quinine is 30 mg salt/kg body weight (usually divided into three equal administrations at 8 h intervals).

4.6.2.2 Artemisinin derivatives

Various artemisinin derivatives have been used in the treatment of severe malaria including artemether, artemisinin (rectal), artemotil and artesunate. The pharmacokinetic properties of artesunate are superior to those of artemether and artemotil as it is water soluble and can be given either by intravenous or intramuscular injection.

Randomized trials comparing artesunate and quinine from South-East Asia show clear evidence of benefit with artesunate. In the largest multi-centre trial, which enrolled 1461 patients (including 202 children <15 years old), mortality was reduced by 34.7%

compared to the quinine group. The results of this and smaller trials are consistent and suggest that artesunate is the treatment of choice for adults with severe malaria.
There are, however, still insufficient data for children, particularly from high transmission settings to make the same conclusion.

An individual patient data meta-analysis of trials comparing artemether and quinine showed no difference in mortality in African children.
Although artesunate has better pharmacokinetic properties than artemether or artemotil, there are relatively few published comparative clinical trials.
Concerns have been raised, regarding the possibility that the intrinsic benefits of artemether as an antimalarial may have been negated by its erratic absorption following intramuscular injection. Artemotil is very similar to artemether, but very few trials have been conducted.

4.6.3 Follow-on treatment

Following initial parenteral treatment, once the patient can tolerate oral therapy, it is essential to continue and complete treatment with an effective oral antimalarial.
Current practice is to continue the same medicine orally as given parenterally to complete a full 7 days of treatment. In non-pregnant adults, doxycycline is added to quinine, artesunate or artemether and should also be given for 7 days.
Doxycycline is preferred to other tetracycline because it can be given once daily, and does not accumulate in renal failure.

5.0. HIV AND MALARIA COINFECTION

In large parts of tropical Africa the burden of Malaria is greatest and where severe diseases and mortality are largely confined to poor people of all ages. In these settings, malaria is by far the commonest cause of fever and most of them have malaria parasitemia.[38, 39, and 40]

In Africa, the HIV pandemic has been superimposed on the long standing malaria pandemic, where p. falciparum malaria is consistently one of the major causes of death.

The high prevalence of both HIV and malaria infection in Africa means that even small interactions between the 2 could have substantial effects on populations.

The current understanding of the human immune response to malaria and HIV leads scientists to expect that either infection might influence the clinical course of the other. Many other types of infections are associated with at least a transient increase in HIV viral load[41, 42]. Hence, it is logical to expect malaria to do the same and potentially to accelerate HIV disease progression.

On the other hand, the control of malaria parasitemia is immune mediated, and this prevents most malaria infections from becoming clinically apparent in semi – immune adults in endemic areas.

The immune deficiency caused by HIV infections should increase parasitemia and therefore increase the frequency of clinical attacks of malaria.

The underlying epidemiology and intensity of malaria transmission, the duration of HIV infection and consequent immunosuppression appears to be critical in determining the consequences of co-infection, though no direct evidence has been found to suggest that HIV alters malaria transmission[43, 44].

Investigators have speculated that because HIV infection increases parasitaemia and reduces the response to therapy, it will increase the reservoir of infection in the human population and hence increase transmission[45, 46, and 47]. In an area with high HIV prevalence 30%, it has been estimated that 20% of malaria infection could be attributable to HIV, assuming gametocytaemia parallels asexual parasitaemia[48]. However, the

relationship between asexual parasitaemia and gametocytaemia is not straightforward and the effect of HIV infection on gametocytes remains unclear.

A community based study in rural Masaka, Uganda found increase of clinical malaria incidences among HIV positive adults compared to HIV negative adult[48]. Also in another study done by French N, et al found out that malaria incidence, level of parasitemia and fever episodes were inversely related to CD4 count when an alternative cause of acute febrile illness such as bacteremia were excluded through laboratory tests.

A study conducted in Blantyre, Malawi among HIV infected children admitted to the Hospital found that HIV was less prevalent among children with malaria (11%) or surgical conditions (11%) and case fatality in HIV infected children was 30%compared to 9%in non –HIV infected children [49].

Another study on Bacteremia in Malawi on children with severe malaria found that HIV prevalence was 16% and was highest in those with severe anemia (20.4%) [50]

Many studies in early nineties on malaria and HIV interaction in adults living in areas of stable Malaria have been conducted but came with inconclusive results[51, 52, and 53].

Most studies have suggested that treatment with artemesinin, sulfadoxicine – pyrimethamine (SP) and artemether - lumefantrine were less effective in HIV – infected than in uninfected men and non pregnant women.

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 high frequency of new infections rather than recrudescence of existing infections[54].

So in most study findings which already had done illustrate the difficulties in, differentiating between malaria and other causes of febrile illnesses. The extent to which HIV infections complicates this is largely unknown.

Malaria and HIV data from Kisumu, Kenya, an area of high HIV and malaria prevalence, was entered into the model. The impact of HIV/malaria interactions on each other's prevalence in Kisumu and other settings with varying malaria and HIV prevalence was assessed. In Kisumu, the interaction resulted in an HIV epidemic peak 8 % higher and a

malaria peak 13 % higher than the levels in a scenario with no HIV/malaria interaction. The model shows that since 1990,

Kisumu alone showed an excess of 8,500 HIV infections and 980,000 malaria attacks due to the interaction. In general, malaria accelerated the spread of HIV.

In scenarios where both malaria and HIV prevalence is high, the impact of the interaction was minimal. However, when baseline prevalence was high while the other was low, co-infection increased HIV or malaria prevalence. For example, in a scenario with 1 % malaria and 37.8 % HIV prevalence, co-infection increased malaria prevalence about 9 fold (to 9.2 %) while it had minimal impact on HIV prevalence (38.5%).

Studies on adults in areas of high malaria transmission showed that HIV-1 infection increased case fatality among hospitalized persons with severe malaria by 1.6- to 2.5-fold, while the incidence of severe malaria, a precursor of fatal episodes, increased by 2.7-fold. These data collectively suggest that HIV-1 increases malaria deaths by increasing the proportion of severe cases, case fatality among them, and the failure rate of antimalarial treatment. Malaria and HIV and AIDS mutually reinforce each other and contribute synergistically to morbidity, mortality and burden on health systems. Especially in Southern Africa, where HIV is highly prevalent and malaria is unstable in some parts and stable in other parts especially in the eastern and coastal areas of Tanzania and Mozambique, and therefore affects a relatively large proportion of adults, HIV infection has probably contributed to observed increases in malaria cases during the 1990s.

In Central Africa, where large areas of countries have malaria transmission at high intensity, malaria is likely to be an important contributor to morbidity and mortality in HIV and AIDS patients. In areas of unstable malaria transmission, HIV infection augments the risk of developing severe and fatal malaria. In areas of stable endemicity, HIV infection among adult men and non-pregnant women increases the incidence of clinical malaria and its severity and case fatality. These effects were most pronounced in HIV and AIDS patients with advanced immunosuppression.

Conversely, there is some evidence that malaria may exacerbate HIV infection. Acute malaria episodes temporarily increase viral replication and hence HIV viral load, which may accelerate disease progression and contribute to heterosexual HIV transmission.

In addition, as an important cause of anemia, malaria frequently leads to blood transfusions, which is a potential risk factor for HIV infection. The increased disease burden resulting from co infection with HIV and malaria highlights the need for better integration of health services for both diseases. HIV infected adults should be targeted for free or subsidized distribution of ITNs.

The recurrent non-malarial fevers in HIV and AIDS patients could cause considerable overuse of antimalarial drugs under the policy of presumptive antimalarial treatment of all acute fevers . To reduce costs and the risk of drug resistance, capacity for laboratory diagnosis of febrile disease should be increased in countries with high HIV prevalence and high malaria incidence. Prompt and effective combination treatment is particularly important for HIV-infected individuals who might be prone to treatment failure with conventional antimalarial drugs [55].

By preventing acute increases in viral load, good coverage of antimalarial treatment could contribute to limiting HIV disease progression and transmission [56]A recent study in Uganda in HIV-infected adults found a reduction in febrile parasitaemia of 76% [95% confidence interval (CI), 62-85) associated with cotrimoxazole prophylaxis, of 92% (CI, 83-96%) associated with cotrimoxazole and antiretroviral treatment (ART), and of 95% (CI, 92-97) when insecticide-treated bed nets were added to cotrimoxazole and ART. This study demonstrates that the effects of these three interventions are cumulative, and that malaria infection can be successfully controlled in HIV-infected adults[57].

5.1 ANTIMALARIAL IN HIV AND AIDS INFECTION

Increasing numbers of people in malaria endemic areas are living with HIV infection. It is becoming increasingly apparent that, as HIV progresses and immunosuppression worsens, the manifestations of malaria also worsen. In patients with partial immunity to malaria, the severity of the infection increased.[58]

There is insufficient information at the present time on how HIV infection modifies the therapeutic response to antimalarials. However, increasing parasite burdens and reduced host immunity, both of which occur with HIV infection, are associated with increased treatment failure rates.

At this time, there is insufficient information to modify the general malaria treatment recommendations for patients with HIV and AIDS. Current UNAIDS and WHO recommendations on the prophylaxis of opportunistic infections with cotrimoxazole (trimethoprim - sulfamethoxazole) in people living with HIV and AIDS remain unchanged. However, treatment with sulfadoxine–pyrimethamine should not be given to patients on cotrimoxazole as there is probably an increased risk of sulfa-related adverse effects (and in any case as both medicines have similar antimalarial activity, the malaria infection is likely to be resistant to sulfadoxine–pyrimethamine).

Depending on the malaria transmission setting, HIV-infected individuals are at increased risk of asymptomatic parasitaemia, clinical malaria or severe and complicated malaria. Therefore, they have an even greater need for malaria control measures than individuals not infected with HIV.

CHAPTER 2

6. 0 PROBLEM STATEMENTS

HIV and malaria are 2 diseases that account for significant morbidity and mortality in Africa. About 30% of death due to malaria occurs in adults[59] .However despite 30% of deaths which is due to malaria in adults the problem has been given little attention in this group compared to much effort directed to malaria in children and pregnant women. Yet this group has been severely affected by both HIV and malaria as well.

Many studies evaluating the effects of HIV on the management of malaria have been done in adults and children with contradicting findings [33, 34, 35, 36].Birku et al; looked at delayed clearance of plasmodium falciparum in patients with human immunodeficiency virus co infection treated with artemisinin and found out that parasite clearance was low in HIV-seropositive i.e. 12-fold higher in the seropositive patients than in the HIV negative patients at the same period, so they concluded that the host's immunity affects the activity of antimalarial drugs and their data suggested for the first time that clearance of P.falciparum after administration of artemisinin is delayed in patients with HIV co infection.

Whitworth J, et al reported on the study done in Uganda on effect of HIV -1 and increasing immunosuppresion on Malaria parasitemia and clinical episodes in adults in rural Uganda; Found out that parasitemia was more common at visits by HIV -1 positive individuals, lower CD4-cell counts were associated with higher parasites densities and clinical malaria, compared with HIV negatives individuals. So they concluded by saying that HIV-1 infection is associated with an increased frequency of clinical malaria and parasitemia which tends to become more pronounced with advanced immunosuppression. Put together, these studies suggest that HIV-associated immunosuppression interferes with parasite control and may cause some loss of the specific disease-protective immune response that protects parasitaemic persons from developing clinical illness.

But these studies did not control possible confounding factors such as use of antiretroviral therapy, CD4 cell counts, use of co-trimoxazole prophylaxis and adherence factors which might have led to the observed differences in their findings.

7.0 RATIONALE

Studies have reported HIV and AIDS and malaria co infection as a major cause of morbidity and mortality but currently there is little updated information on the relevance of HIV and Malaria co infections especially in Tanzania.

Study in Malawi, on impact of HIV–associated immunosuppression on malaria infection and disease, found out that the incidence of clinical malaria episodes was higher in participants with CD4 cell counts less than 200 cells/mm3 than in those with CD4 cell counts more than 500cells /mm3.[60]

The trend was preserved when increasingly specific definitions of malaria disease were used .The prevalence of malaria infection was not associated with CD 4 cell counts.

In per – visit analysis, lower CD4 cell Counts were associated with higher incidences of Pneumonia, Sepsis, and tuberculosis but not malaria; Severe malaria was rare, with only 3 cases in 591 person –years of observation. Parasite density and CD4 cell count were independent risk factors for fever.

Currently little is known about HIV and Malaria co- infection, its magnitude and effects on a patient.

So exploring its prevalence and its effects of HIV and AIDS and malaria co infection at Amana municipal hospital would be a stepping stone towards better understanding of these problems.

8.0 OBJECTIVES

8.1 Broad Objective

To determine the prevalence of HIV and Malaria co-infection among HIV patients admitted to medical wards at Amana Municipal hospital, Ilala District, Dar es Salaam.

8.2 Specific objectives

1. To determine the prevalence of HIV and Malaria co infection among HIV patients admitted to medical wards at Amana hospital.
2. To determine socio-demographic characteristics of patients with HIV and Malaria co infection among HIV patients admitted to medical wards at Amana hospital
3. To determine clinical features of patients with HIV and Malaria co infection among HIV patients admitted to medical wards at Amana hospital.

4. To determine the level of malarial parasitaemia, hematological indices, biochemical indices, and CD4 cell counts among patients with HIV and malaria co-infection admitted to medical wards at Amana hospital.

5. To determine the correlation between hospital stay and deaths with the mean CD4 T-cell counts among patients with HIV and malaria co-infection patients admitted to medical wards at Amana hospital.
6. To determine the correlation between hospital stay and deaths with mean malarial parasite densities among patients with HIV and malaria co-infection patients admitted to medical wards at Amana hospital

9.0 METHODOLOGY

9.1 STUDY DESIGN AND STUDY SITE

This was a descriptive cross- sectional study which was conducted at Amana municipal hospital in Dar es salaam. The study site was selected on the basis of convenience and availability of malaria patients in peripheral hospital as the hospital serves as a district hospital. Amana hospital receives a total of 800 patients as outpatients and on average a total of 11 patients are admitted to medical wards per day.

9.2 STUDY POPULATION

The study population was known HIV and AIDS patients admitted to medical wards in Amana Hospital.

9.3 INCLUSION CRITERIA

Confirmed HIV and AIDS patients, aged 9 years and above admitted to medical wards at Amana hospital were recruited into the study, after obtaining their consent or that of their parents or guardians in case of children.

9.4 EXCLUSION CRITERIA

All patients who were known to have the following conditions:

1. HIV in pregnancy
2. HIV in sickle cell disease
3. HIV in diabetic mellitus patients
4. HIV in Non HIV associated malignancy
5. HIV in end stage -organ diseases such as severe heart failure, renal failure, and liver failure.

9.5 SAMPLE SIZE

Sample size was obtained from the following formula, taking the prevalence of HIV and malaria co-infection to be 12% as documented by Onyenekwe.C.C et al in a study from Southeastern Nigeria [61]

$$N = \frac{D2P(1-P)}{\delta}$$

Where N	=	Sample size
D	=	Critical value 1.96
P	=	Prevalence 12%
δ	=	Maximum likely error 5%
N	=	162 +10% = 180

9.5.1 Patients' recruitment

Patients were consecutively recruited into the study on the day of admission, if they fulfilled the inclusion criteria. All consented HIV and AIDS patients admitted to medical wards, at Amana, Ilala municipal hospital were identified and recruited.

9.5.2 Clinical intervention

Recruited patients were interviewed to obtain socio-demographic information as well as relevant symptoms. Socio-demographic information sought for included age, sex, marital status, education level, occupation and HAART use. Relevant symptoms asked for were fever, headache, nausea, vomiting, joint ache, myalgia, fatigue, chills and rigors. After interview each patients underwent a thorough physical examination and the information was entered into data collecting sheets for record keeping and analysis.

The duration of hospital and death were ascertained from patients' record files.

9.5.3 Laboratory Work-up

A venous blood sample was collected from each patient for the CD4 T-cell count, FBP, and comprehensive chemistry panel which include Alanine aminotransferase, Creatinine levels, serum Potassium determination. Peripheral blood was taken for RBG determination.

9.5.4 Diagnosis of Malaria

The rapid diagnostic test used in this study was Paracheck Pf™ device (Orchid Biomedical, India), which is based on the detection of P. falciparum-specific histidine-rich protein 2(HRP2 Pf) in blood. This was used to screen all patients recruited into the study. Those who were found to be positive on RDT had thick blood smears subjected to microscopic examination.

Here a blood specimen collected from the patient was spread as a thick blood smear, stained with a Giemsa for 30minutes and then washed off, followed by examination under 100X oil immersion objective for detection and quantification of malaria parasites. In this study diagnosis of malaria was based on finding malaria parasites in the thick blood smear of HIV patients. A slide was considered negative when no parasite was detected in the process of counting 200 leukocytes on a thick film.

9.5.5 CD4 cell counts measurement

To achieve the quality of the results MUHAS/HAVARD/ RESEARCH laboratory was used to analyze CD4 cell counts.

The laboratory has two types of machines which are FACS count and FACS calibur. In this study, FACS count machine was used to analyze CD4 cell counts of all patients.

After the blood was collected from the patient and put in a purple coloured stopper tube and transported in a cool box without ice packs at room temperature. The BD FACS count reagent container was taken and vortexed to mix its contents, and after which 50ul of reagent was drawn and put in a test tube.

Blood which was in a purple coloured stopper tube was taken and put in a test tube and mixed properly to avoid clotting.

Using a pipette, 50ul of blood was drawn from a test tube and mixed with BD FACS counts reagent in a test tube and closed with a cap then the mixture was put in a dark place, at room temperature for 60 to 120 minutes. After about 1 to 2 hours 50ul of fixative solution was drawn and mixed with an incubated blood then vortexed for 5 seconds. Here fixative solution is used to stop reaction and protect the cells from damage. Lastly the mixed solution was put in the FACS count machine for analysis.

10.0 PATIENTS DISPOSAL:

All patients were managed as per National malaria control program guidelines. Patients with HIV who were on anti retroviral therapy were advised to continue with their medications and those who were not on Antiretroviral and fulfilled the criteria for anti retroviral drugs initiation were sent to the nearby CTC clinic for HIV treatment and management.

11.0 ETHICAL CONSIDERATION

Ethical clearance for carrying out this research was obtained from the Research and Publication Committee of Muhimbili University of Health and Allied Sciences (MUHAS), and the Ethics Committee of Amana hospital. Informed consent for participation in the study was obtained from the individual respondents and the guardians and parents of the children.

In addition to consenting, individual participants were informed on their anonymous data use. For strict confidentiality, none of the participants' names appeared on the data collecting sheets which were separately coded.

12. 0 DATA ANALYSIS.

The collected data was entered into the SPSS version 15 computer statistical programme software, followed by data coding, checking and cleaning. The data double entry was done to ensure appropriate data consistency and quality.

Univariate analyses were used for descriptive statistics characterizing study participants. Comparison of proportions was tested using the Chi-square test and Fisher's exact test was adopted when the expected value in a cell was less than five. The odds ratios (OR) and 95% confidence intervals (CI) was used to quantify the strengths of predictors.

All statistical analysis was performed at a type I error rate of 0.05 and at confidence interval of 95% CI. The differences were considered significant statistically significant if p values were less than 0.05.

CHAPTER 3

13.0 RESULTS

During the study period, a total of 202 patients were screened, of these 180 fulfilled the inclusion criteria and consented to participate in the study. The rest i.e. 22(11%) patients were not included. Of these 15/22(68%) did not consent and 7/22 (32%) did not meet inclusion criteria. Among those who did not meet the inclusion criteria, 4/7(57%) had diabetes mellitus and 2(43%) had known severe end –stage organ disease.

Among 180 patients who fulfilled inclusion criteria and consented to participate in the study, 81 patients had positive rapid diagnostic test (RDT) and only 46 patients with positive RDT, had also positive blood slides for malaria parasites.

Characteristics of HIV and AIDS patients have been shown in table 1 below. A higher proportion of patients were female 68%, (95%C.I: 60.89 – 74.91) compared to male 32%, (95%C.I: 25.09 – 39.11).

The overall mean age of the study participants was 37.4(±1.42) years with a range of 9 – 69 years.

Eighty six percent of males and 87% of females were in the sexually active age group of 15- 49 years. The married couples comprised the majority of study participants, in which 49% of males were married while to 41% of females were also married ($p= 0.16$).

Males appeared to be more educated than their females' counterparts, with 46% of males having attained secondary school education compared to only 28% of females with secondary education ($p < 0.001$).While none of the males had informal education, 18% of the females had informal education.($p < 0.001$)

Fifty three percent of male were formally employed compared to 23% of females. Only 9% of males had reported to have no employment compared to 31% of females with no employment.

According to WHO grading classification of anemia, males predominated in grades 1, 2, and 3 while females predominated the lower grades of anemia i.e. grade 4 and 5($p = 0.01$).

Table1: Socio- demographic, HAART use status, and laboratory indices of HIV and AIDS patients admitted to medical wards at Amana hospital (N= 180).

	Male (%)	Female (%)	p-value
	n = 57 (31.7)	n = 123 (68.3)	
Age: (yrs)			
9 - 15	1 (2)	1 (1)	
15 – 49	49 (86)	107 (87)	0.844*
≥ 50	7 (12)	15 (12)	
Marital status			
Single	20 (35)	39 (32)	
Married	28 (49)	51 (41)	
Living together	5 (9)	13 (10)	
Divorced	3 (5)	8 (7)	
Widowed	1 (2)	12 (10)	0.16*
Education Level			
No formal education	0 (0)	22 (18)	
Primary education	28 (49)	63 (51)	
Secondary education	26 (46)	35 (28)	
Post secondary	3 (5)	3 (3)	<0.001*
Occupation			
Formal employment	30 (53)	28 (23)	
Informal employment	22 (38)	56 (46)	<0.001
No employment	5 (9)	39 (31)	
HAART use			
Yes	30 (53)	66 (54)	
No	27 (47)	57 (46)	0.887
HB(WHO Anemia Grading)			
Grade1	19 (33)	25 (20)	
Grade2	16 (28)	28 (23)	
Grade3	13 (23)	22 (18)	
Grade4	2 (4)	13 (11)	
Grade5	7 (12)	35 (28)	0.007*
CD4 cell (CDC-Classification)			
≥ 500	12 (21)	15 (12)	
200 – 499	21 (37)	58 (47)	
< 200	24 (42)	50 (41)	0.16

p- value denotes difference between HIV patients in terms of gender

* Fisher's exact test

13.1 Prevalence of HIV and Malaria co – infection

Among the Patients participated in study, 25.6% had a diagnosis of HIV and Malaria co infections, in whom the majority 38/46 (82.6 %) where in the age group of 15 – 49years. Females comprised 36/46 (78.2%) of the individuals who were diagnosed to have both HIV and Malaria co infections.

The overall prevalence of HIV and Malaria co-infection was higher among females (29.3%) as compared to males (17.5%) p= 0.09.The prevalence of HIV and Malaria co-infection was 26.6% among the married couples while that of patients who were single was 25.4%, however this difference was not statistically significant, p=0.824.

There was no significant association between the educational level status and the prevalence of HIV and Malaria co-infections. However, highest proportions of subjects with HIV and Malaria co-infections 28/113(25%) occurred in patients with primary school education or below.

Similarly, the prevalence of HIV and Malaria co-infection was not associated with occupation, though patients who had no employment has highest prevalence of 29.5%, p = 0.715.

Prevalence of HIV and Malaria co-infections in patients on HAART (21%) was lower compared to patients with no HAART use (31%); however this was not statistically significant ,(p= 0.12).

Similarly, the prevalence of HIV and malaria co-infection was not associated with CD4 cell counts, though this study found higher prevalence of HIV and malaria co-infections in patients with CD4 cell counts between 200 to 499um/mm3, p= 0.132. (Table2)

Table2: Distribution of HIV/AIDS and Malaria co-infection by socio- demographic characteristics, HAART use status and CD4 cell classification of patients admitted to medical wards at Amana hospital (N = 180)

Characteristic	Total Number of HIV patients	Number of HIV patients with Malaria	Proportion with Malaria (%)	P-value
Sex: Male	57	10	17.5	
Female	123	36	29.3	0.19
Age				
9 – 15	2	2	100	
15 – 49	156	38	24.3	
≥ 50	22	6	27.3	0.323
Education Level				
Informal education	22	6	27.3	
Primary education	91	22	24.2	
Secondary education	61	16	26.2	
Postsecondary educ	6	2	33.3	0.979
Marital status				
Single	59	15	25.4	
Married	79	21	26.6	
Cohabiting	18	3	16.7	
Divorced	11	4	36.4	
Widowed	13	3	23.1	0.924
Occupation				
Formal employment	58	13	22.4	
Informal employment	78	20	25.6	
No employment	44	13	29.5	0.82
HAART use				
Yes	96	20	21	
No	84	26	31	0.12
CD4 CELL(CDC-Classification)				
≥ 500	27	5	18.5	
200 – 499	79	26	33	
< 200	74	15	20.3	0.13

13.2 Characteristics of Patients with HIV and Malaria co –infections admitted to medical wards at Amana hospital by demographic and HAART use status.

The majority of patients with HIV and malaria co-infections were in the sexually active age group 15-49 years. (p = 0.261)

A high proportion of women were married (53%) compared to males (20%), however fifty percent of males were found to be single while 28% of females were also living single. (p= 0.201)

The use of highly active antiretroviral therapy (HAART) did not influence the HIV and malaria co-infection in both sexes, though the majority 26/46 (56.5%) of patients were not using HAART .p=0.802 (table3)

13.3 Laboratory indices of patients with HIV and Malaria co-infections admitted to medical wards at Amana hospital

Table4 shows that, thirty percent of males had grade1 anaemia while only seventeen percent of females were in the grade 1 anaemia by WHO grading classification. (p< 0.001)

Data for malaria parasites was stratified into three groups, the malaria parasites 1 to 500 per 200wbcs, 501 to 1000 per 200wbcs and above 1000 malaria parasites per 200wbcs. About 80% among males and 86% of females had 1 to 500 malaria parasites per 200 wbcs while 10% of males had malaria parasites more than 1000 per 200wbcs and no one in female sex had malaria parasites more than 1000 per 200wbcs.

Table3: Demographic characteristics and HAART use status of Patients with HIV and Malaria co-infections admitted to medical wards at Amana hospital (N = 46)

Variable	Male n = 10(22%)	Female n= 36(78%)	P- value
Age			
9 – 15	1(10)	1(3)	
15 – 49	9(90)	29(80)	
≥50	0(0)	6(17)	0.261*
Marital status			
Single	5(50)	10(28)	
Married	2(20)	19(53)	
Cohabiting	1(10)	2(6)	
Divorced	2(20)	2(6)	
Widowed	0(0)	3(8)	0.201*
Education level			
Informal education	0(0)	6(17)	
Primary education	4(40)	18(50)	
Secondary education	6(60)	10(28)	0.193*
Post secondary education	0(0)	2(6)	
Occupation			
Formal employment	5(50)	8(22)	
Informal employment	3(30)	17(47)	
No employment	2(20)	11(31)	0.22*
HAART use			
Yes	4(40)	16(44)	
No	6(60)	20(56)	0.802*

* Fisher's exact test

Table4: Laboratory indices of Patients with HIV and Malaria co- infections admitted to medical wards at Amana hospital (N = 46)

Variable	Male n= 10(22%)	Female n= 36(78%)	p- value
Haemoglobin(WHO grading classification)			
Grade1	3(30)	6(17)	
Grade2	2(20)	9(25)	
Grade3	3(30)	9(25)	
Grade4	0(0)	3(8)	
Grade5	2(20)	9(25)	0,01*
CD4 Cell counts(CDC-classification)			
≥ 500	3(30)	2(6)	
200- 499	4(40)	22(61)	
< 200	3(30)	12(33)	<0.001*
RBG(mmol/L)			
Hypoglycemia	0(0)	5(12)	
Normal	10(100)	36(88)	<0.001*
Malaria Parasites/200wbc			
1 – 500	8(80)	31(86)	
501 – 1000	1(10)	5(14)	
> 1000	1(10)	0(0)	0.004*
ALAT(U/L)			
Normal	5(50)	23(56)	
Elevated	5(50)	13(44)	0.395
Creatinine (umol/L)			
Normal	8(80)	29(81)	
Elevated	2(20)	7(19)	0.858*
Potassium(mmol/L)			
Mild hypokalaemia	2(20)	8(22)	
Normal	7(70)	21(58)	
Mild hyperkalaemia	1(10)	7(20)	0.102*

* Fisher's exact test

13.4 Main symptoms of HIV and AIDS patients with malaria and HIV and AIDS patients without malaria co-infection

The frequency of symptoms among the study participants in relation to HIV and malaria co-infection and HIV without malaria co-infection is shown in table 4.

A high proportion (93.5%) of patients with HIV and malaria co-infections presented with fever ($p < 0.001$).

Headache presented in 52.2% of HIV and malaria co-infected patients.($p=0.02$) Other symptoms which were common at presentation in patients with HIV and malaria co-infection and statistically significant included myalgia (32.6%) and fatigue 78.3%, ($p < 0.001$).

Table 5: Main symptoms of HIV and AIDS patients with and without Malaria co- infections admitted to medical wards at Amana hospital (N = 180)

	HIV without Malaria	HIV with Malaria	
	n=134(74.4)	**n=46(25.6)**	**p - value**
Fever			
Yes	66(49.3)	43 (93.5)	
No	68 (50.7)	3(6.5)	< 0.001
Headache			
Yes	44 (32.8)	24 (52.2)	
No	90 (67.2)	22 (47.8)	0.02
Nausea			
Yes	44 (32.8)	16(34.8)	
No	90 (67.2)	30(65.2)	0.809
Vomiting			
Yes	48 (35.8)	12(26.1)	
No	86 (64.2)	34(73.9)	0.22
Myalgia			
Yes	12 (9.0)	15(32.6)	
No	122 (91.0)	31(67.4)	< 0.001
Joints ache			
Yes	33 (71.7)	13(28.3)	
No	101 (75.4)	33(71.7)	0.626
Chills & Rigors			
Yes	1 (0.70)	2(4.3)	
No	133 (99.3)	44(95.7)	0.1
Fatigue			
Yes	45(33.6)	36(78.3)	
No	89(66.4)	10(21.7	0.001

13.5 Laboratory indices of HIV and AIDS patients with malaria co-infection and those without co-infection

Table 6 below shows the comparison of laboratory indices. In terms of the severity of anaemia by WHO grading system, lower grades were found more in HIV and malaria co-infection than HIV without malaria co-infection but statistically was not significant (p = 0.507) and similarly in CD4 cells counts by CDC –classification it was found no difference between the two groups(p= 0.06).

Table6: Laboratory indices of HIV/AIDS Patients with and without Malaria co- infections admitted to medical wards at Amana hospital (N = 180)

	HIV without Malaria	HIV with Malaria	
	n= 134 (74.4%)	n= 46 (25.6)	p-value
HB(WHO Anemia Grading)			
Grade1	35(26)	9 (20)	
Grade2	33(25)	11(24)	
Grade3	23(17)	12(26)	
Grade4	12(9)	3(6)	
Grade5	31(23)	11(24)	0.507
CD4 cell (CDC- classification)			
≥ 500	22(16)	5(11)	
200 – 499	53(40)	26(57)	
<200	59(44)	15(33)	0.06
RBG(mmol/L)			
Hypoglycemia	6(4)	5 (11)	
Normal	128(96)	41(89)	0.06
Creatinine (umol/L)			
Normal	96(72)	37(80)	
Elevated	36(28)	9(20)	0.185
ALAT(U/L)			
Normal	98(73)	28(61)	
Elevated	35(27)	17(39)	0.071
Potassium(mmol/L)			
Mild Hypokalaemia	39(30)	10(22)	
Normal	73(54)	28(61)	
Mild Hyperkalaemia	22(16)	8(17)	0.430

13.6 The comparison of clinical outcome (hospital stay and Death) of patients with HIV and Malaria co-infections and HIV patients without co-infection

The comparison of clinical outcome (hospital stay and death) of HIV patients with malaria co-infection and HIV patients without malaria co-infection is shown in table6 below.

Among the 46 patients with HIV and malaria co-infection, 46% stayed longer (≥ 5 days) in the hospital while only 25% of those without the co-infection had a long hospital stay. On the other hand sixty one percent of those without co-infection stayed shorter (< 5 days) in hospital as compared with 41% of those with co-infection. This difference was statistically significant, p –value <0.001

Table7: Comparison of duration of hospital stay and death to HIV patients with and without Malaria co- infection, admitted to medical wards at Amana hospital (N = 180).

Variables	Short hospital stay n (%)	Long hospital stay N (%)	Death n (%)	Total
HIV and Malaria co-infection	19(41)	21(46)	6(13)	46
HIV without Malaria co-infection	82(61)	33(25)	19(14)	134
Total	101(56)	54(30)	25(14)	180

Chi-square = 10.17, p –value = 0.01

13.7 The correlation of mean CD4 cell counts with the mean duration of Hospital stay and death for HIV and Malaria co-infected patients

The mean duration of hospital stay for the patients of HIV and malaria co-infection who stayed in the wards for less than five days was 4 days and the mean hospital stay for those who stayed in the hospital medical wards for more than five days was 7days.
The mean hospital stay for HIV and malaria co-infected patients who died was 2.8 days. As shown in the figure1 below. HIV and malaria co-infected patients who stayed for less than five days in the wards had a higher mean CD4 T- cell count of 372 cells/ul while those who stayed in the wards for more than five days, had a mean CD4 T- cell count of 207 cells/ul. Patients with HIV and Malaria co-infection who died in hospital had a lower mean CD4 T-cell count of 127cells/ul. However, there was no association found between CD4 cell counts, duration of hospital and death.

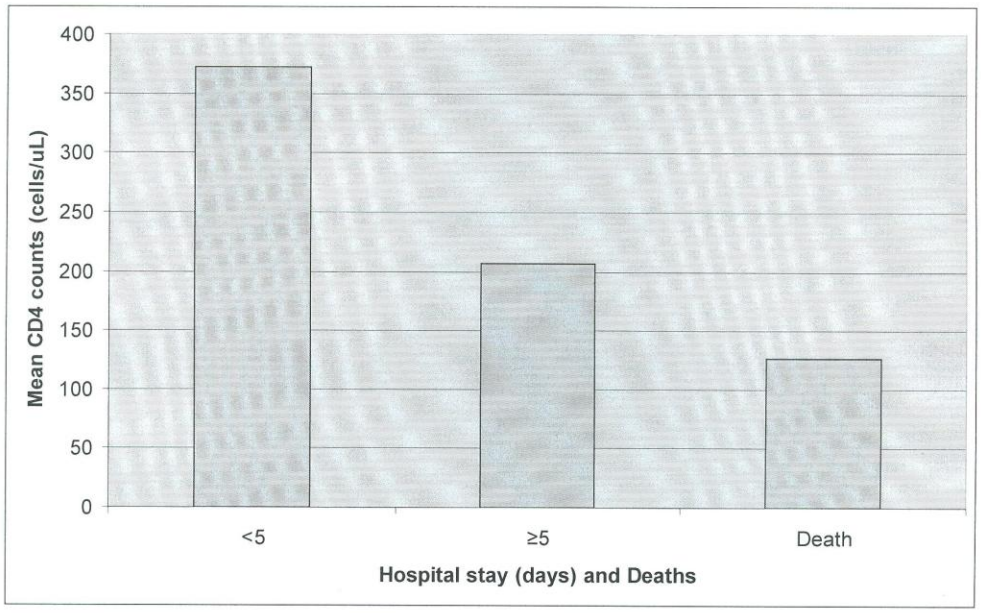


Figure1: The correlation of Mean CD4 cell counts with the duration of hospital stay and death of HIV and Malaria co-infections admitted to medical wards at Amana hospital.

13.8 The correlation of mean malarial parasites with the mean duration of Hospital stay and death for HIV and Malaria co-infected patients at Amana hospital

As shown in figure 2 below. The mean malaria parasites density was highest (1072mps/200wbcs) among HIV and malaria co-infected patients who died in hospital followed by the one who had longer hospital stay (246mps/200wbcs) and it was lowest (190mps/200wbcs) among those with a short hospital stay.

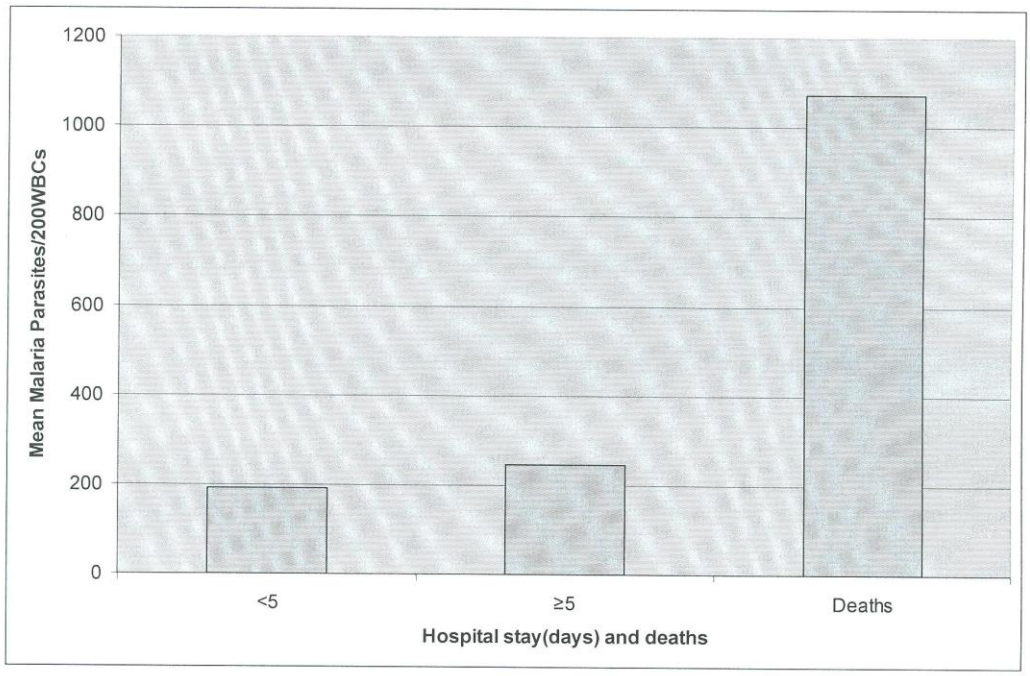


Figure2: The correlation of Mean Malarial Parasites with duration of hospital stay in days and Death of HIV and Malaria co-infections admitted to medical wards at Amana hospital.

CHAPTER 4

14.0 DISCUSSION

Prevalence of HIV and Malaria co-infection at Amana hospital

This was cross-sectional study aimed at establishing prevalence of HIV and malaria co-infection among HIV patients admitted to medical wards at Amana hospital. The study recruited 180 HIV and AIDS patients, in which 68.3% were females and 31.7% were males.

In this study, it has been found that Malaria is a significant problem among HIV patients admitted to medical wards, with overall prevalence of HIV and malaria co –infection 25.6%. This prevalence is higher than 11.8% prevalence of a similar study done in malaria endemic area of southern Nigeria[61]. This prevalence in a current study represents a big burden to the health care system which is already overwhelmed.

There are only few cross –sectional studies that have mentioned the prevalence of HIV and malaria co-infection. Some of these studies have been done in developing countries such as Botswana, Zimbabwe, Swaziland, South Africa and Namibia, and reported slightly higher figure (28%) [62].

The prevalence of HIV and malaria co-infection was also slightly high a 29.4%, in a prospective cohort study which was undertaken among adult hospital attendees in Douala, Cameroon.[63]

The current study has a lower prevalence than the one found in a cross-sectional study, which based on data from 104 HIV-infected patients from the French Hospital Database on HIV cohort adults returning from areas of endemic malaria, where they found that 40% had HIV and malaria co-infection.[55] The difference observed in prevalence between my study and France hospitals study, could be due to the fact that, most patients were living in non malarial zone and did not have immunity against malaria, which normally is acquired during childhood and the level of technology in diagnosis of malaria and HIV.

The prevalence found in present study which took place in urban area, is similar to what was found in a cross-sectional study in rural Tanzania, where by there was an increase in the parasitaemia prevalence, and non-significant increase in rates of non-severe malaria, among HIV sero positive adults compared with those who were sero –negative [63].

The prevalence of HIV and malaria co-infection, found in this study is higher than that (7.8%) of a study done in Northern Uganda at Lacor Hospital[64]. This is could be due to the fact that the Lacor hospital study involved the smaller sample size.

In another in Uganda, on effect of HIV-1 Infection on Antimalarial Treatment Outcomes in Uganda, reported HIV and malaria co-infection prevalence to be 31% [54], which is slightly higher than the one found in this study.

In yet a hospital based study done in Burundi in an area of high prevalence of HIV infection, the prevalence of HIV and malaria co-infection was 38.7% [65].This is higher than what has been found in this study. However, this high prevalence could be due to the fact that many hospital studies tend to portray a much higher prevalence than the community based studies. .

The prevalence of HIV and malaria co-infection was noted to be high (33%) and (20.3%) in patients with moderate and severe immunosuppression respectively, this high prevalence was also reported in Ugandan [32] and Malawian[66] studies on HIV and malaria co-infection. This high prevalence of HIV and malaria co-infection in moderate and severe immunosuppression was ascribed to the failure of the body to fight against infections in severe immunosuppression.

Social demographic of HIV and Malaria co-infected patients

Most of the patients with HIV and AIDS and malaria co-infection were in the age group 15 – 49 years. This is the most sexually active age group and has been severely hit by HIV and AIDS.

The study found that among HIV and malaria co-infected patients, 22% of women had formal employment and about 31% had no employment at all, compared to 50% and 9% of men who had formal and no employment respectively ($p = 0.22$).

The finding of more than a quarter of women without any form of employment, is related to the poverty of these individuals, as malaria has been linked with the poverty, so these women could be prone to mosquitoes and hence malarial infection.

Decline in co-infection among patients on HAART is due to the well established fact that HIV patients who are on HAART tend to have improved immunity. In this study use of HAART has been shown to reduce incidence of malaria in co-infected patients, though

did not reach significant level, as it was seen in the Ugandan study, on effect of co-trimoxazole prophylaxis, antiretroviral therapy, and insecticide-treated bed nets on the incidence of malaria among HIV infected adults.[57]

Clinical characteristics of HIV and AIDS and Malaria co-infected patients

In this study, the top symptoms were fever, headache, myalgia, nausea, vomiting, fatigue, joints ache, chills and rigors. However, fever, headache and myalgia in HIV and malaria co-infection were significantly differed from patients without co-infection.

The symptoms of fever, headache and myalgia were also the most common presenting symptoms of HIV and malaria co-infected patients in a study done in Malawi on the effect of Plasmodium falciparum malaria on HIV -1RNA blood concentration[41].

Study in Blantyre, Malawi on prospective cohort study in HIV positive patients, found that fever was the commonest symptom in HIV patients presented with clinical malaria and it was increasing as the severity of immunosuppression increase [66].

The study done in South Africa in an area of unstable malaria transmission, found the predominant symptoms to be vomiting and confusion which are the signs of severe malaria [34].This is in contrary to our findings, and could be due to the fact that people who live in unstable malaria transmission area do not develop strong immunity against malaria, so are prone to develop severe malaria compared to people from stable malaria zone. This may lead to observed difference in common presenting symptoms between the two studies.

The current study has shown that, fever was associated with moderate to severe immunosuppresion. This finding is similar to study done in Ugandan adults, the odds of parasitaemia, and the risk of malarial fever increased with decreasing CD4 cell count, such that individuals with CD4 cell counts < 200 cells/µl were more than twice as likely to suffer malarial fever as individuals with > 500 cells/µl.[32,48]

Similarly, a hospital-based case-control study in northern Uganda found an association between HIV infection and symptomatic malaria with fever as a predominant symptom.[64]

A recent study in a cohort of Malawian adults reported a moderate association between malaria parasitaemia and HIV infection. High parasite densities with fever were associated with low CD4 cell counts. [66]

The intensity of malaria parasite density and the level of immunosuppression appear to be critical in determining the consequences of co-infection. In this study the association between long hospital's stay as a consequences of HIV and malaria co-infection was established by comparing the HIV and malaria co-infection and HIV without co-infection. The majority of patients with HIV and malaria co-infections stayed longer in the hospital than the patients of HIV without malaria co-infection. $p = 0.001$ (Table6).

To my knowledge there is no cross-sectional study done in Tanzania so far to describe the factors that influence the long duration of hospital stay for HIV and malaria co-infected patients. Those study which have been done out side Tanzania, many of them did not report CD4 cell counts and so did not distinguish between HIV infection and the associated immunodeficiency; and most were facility-based case-control or cross-sectional designs with limited ability to assess any longitudinal population-based impact of the two infections and their interaction. However, some prospective studies done have shown significant relationship between long duration of hospital stay due to delayed response from antimalarial treatment and severity of immunosuppression in HIV and malaria co –infection, [67].

15.0 STUDY LIMITATIONS

This study has several important limitations. Due to financial constrains, this study could not do viral load, which could explain the burden of the HIV one could have in relation to the findings we have reported.

Blood slides for malaria diagnosis was performed by investigator with the help from a laboratory technologist at the site, without quality control from the third person at the reference laboratory for confirmation, this was not done due to little time provided for the accomplishment of the study and lack of fund .

16.0. CONCLUSIONS

The malaria infection was high in patients presenting with HIV. This finding supports the implementation of routine HIV counseling and testing for patients with uncomplicated falciparum malaria and malaria testing for HIV patients who attend the CTC clinics.

The co-infection was common at Amana municipal hospital because of presence of both diseases at high levels.

- It was high in:

1. (15 – 49) age group
2. Female with grade 4&5 anemia by WHO grading classification
3. Moderate to severe immunosuppression

- It was common in females and unemployed patients
- Fever was common symptom among patients with HIV and malaria co-infection
- It was associated with long hospital stay and death.

17.0. RECOMMENDATIONS

1. Interactions between HIV and malaria necessitate collaboration between HIV and malaria programmes.

2. HIV and Malaria programmes should contribute to strengthening health systems and capacity for equitable service delivery, to address the needs of poorer communities that are most at risk of these diseases.

3. There is a need for prospective studies with larger sample size to find the magnitude of this problem in the country.

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