ADDIS ABABA UNIVERSITY

FACULTY OF MEDICINE

DEPARTMENT OF COMMUNITY HEALTH

MALARIA AND HIV CO-INFECTION IN HADYA ZONE, SOUTHERN ETHIOPIA

By

Adamu Addissie, MD

A thesis submitted to the School of Graduate Studies of Addis Ababa University in partial fulfillment for the degree of Master of Public Health

April 2004
Addis Ababa

Addis Ababa University
Faculty of Medicine
Department of Community Health

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DECLARATION

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

Name: _____

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The thesis has been submitted for examination with my approval as a University advisor.

Name: _____

Signature: _____

Date: _____

DEDICATION

I dedicate this thesis:

- To my beloved family: my dad Ato Addissie; my mom Woizero Aster; my younger brothers Denamo, Yisak and Thomas, and my only and younger sister Helen. My parents, it is your constant support and inspiration that brought me here and I hope that the other children also will follow on the track that you already have shown us.

  AND

- To my great grand father the late 'Ababa Fogie', as many used to call him with traditional respect, who passed away during the week of my thesis defense. He has been an inspiration and role model for the whole family in many aspects especially modern education.

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LIST OF ABBREVIATIONS

AAU	Addis Ababa University
AIDS	Acquired Immunodeficiency Syndrome
ARI	Acute Respiratory Infections
CFR	Case Fatality Ratio
CI	Confidence Interval
DALYS	Disability Adjusted Life Years
DCH	Department of Community Health
DDPC	Department of Disease Prevention and Control
EB	Epstein Barr Virus
ELISA	Enzyme Linked Immuno Sorbent Assay
FM	Faculty of Medicine
GMPD	Geometric Mean Density of Parasitemia
HAPCO	HIV/AIDS Prevention and Control Office
HIV	Human Immune Deficiency Virus
HIV 1	Human Immune Deficiency Virus Type 1
HIV 2	Human Immune Deficiency Virus Type 2
HIVSN	HIV Sero-negative Group
HIVSP	HIV Sero-positive Group
HSDP	Health Sector Development Program
IL-10	Inter Leukine Type 10

ITNs	Insecticide Treated Mosquito Nets
MOH	Ministry of Health
NOCMVD	National Organization for Control of Malaria and Other Vector Borne Diseases
PI	Principal Investigator
PR	Prevalence Ratio
RBM	Roll Back Malaria
RR	Relative Ratio
SCM	Severe Complicated Malaria
SD	Standard Deviation
SNNPR	Southern Nations Nationalities and Peoples Region
SSA	Sub Saharan Africa
STD	Sexually Transmitted Diseases
T-cell	Thymus cell
TNF	Tumor Necrotic Factor
UNAIDS	Joint United Nations Program on HIV/AIDS
URTI	Upper Respiratory Tract Infection
WHO	World Health Organization

ABSTRACT

Back Ground: Malaria and HIV/AIDS are the major priority medical challenges facing sub-Saharan Africa in general and Ethiopia in particular and yet little has been known so far on the clinical and public health implications of HIV and Malaria co-infection. Even if the statistical effect is modest, any interaction between these two infections would have public health significance.

Objectives: A cross sectional health institution based study was conducted between mid October 2003 and mid January 2004 in three health facilities in Hadya Zone, Southern Ethiopia. The objectives of the study were to determine the prevalence of HIV malaria co-infections in the area and to describe the clinical manifestations of malaria in HIV positive and HIV negative malaria patients.

Subjects and methods: A total of 337 microscopically confirmed malaria patients in the age range of 15-34 years were included in the study. A structured questionnaire was used to collect data on socio demographic and clinical variables. Physicians used a checklist of physical findings during physical check up of patients. Anonymous HIV testing was done on the blood samples of the patients using single ELISA technique by an experienced laboratory technologist.

Results: The HIV serostatus assessment revealed that 4.2% (14 out of 337) of the patients were seropositive for HIV. No socio demographic difference was detected between HIV positive and HIV negative malaria patients.

Conclusions and Recommendations: The study concluded that the current HIV prevalence among *P.faciparum* malaria patients was not different from the HIV seroprevalence in the general population in the area, based on the prevalence findings from the national sentinel reports. No strong evidence suggesting an association between HIV and malaria was identified. The need for further studies with improved methodologies and designs is emphasized.

Key Words: HIV, Malaria, Coinfection, Health Institution, Ethiopia

1. INTRODUCTION

Two of the greatest medical challenges facing Africa today are human immunodeficiency virus (HIV) and malaria infections. Although these two infections are of major public health and clinical importance in the Sub Saharan Africa (SSA) in general and in Ethiopia in particular, their interaction is little understood (1). It is estimated that over 40% of the world's population lives in areas where there is high risk of malaria infection (2, 3). WHO estimates 300 - 500 million cases and 1.5 - 2.5 million deaths a year globally; Africa accounts for 90% of cases and the great majority of deaths (3, 4).

According to UNAIDS's latest report in July 2002; approximately 70% of the worlds 40 million HIV positive population live in Sub-Saharan Africa. UNAIDS also reports that out of the 5 million newly infected persons in 2001, 3.5 million live in Sub-Saharan Africa (5).

Man has known malaria for centuries and HIV has been around only for two decades. Malaria has already killed millions and continues to kill nearly three million every year. As of 1999 nearly 36 million people around the world have been infected with HIV and five million have died of AIDS related illness. In the coming millennium both diseases are expected to infect and kill many more around the world. And the biggest tragedy is that HIV infection is on the dramatic increase in those countries where malaria is already an uncontrollable problem (6).

Being the two most common infections in sub-Saharan Africa and to a lesser extent in other developing countries little is known on the clinical and public health implications of HIV and malaria co-infection. And yet the association between the two infections has important implications. It is estimated that 22 million Africans are already infected with HIV-1 and 500 million Africans get infected with malaria every year. Therefore, any interaction between these two infections will have public health significance, even if the statistical effect is modest (7).

On a population basis, an increased prevalence of malaria and parasite density in HIV infected individuals could lead to increased malaria transmission affecting both HIV positive and negative individuals, assuming that the frequency, duration and density of gametocytemia rise in parallel with asexual parasitemia, which is currently unproven. The increased risk of clinical malaria in HIV positive subjects could also increase the burden on clinical services in areas where HIV-1 is prevalent. The population attributable fraction of adult malaria due to HIV-1 would be expected to rise in parallel with HIV-1 prevalence. In a region with HIV-1 prevalence of 30% such as parts of Southern Africa, the population attributable fraction could reach 20% for parasitaemia and 35% for clinical malaria (7).

Research questions that need addressing in the relationship between these two illnesses include establishing the precise mechanism where by immunity to malaria is impaired by HIV-1; whether mortality from severe malaria is increased by HIV-1 in some situations; whether response to malaria treatment is diminished by HIV-1; whether the current

HIV-1 epidemics is having an effect on malaria control programs in Africa and whether improved clinical management of malaria in HIV-1 infected subjects, such as avoiding mosquito bites or chemoprophylaxis, slows the progression of HIV disease (7).

Recent studies have shown presence of interaction between malaria and HIV-1 in pregnant women and non-pregnant adults in Africa. In East and Southern Africa, where HIV-1 prevalence approaches 30%, about a quarter to third of clinical malaria in adults and malaria in pregnancy can be accounted for by HIV-1. If confirmed by further study, this has significant public health implications (8). Thus, the worsening of malaria in Africa could in part be due to the expanding HIV-1 epidemic. Also, if present observations of a transient increase in viral load during malaria episodes and its reversibility with effective treatment of malaria hold in, malaria control may be beneficial in curbing HIV-1 transmission and the rate of disease progression.

The interaction between HIV infection and malaria could work in either direction. HIV infection might reduce immunity to clinical malaria resulting in more frequent infection among the semi-immune and more severe disease among the semi-immune and non-immune; conversely malaria might enhance the progression of HIV infection to clinical AIDS (1).

The effect of HIV infection on the pattern of malaria might take the form of an increased

incidence of successful as opposed to aborted infections, an increased incidence of clinical as opposed to asymptomatic infections, or an increased incidence of severe rather than mild malaria (1).

Perhaps the other most critical challenge would be to make the most out of increasing resources for control of malaria and HIV-1. Anemia related deaths could be reduced by a joint program of prevention of malaria associated anemia and provision of a safe blood supply. High rate of attendance at antenatal clinics in Africa suggests that the effect of HIV-1 and malaria in pregnancy could be countered in routine antenatal care by the incorporation of malaria prevention, through intermittent preventive treatment and the use of insecticide treated bed nets, and access to HIV diagnoses and antiretroviral drugs (8).

Therefore, continued investigation in to the interaction of HIV-1 and malaria, and joint programming of key intervention strategies could lead to immediate and long-term benefits in disease control. Such studies also could help in dealing with certain misconceptions in HIV transmission in malarious areas (9). Our improved understanding of HIV disease progression combined with newer laboratory techniques for easier diagnoses of HIV infection and quantification of viral load provide an opportunity to revisit and further investigate these important areas of potential overlap between malaria and HIV.

It was with the above mentioned perspectives that the current study was designed to assess the magnitude of HIV infection among malaria patients in southern Ethiopia.

2. LITERATURE REVIEW

2.1. MALARIA

Malaria is a disease caused by protozoan parasites belonging to the genus *Plasmodium.* The four species of the parasite in human are *P. falciparum, P. vivax, P. malariae* and *P. ovale*. *Plasmodium falciparum* and *Plasmodium vivax* account for more than 95 % of cases of malaria in the world. *P. falciparum* is the cause for the severe form of the disease and most deaths due to malaria. Malaria is transmitted by the bite of infective female anopheles mosquitoes (10, 11).

Globally, almost half of the world's population is at risk of the disease; the poor and the most under privileged are most severely affected. Each year, malaria causes more than 2.5 million deaths and 300-500 million clinical illnesses; majority are in sub-Saharan Africa. It is estimated that over 80% of malaria clinical cases occurring in the world each year are in Africa. Malaria accounts for 10-30% of all hospital admissions, and is responsible for 15-25 % of all deaths of children, under the age of five. According to recent studies undertaken in various health facilities in Africa, malaria constitutes 20-60% of out patient consultations and about 10% of hospital admissions (3, 4, 11).

2.1.1. THE SITUATION OF MALARIA AND ITS EPIDEMIOLOGY IN ETHIOPIA

Malaria is one of the country's foremost health problems top ranking in the list of common infectious diseases. Three quarter of the total land mass is regarded as malarious and about 68% of the total population is at risk of malaria infection (12). Reports indicate that clinical malaria accounts for 10% - 40% of all out patient consultations, with corresponding proportional morbidity among children under 5 years in age being 10% - 20%. In recent years, on average, about 400,000 to 600,000 people with positive blood films for malaria are treated every year. It is estimated that the actual number of malaria cases seen at health facilities with out microscopic diagnostic services and by the community health workers is 3-4 times the number of cases treated at health institutions with diagnostic facilities. In addition, since quite a significant number of people do not have access to health services, the actual number of malaria cases that occur annually throughout the country is estimated in the range of 4-5 million. According to MOH reports, malaria accounted for 13% - 26% of all in patient admissions in the various health facilities with proportional mortality and case fatality rates of 13 - 35 % and 15 -17 %, respectively (12,13).

Malaria is also a significant impediment to socioeconomic development in Ethiopia. Fertile lowlands and major river valleys have not been fully inhabited and developed largely due to high malaria transmission in these areas. Due to fear of malaria in these areas the population has settled largely on the highlands; this has caused over population,

ecological degradation, reduced productivity and hence famine and poverty (12, 14).

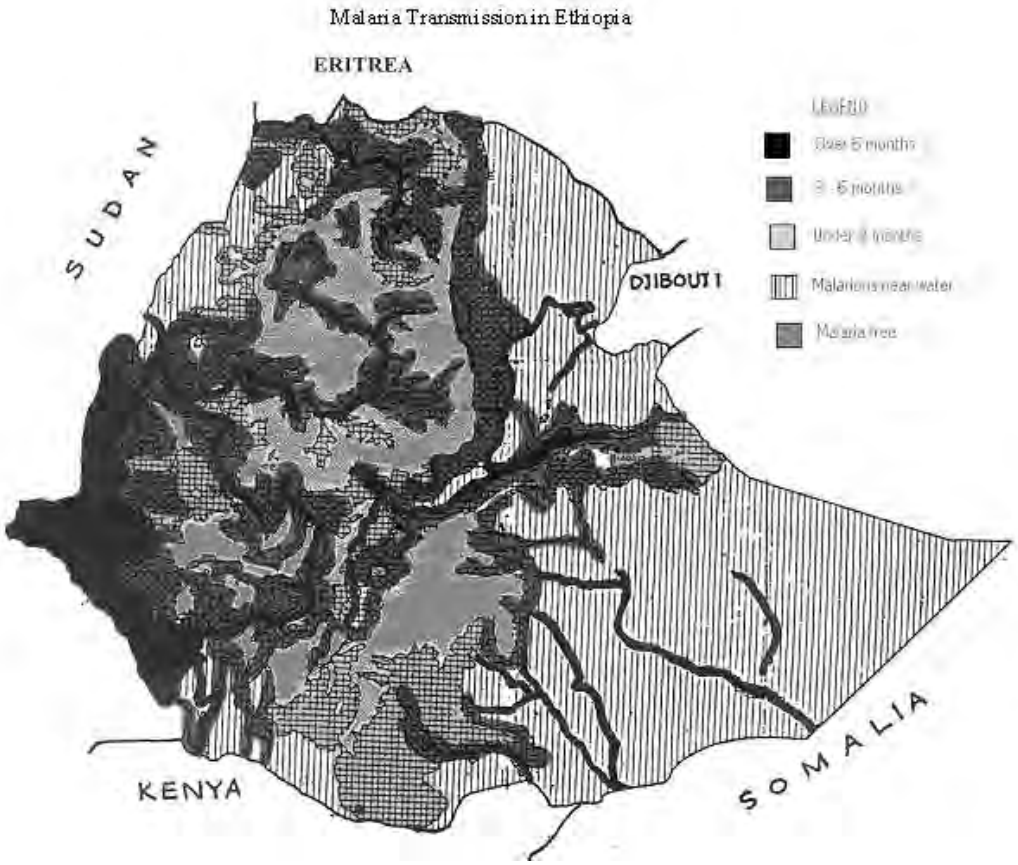
In endemic and malaria epidemic prone areas, the disease strikes during planting and harvesting seasons, cutting down productivity capacity at a time when there is the greatest need for agricultural work. The disease is also associated with loss of earning, low school attendance, and high treatment cost. Malaria also impedes flow of trade, foreign investment and commerce. During epidemics, malaria generally causes panic in the general population; economic activities, particularly agricultural activities are paralyzed. Health facilities are also overwhelmed and lots of resources are spent on dealing with the emergency situation. Generally, malaria accounts for 30% of the disease burden (DALYs) in all age groups (12, 13, 14).

In Ethiopia, *Plasmodium falciparum* and *Plasmodium vivax* are the two most dominant malaria parasites, distributed all over the country and accounting for 60% and 40% of malaria cases, respectively. *P. malariae* accounts for less than 1% and *P. ovale* is rarely reported. The parasite is principally transmitted by the major mosquito vector known as *Anopheles arabiensis* (12, 13).

Altitude and climate (rainfall and temperature) are the most important determinants of malaria transmission in Ethiopia. Transmission is seasonal and largely unstable in character (Figure 1). The major transmission season of malaria follows the June-September rains and occurs between September and December while the minor transmission season occurs between April and May following the February-March rains.

Areas with bimodal pattern of transmission are limited and restricted to a few areas that receive the small (*Belg*) rains. The major transmission season occurs almost in every part of the country. Accordingly, there are four eco-epidemological strata of malaria transmission in the country:

- malaria free high land areas above 2500 meters altitude,
- high land fringe areas between 1500-2500 meters which are affected by frequent epidemics,
- low land areas below 1500meter with seasonal pattern of transmission and
- stable malaria areas (characterized by all year round transmission) (12, 14).



Map 1 The epidemiology of malaria transmission in Ethiopia.

(Adopted from Professor Stanley Foster's Lectures)

2.1.2. CURRENT MALARIA CONTROL ACTIVITIES

The control of malaria in Ethiopia has a history of more than four decades, which initially began as a pilot control project in 1950s and launched a national eradication campaign in the 1960s followed by a control strategy in the 1970s. In 1976 a vertical organization known as the National Organization for the Control of Malaria and other Vector Borne Diseases (NOCMVD), evolved from the Malaria Eradication Services (MES). Until 1993, this organization had been operating with one central office, 17 regional or zonal offices, 70 sector offices and more than 1400 malaria detection and treatment posts. Some of the major contributions attributable to malaria control program activities in the country include, reduced prevalence and level of transmission in many areas, the opening up of the fertile arable lowlands and major river valleys for expanded agriculture and settlement, rapid growth of many urban centers in the lowlands and the general population increase in these areas (12).

Currently, the major malaria control measures being employed in the country include vector control and prompt case management. The vector control activities mainly rely on insecticide sprays, environmental management and insecticide treated nets (ITNs). The anti malarial drugs being used for malaria case management include chloroquine, sulfadoxine-pyremethamine and quinine. To this effect, the federal MOH has developed national guidelines for professionals involved in malaria case management (12, 15).

Concurrently, the global Roll Back Malaria (RBM) initiative, which aims at reducing the malaria burden by half in ten years, was initiated in 1998. In line with the global RBM objectives, malaria control in Ethiopia aims at reducing overall burden of malaria by 25% as compared to the 2000 level, over the coming five years. Furthermore it aims to maintain malaria free areas from introduction and establishment of the disease through strong surveillance and preventive measures (12).

Despite decades of sustained control efforts, malaria still remains as the major cause of morbidity, mortality and socioeconomic problem in Ethiopia. Various reports from health institutions in the country show that the problem is growing intense and there is a general build up and increase of malaria nation wide with common occurrence of epidemics. The problem is partly due to development of chloroquine resistant strains of *P. falciparum*, the commonest cause of malaria in Ethiopia and other possible factors (12, 16).

2.2. HIV / AIDS

HIV/AIDS is a new emerging phenomenon. The disease was first recognized in the United States in 1981. AIDS is characterized by presence of HIV infection together with presence of reliably diagnosed opportunistic infections that are indicative of underlying deficiency in cell mediated immunity in the absence of known causes of other underlying immune defects.

The etiologic agent for AIDS is *human immune deficiency virus* (HIV), which belongs to

the family of human retroviruses and the subfamily of *lentviruses*. The virus has two serotypes and the most common cause of HIV disease through out the world is HIV-1 (17).

HIV is transmitted by sexual contacts; by blood or blood-products; and from infected mother to infant intrapartum, perinatally, or via breast milk. There is absolutely no evidence that HIV is transmitted by casual contact or that the virus can be spread by insects such as by a mosquito bite (17).

The clinical consequences of HIV infection encompass a spectrum ranging from an acute syndrome associated with primary infection, prolonged asymptomatic state to advanced disease. The diagnoses of HIV infection is based on demonstration of antibodies to HIV or the direct detection of HIV or one of its components. The standard screening test for HIV is *enzyme linked immunosorbent assay* (ELISA). This solid-phase assay is an extremely good screening test, with a sensitivity of over 99.5 percent. The majority of diagnostic kits contain both HIV-1 and HIV-2 and thus either will be detected on routine screening. Though extremely sensitive, ELISA is not optimal with regard to specificity. Therefore, positive test results should be confirmed with a more specific assay (17).

It is estimated that there are more than 40 million HIV positive people in the world. Out these, 70 % live in sub-Saharan Africa. UNAIDS reported that out of those 5 million newly infected with the virus in 2001, 3.5 million live in sub-Saharan Africa (5).

2.2.1. HIV/AIDS SITUATION IN ETHIOPIA

Being located in SSA, Ethiopia is one of the countries most seriously affected by HIV/AIDS in the world. The earliest evidence of HIV infection in Ethiopia was found in 1984, with the first case reported in 1986. Since 1984, a cumulative total of 107,575 AIDS cases were reported to the Ministry of Health. The prevalence of HIV was low in 1980's but increased rapidly in the 1990's (18, 19).

The major avenue of transmission of HIV infection in Ethiopia is heterosexual intercourse. The practice of multiple sexual partnerships, particularly in urban areas, is a major contributory factor to the rise in HIV prevalence. Illegal medical practices and harmful traditional practices are also potential routes of transmission. It is believed that 30 to 40 % of babies born to HIV positive mothers are likely to contract the virus (18, 19).

The 2001 estimate of HIV prevalence in Ethiopia is 6.6 % with differing levels of magnitude in urban and rural parts of the country. The urban prevalence is 13.7 % where as the rural is 3.7 %. The number of persons living with HIV/AIDS is estimated at 2.2 million, including 2 million adults and 200,000 children. Approximately 10 percent of these (219,400) are full blown AIDS cases (18).

Data on age specific HIV prevalence rates have shown that the highest infection rates are concentrated among the age groups 15 to 24 years followed by the age group of 25 to 34 years. The HIV prevalence as well as the number of infected persons seems to decline

with age (18).

The age and sex distribution of reported AIDS cases shows that about 91% of infections occur among adults between 15 and 49 years. Given that the age range encompasses the most economically productive segment of the population, the epidemic impacts negatively on labor productivity. Work time is lost through frequent absenteeism, and decreased capacity to do normal work as the disease advances. There are also social consequences of the epidemic as care givers and income generating members of the family die leaving behind orphans and other dependents. These events lead to an aggravation of the problems of poverty and social instability (18).

2.2.2. HIV/AIDS CONTROL MEASURES

The Federal Government of Ethiopia vested responsibility for the planning and implementation of preventive and control programs against HIV/AIDS in the Department of Disease Prevention and Control (DDPC) of the MOH. Similar units operate at the regional and sub regional levels (18).

An HIV/AIDS Prevention and Control Office (HAPCO) was established to mobilize multi-sectoral and grass root efforts in the fight against HIV/AIDS. The office's major tasks call for reviewing and updating existing policies and guidelines, to ensure consistency with new scientific insights and methods of dealing with the epidemic. Now, advocacy and coordination are also part of HAPCO's responsibilities. The composition of

HAPCO reflects the type and focus it should bring to the battle against HIV/AIDS, i.e. creating a policy environment that would facilitate the involvement of relevant government sectors and non governmental organizations and civil society institutions (18).

2.2.3. CURRENT TREND AND PROJECTIONS OF HIV INFECTION

Although the government has made progress in the areas of education, access to health care and economic development, the AIDS epidemic is eroding those gains. The limited empirical data that are available show that hospital bed occupancy rates for HIV/AIDS cases are increasing. The health care sector, military and mobile work forces are likely to be significantly affected.

According to a projection model used for estimating the number of people living with HIV/AIDS (PLWHAS), the estimate was 2.2 million HIV positive and AIDS cases in 2001. The figure would increase in a more or less consistent manner over the coming 12 years. For example, from 2.2 million persons in 2001 it would increase to 2.6 million in 2006 and to 2.9 million by 2010. If the existing trend continues, the total number of people with full blown AIDS in 2014 would be 322, 310 (18).

The HIV /AIDS situation in the southern part of the country has also similar trend. Estimates of HIV prevalence in Southern Nations Nationalities and Peoples Region (SNNPR) according to the sentinel surveillance report (1989-2001) show that the HIV

prevalence in the region in the year 2001 ranges between 1.5% in Attat (rural site) to 11.6% in Soddo (an urban site). There was decline in the prevalence rates or similar rates were observed in most of the sites. Unlike other sites, in Hosanna town, the capital for Hadya Zone, there was a steady increase in the prevalence of HIV from 3.6 % in 1998 to 4.8 % in 1999-2000 and 5.9 % in 2001 (18,20).

2.3. AREAS OF POTENTIAL OVERLAP BETWEEN HIV AND MALARIA INFECTIONS.

With what we know of HIV infection, it is only natural that one expects as far poorer outcome for malaria infection in HIV patients. But on the contrary, the reports available indicate either no effect or even a protective effect of HIV infection against death from complications of *P.falciparum* malaria (6).

Studies showed that although high level of malaria parasitaemia has been observed in African children with symptomatic HIV infection, these children have been found to be 'protected' against cerebral malaria. This has been attributed to lower levels of TNF in HIV infected children. TNF is reported to have a potentiating effect on the endothelial adherence and clogging of microcirculation by parasitized red cells. In an animal study using mice, murine AIDS was found to confer protection against the severity of neurological manifestations of experimental cerebral malaria and this protection was higher with longer duration of immunodeficiency. IL-10 from splenic cells was shown to play a crucial role in this protection (6).

In Africa, human immunodeficiency virus type-1 (HIV-1) infection is a serious emerging infectious disease, and *P.falciparum* malaria infection is the most prevalent infectious diseases. Studies to date have not demonstrated a direct, biologic association between HIV infection and *P.falciparum*; that is, malaria has not appeared as an opportunistic infection, nor does it accelerate progression of HIV related diseases. However, altered cell mediated immunity in HIV infected person could influence the frequency and course of malaria infection. Inadequate sample sizes and the cross sectional nature of previous studies might have limited their ability to adequately asses any interaction between the two infections. The one confirmed area of overlap reported was the increased risk of HIV transmitted through blood transfusion to persons with severe malarial anemia (21).

There are also evidences that T-cell function is impaired during acute episodes of malaria. Proliferate responses to a variety of antigens are depressed during acute episodes of malaria when assessed by tests carried out on peripheral blood mononuclear cells. It is possible, however, that this anergy is due in part to sequestration rather than depletion of competent cells. Of particular importance here is the observation that T-cell control over EB virus infection is lost transiently in children with acute *falciparum* malaria. Thus, one might expect malaria infection to have an adverse effect on HIV infection both by stimulating T-cell turn over and by impairing T-cell cytotoxic function. Malaria infection may damage the placenta in such a way as to facilitate transmission of HIV in-utero (1).

There could as well be several other areas of interest to be assessed for potential overlap

between these two illnesses (21):

- Safety and efficacy of anti-malarials : the high incidence of febrile episodes among HIV infected persons may result in greater exposure to anti-malarial drugs and thus a higher risk of adverse drug reactions, particularly to sulfonamides.

- Chloroquine as a cofactor for HIV replication: data from invitro studies indicate that chloroquine may be a cofactor for increased viral replication

- Malaria as a cofactor for HIV progression: malarial parasitaemia and the released antigens may be a cofactor for increased viral load and subsequent progression of HIV related disease.

- HIV as a confounder in studies of malaria related mortality: the impacts of malaria control efforts on reduction of severe morbidity and mortality may be less than expected in areas where HIV prevalence is high.

- Malaria and HIV during pregnancy: recent studies indicate that HIV infected pregnant women are at increased risk of peripheral, placental, and cord blood parasitaemia which may be a cofactor for mother to infant transmission of HIV and for earlier progression of HIV related disease, and that HIV impairs the efficacy of sulfadoxine-pyremethamine for control of placental parasitaemia.

2.3.1. HIV AND ASYMPTOMATIC OR UNCOMPLICATED MALARIA

INFE CTION

Chandra and Greenwood (1998) tried to asses different studies done in these areas (1). About seven different studies were done between 1986 and 1991 in urban hospitals in Uganda, Rwanda, Zambia, and Zaire and one in a rural dispensary in Tanzania. The range of the study population varied widely between studies and one study was restricted to 18-35 years old women. The prevalence ratio (PR) of peripheral parasitaemia among the HIV seropositive group (HIVSP) compared to the HIV seronegative group (HIVSN) ranged from 0.72 to 0.94 in children (<13years) and from 3.3 to 0.69 in adults (>11years). However only one difference from a study of adults in rural Tanzania, was statistically significant (1).

The rate ratio (RR) of none severe malaria (fever + parasitaemia) among HIVSP was higher compared to HIVSN in two cohort studies but differences between groups were only of borderline significance. In addition, there was no significant difference in the proportion of slides positive for malaria among fever cases or in the parasite density between HIVSP and HIVSN groups. During a 13 months period follow-up of 5-9 months old children with HIV-1 infection, there was no any statistically significant difference in the incidence of malaria in 36 children who developed AIDS and in 37 children who did not develop AIDS (1).

2.3.2. HIV AND SEVERE MALARIA

In two studies done in urban Burundi, and Zambia among admitted adults with severe malaria, the case fatality ratio (CFR) was more than twice as high in the HIVSP compared to the HIVSN group. However, the sample sizes of these studies were too small to draw any statistically significant conclusion (1).

In another study done in Zimbabwe, after adjusting for confounders, the risk of developing severe and complicated malaria was significantly more in HIV positive patients than in HIV negative patients (22)

2.3.3. HIV AND MALARIA IN PREGNANCY

In a secondary analysis of data, from a cohort of mothers enrolled in a trial chemoprophylaxis during pregnancy undertaken in rural Malawi from 1987 to 1989, it was observed that the prevalence of parasitaemia at the time of enrollment was similar among HIVSP and HIVSP primigravidae, but it was higher among HIVSP multigravidae compared to HIVSN multigravidae. The geometric mean density of parasitemia (GMPD) was higher in HIVSP primigravidae than HIVSN primigravidae. While the GMPD decreased with gravidity it was consistently higher in HIVSP than HIVSN pregnant women at all parities. The incidence of placental malaria was also higher among HIVSP than HIVSN women, and this difference was more marked among multigravidae (1).

2.3.4. HIV AND RESPONSE TO ANTIMALARIAL TREATMENT

Chloroquine, the most commonly used ant-malarial drug in Africa has in-vitro anti HIV-1 activity. Prospective studies addressing the role of chloroquine as an anti-HIV-1 agent are being planned in sub-Saharan Africa (8).

Two studies have examined the prevalence of treatment failure on day 7 following treatment with Quinine given a dose of 20 mg/kg daily for 5 days in HIVSP and HIVSN children in urban Zaire; there was no significant difference in the level of treatment failure in the two groups (1).

In an Ethiopian study, nineteen hospital admitted adult malaria patients with *P. falciparum* infection (7 HIV sero positives and 12 HIV sero negatives), were followed for their response to anti malarial therapy (*artemisinin*) so as to investigate the effect of *artemisinin* on the rate of clearance of *P. falciparum* in patients with or with out human immune deficiency virus (HIV) co-infection. The findings of the study indicated for the first time that clearance of *P.falciparum* after administration of *artemisinin* is delayed in patients with HIV co- infection (23).

2.3.5. MALARIA AND PROGRESSION TO HIV INFECTION

In community based study in Guinea Bissau, no significant difference in provirus load of HIV- 2 was found between subjects who had peripheral parasitemia and those who did not; the geometric mean provirus load in the two sub groups were 103 (95% CI : 37-287) and 146 (95% CI : 96-220) respectively (1).

3. OBJECTIVES

3.1. GENERAL OBJECTIVE

- The general objective of the study is to determine the prevalence of HIV-malaria co-infection, in malaria patients in Hadya Zone, Southern Ethiopia and determine if this rate is different from the HIV prevalence rate in the general population.

3.2. SPECIFIC OBJECTIVES

- To assess the knowledge of the study population about malaria illness and treatment seeking behavior.

- To measure the seroprevalence of HIV among malaria patients in Hadya Zone.

- To describe the clinical manifestation (in terms of reported symptoms, physical findings and blood microscopy results) of malaria in HIV seropositive and seronegative malaria patients.

- To assess the presence of HIV/AIDS related risk factors among the study population.

- To compare the rate of HIV in malaria patients with that of the general population.

4. SUBJECTS AND METHODS

4.1. STUDY DESIGN

The study used a health institution based descriptive cross sectional design.

4.2. STUDY AREA AND PERIOD

The study was conducted in Hadya Zone, Southern Ethiopia, between October 2003 and mid January 2004. The period coincides with the major season of peak malaria transmission in the country.

The study area, Hadya zone is one of the 13 zones in the southern nations and nationalities region (SNNPR) and has a population of approximately 1,174,118 (586,316 males and 587,802 females; 87,671 urban and 1,086,447 rural). The capital town of the zone, Hosanna is located 230 kilometers from the national capital Addis Ababa, 210 kilometers from the regional capital Awassa and 102 kilometers from the farthest woreda in the zone, Badawacho woreda (24, 25).

The total area of the zone is 5000 km^2 and has three climatic zones. Dega (>2500 meters, 24%), Woinadega (1500-2500 meters, 65%) and Qolla (<1500 meters, 11 %). The economic livelihood of the people in the zone is based on livestock (14.6 %), crop production (77.4 %), trade (6.7 %) and other activities (1.25 %) (24, 25).

The region is well known for both endemic and epidemic forms of malaria transmission. Malaria is also a leading cause of outpatient visit, hospital admission and hospital death in the region. As can be seen from different reports, the magnitude of infection is on the increase (26).

In both regional (SNNPR) and zonal (Hadya) levels, malaria was top on the list as a cause of out patient morbidity in 1997/98. In Hosanna hospital, the referral hospital for three zones including Hadya zone, malaria was the major cause of hospital death and inpatient load for the same period. And the five most common diseases in the zone at woreda level in 2001 in decreasing order were malaria, upper respiratory tract infections, intestinal parasites, gastritis and diarrhea (24, 25, 27). The region's (SNNPR) HIV prevalence based on blood donor report for year 2001 was 5.1 % where as the sentinel site report for Hosanna (zonal town) for the same year was 5.9 % (18, 20).

The health services coverage of the zone is 42.42 %. There are five health institutions with operating laboratories in the zone, one of them being capable of performing HIV testing. There is also a regional research and health laboratory branch located at Hosanna responsible for the activities of diagnostic and research laboratory activities in three zones (Hadya, Kambata Tembaro (KT) and Guraghe) (24, 25).

The study was conducted in three health institutions in Hadya zone. These were one hospital (Hosanna hospital) and two health centers (Hosanna and Shone health centers) (See Annex IV). Health institutions were selected from malaria endemic locations in the

zone based also on the availability of infrastructures (laboratory facilities and qualified health professionals who are able to carryout the required procedures in the study) that are required to conduct the study. The requirements were laboratory setups with a functional refrigerator and centrifuge, presence of a physician (or a health officer) and a qualified medical laboratory technician.

4.3. SOURCE AND STUDY POPULATION

Patients diagnosed to have symptomatic, slide positive *P. falciparum* infection in the three health institutions in Hadya Zone were the source population for the study. Adult patients in the age range of 15-34 years with symptomatic slide positive *P. falciparum* malaria were included in the study. According to the MOH's report for the year 2001, this was the age range with peak HIV infection (18, 20).

4.4. SAMPLE SIZE AND ENROLLMENT PROCEDURES

The minimum sample size required for the study was calculated using statistical formula for a single population proportion (28).

$$N = \frac{(Z\ \alpha/2)^2\ P\ (1-P)}{d^2}$$

Where,

N = the number of subjects to be included in the study (i.e. the sample size)

Z = standard normal distribution curve value for 95% confidence interval which is 1.96 (where α=0.05)

P = proportion of co infection (the approximate proportion of *P.falciparum* cases who would turn out to be HIV positive) taken from other African studies, which is equal to15 %

d = absolute precision (which is taken at 0.04)

In addition expecting the issue of HIV testing to be sensitive, a non-response rate of 10 % was added and an effective sample size of 337 was computed. All patients with slide positive *P. falciparum* malaria infection diagnosed in the three health institutions who are willing to participate in the study were included until the required sample size was attained.

The total required sample size was distributed to the three health institutions based on the proportions of the total number of malaria patients reported to the Zonal Health Department by each institution in the year 2002/2003 (27). Accordingly, 149 (44.2%) patients from Hosanna health center, 130 (38.6 %) patients from Shone health center and 58 (17.2 %) patients from Hosanna hospital were included in the study.

Self reported febrile patients suspected to have malaria infection were investigated microscopically for *P.falciparum* malaria. Once the infection was microscopically

confirmed, those patients who fulfilled the inclusion criteria (*P. falciparum* positive and in the age group 15 – 34 years) and willing to participate in the study were referred to the study team and enrolled into the study. After interview and clinical evaluation, venous blood samples were taken for routine hemoglobin and random blood sugar checkup. On the same sample serology was performed for HIV antibodies, anonymously.

4. 5. STUDY VARIABLES

The following dependent and independent variables were used for data collection purpose.

4. 5. 1. DEPENDENT VARIABLE

HIV serostatus (serological status of HIV-1 infection)

- HIV-1 negative = a negative test result with the first ELISA
- HIV-1 positive = a positive test result with the first ELISA

4. 5. 2. INDEPENDENT VARIABLES

- Socio demographic characteristics
- Socio economic variables
- Knowledge about malaria illness and health seeking behaviors
- Risk factors for HIV/AIDS infection

- Clinical and laboratory data
    - Reported symptoms of malaria and HIV/AIDS
    - Physical signs of malaria and HIV/AIDS
    - Species of malaria parasites
    - Parasitic load

4.6. DATA COLLECTION INSTRUMENTS (MEASUREMENT) AND DATA COLLECTORS.

4.6.1. Structured Questionnaire

A questionnaire which includes the basic socio demographic and clinical variables about the study subjects as well as their knowledge, attitude and practice towards malaria and HIV cause, treatment and prevention was used (Annex I). No personal identifiers were included and individuals were given a unique code number to be attached on the questionnaire and their laboratory specimens (test tubes).

4.6.2. Checklist of Physical Examination (clinical data)

To ascertain presence or absence of signs of severe malaria and major signs of AIDS, physical examination was performed with a check list of important physical examination variables (Annex II).

4.6.3. Laboratory Tests

4.6.3.1. Test to confirm *P. falciparum* malaria infection.

The diagnosis of malaria infection was based on the recognition of *P. falciparum* malaria parasites in the thick and thin blood films stained with *Giemsa* (29). Slides were considered negative when no parasites were detected on examination of approximately 1,000 leukocytes on the thick smear. Parasites when present were counted on the thin smear, against 500 to 2,000 erythrocytes (for parasitemia of 1% or more) or at least 10,000 erythrocytes (for lower parasitemia). In patients with very low parasite densities, parasites count was made against 300 leukocytes on the thick smear. As a result the load was computed in the conventional way using "+" sign, ranging from minimal parasitemia (+) to the maximum parasite loads (+++++) (15).

4.6.3.2. Tests to Determine the HIV-1 Infection

Serological tests were done anonymously on the sample drawn for hemoglobin and random blood sugar determination with out the knowledge of the subjects about the tests, data collectors about the status of the subjects and the laboratory technicians about the identity of the subjects. The blood samples drawn from the subjects were centrifuged and kept at -4 ^{o}C. The isolated serum samples were transferred on the same day to Hosanna Zonal Health and Research Laboratory to be kept at -20^{o}c until transported to the test laboratory. Single ELISA was performed on all specimens at Awassa Regional Research

Laboratory. Serology was performed with commercially available kits by enzyme linked immuno-sorbent assay (ELISA) method. (*Vironestica HIV Uni-Form II plus O*, Boxtel, Netherlands) (30). An ELISA worksheet was employed for the registration of test values (Annex III). Specimens were considered positive for HIV anti bodies if reactive for first ELISA (31).

Physicians collected data regarding socio-demographic and clinical information. If physicians were not available, this task was carried out by health officers. Questions were not probed when administered to the respondents. Data collectors were given a two days training on the techniques of data collection for the study. Blood samples were collected by qualified health assistants who took orientations on the process of blood sample collection using vacutainer tube. Microscopies for *P. falciparum* were performed by qualified and experienced laboratory technicians. Serology to detect HIV-1 antibody was performed by a senior medical laboratory technologist from Awassa Regional Health and Research Laboratory.

4.7. DATA QUALITY ISSUES

The questionnaire was first prepared in English and translated into Amharic and retranslation to English was performed by an independent individual to check for consistency of the meanings of the questions. Pre-testing of the questionnaire was conducted in 34 randomly selected outpatients (10% of the sample size) in Gimbichu Health Center to asses clarity, understandability and flow of questions as well as the time

needed to fill the questionnaire. Based on the findings some questions were restructured.

During the data collection process, the supervising data collector daily checked the questionnaires for completeness. Incomplete or misfiled questionnaires were sent back to the respective data collector for correction.

During the ELISA procedure, comparative control tests were performed for standard control samples provided by the test manufacturer together with the test kit. Five control samples (two positive and three negative controls) were used for every 91 serum samples according to the guidelines provided by the test manufacturers for this purpose. All the procedures in the manual were strictly followed (30).

4.8. DATA ENTRY AND ANALYSIS

Data entry and analysis were performed at the Department of Community Health (DCH), AAU-MF by the principal investigator (PI) using SPSS-10 statistical software package.

The principal investigator before and during the actual data entry performed coding and data cleaning. Any error identified during data entry was corrected after tracing and revising the originally completed questionnaire.

Once the cleaned and edited data were ready for statistical analysis, data analysis was performed by the PI using EPI Info 6.0d and SPSS-10 statistical soft wares. Odds ratios

with 95% confidence interval were used to assess significance of associations between outcome variables and certain independent variables. Logistic regression model was used to assess presence of associations as well as to identify and control for confounding variables. The results of the analysis are presented in tables and graphs.

4.9. OPERATIONAL DEFINITIONS

HIV infection: presence of HIV-1 antibodies in the blood as is detected by single ELISA test.

HIV-1 sero positive: a positive test result for HIV with the first ELISA.

HIV-1 sero negative: a negative test result for HIV with the first ELISA.

Malaria and HIV co-infection: presence of both malaria and HIV infection in an **individual at the same time.**

Malaria infection: presence of *P. falciparum* parasites in the peripheral blood film as is detected by blood microscopy.

Severe complicated malaria: microscopically confirmed *P. falciparum* infection with presence of one or more of the following signs and symptoms

- Altered consciousness (confusion, sleepy, drowsy, coma)
- Severe anemia
- Hypoglycemia

- Convulsion or recent history of convulsion
- Unable to sit or stand up (prostration)
- No urine output in the last 24 hours
- Spontaneous bleeding (gum bleeding, epistaxis, hematemesis, melena)
- Yellowish discoloration of eyes
- Difficult breathing
- Dark urine ('coca-cola' urine; Black Water Fever)
- Failure to respond to treatment in 2-3 days
- Hyperpyrexia (15, 32)

4.10. ETHICAL CONSIDERATIONS

The study was conducted after the proposal was approved by the ethical clearance committee from DCH, FM, AAU and a formal ethical clearance obtained. Before conducting the survey, written permission was obtained from Hadya Zone Health Desk. Data collection consent was obtained from the respective health institutions.

All the study participants were briefed on the purpose and benefit of the study and permission was obtained orally in advance from each patient. They were assured that any information concerning them would never be used by any individual or institution in any way identifying their personal identity.

To keep anonymity, every participant was given a unique identifier code number and

only this code numbers were attached to the questionnaires and test tubes. During data entry and analysis, the investigator identified only these codes which were used to draw associations and conclusions about the study population.

Refusal of a patient to participate in the study did not interfere with the routine doctor-patient relationship. Those who refused to be involved in the study were managed according to the routine procedures in the respective health unit.

Every patient in the study was treated for malaria based on the test results and according to the MOH's national guideline for the management of simple and complicated malaria.

5. RESULTS

5.1. Socio-demographic and socio-economic characteristics of the study population

A total of 337 *Plasmodium falciparum* infected malaria patients between 15 - 34 years of age were included in the study. Of these 233 (69.1%) were males and the rest 104 (30.9%) were females. The male to female ratio was 1**:** 0.40. Thirty two percent of the respondents were 15-19 years old. The mean (SD) age of the patients was 23.8 (2.4) years with a median age of 25 years. Most patients were single (51.3%) followed by the married (47.7%). The rest 10.0% were either widowed or divorced. The majority of patients, 269 (79.8%), were rural residents and the rest 68 (20.2%) were from urban settings. More than 85 % (288) had lived in their current place of residence for 10-20 years or above (Table 1).

With regard to religious composition, 75.7 % (255) were Protestants followed by Orthodox Christians (9.8%) and Muslims (7.7%). The rest 23 (6.8 %) belonged to other religions including Catholic and traditional religions. The majority of the patients, 260 (77.2%), were from Hadya ethnic group and 35 (10.4%) were Kambatas. The rest 42 (11.9%) were from various ethnic groups like Amhara, Gurhage, Silte, Alaba or Wolayita (Table 1).

Table 1 Socio-demographic characteristics of *P. falciparum* patients from three health institutions in Hadya Zone, Southern Ethiopia, 2003 (n = 337).

Variable	Frequency (No.)	(%)
Sex		
Male	233	(69.1)
Female	104	(30.9)
Age		
15-19	109	(32.3)
20-24	72	(21.4)
25- 29	83	(24.6)
30-34	73	(21.7)
Marital Status		
Married	154	(45.7)
Single	173	(51.3)
Widowed and divorced	10	(10.0)
Address		
Rural	269	(79.8)
Urban	68	(20.2)
Duration lived in the area		
0-10 years	49	(14.5)
11-20 years and above	288	(85.5)
Religion		
Orthodox	33	(9.8)
Muslim	26	(7.7)
Protestant	255	(75.7)
Others	23	(6.8)
Ethnic group		
Hadya	260	(77.2)
Kambata	35	(10.4)
Other*	42	(11.9)

* Includes Amhara, Guraghe, Silte, Alaba or Wolayita.

5.2. Socioeconomic status of the study subjects

One hundred thirty (38.6%) of the patients were farmers and 30.0% were students. Housewives were 44 (13.1%); merchants and government employees were 8.1%. The rest 35 (10.5%) were daily laborers, soldiers or jobless. About 33.6 % (113) of the patients had no formal education. Where as, 66.4 % (224) had various levels of formal education either elementary school (34.4%) or secondary school and above (32.1%) (Table 2).

When asked about their current living condition, the majority, 298 (88.4%), answered that they were living with their immediate family, 27 (8.0%) alone, and the rest 12 (3.6%) with friends or other relatives. The source of income for living for 139 (41.2%) of the respondents were themselves, followed by their relatives (40.1%), and spouses (13.6%). Only 41 (12.2%) were able to quantify their monthly income. Majority 296 (87.8%) were either unable or unwilling to do so. Among those who reported their family income, 17 (41.5%) had less than 100 Birr** per month, 9 (21.95%) had 100-250 Birr / month, anther 9 (21.95%) had 251-500 Birr / month and 6 (14.6%) had more than 500 Birr / month (Table 2).

5.3. Health institution accessibility

Of the patients included in the study, 149 (44.2%) were from Hosanna health center, 130 (38.6%) were from Shone health center and the remaining 58 (17.2%) were from Hosanna hospital.

** According to current currency rates one US dollar is exchanged for about 8.5 Ethiopian Birr

Among these patients, 219 (65%) were able to estimate the distance from their home to the current health facility visited and 167 (49.6 %) were able to estimate the distance from their home to any of the nearest health institution. Among those who were able to estimate the distances, 121 (55.3%) traveled more than 10 kilometers to the current health institution, 55 (25%) traveled less than 5 kilometers and 43 (19.6%) traveled 6-10 kilometers. Likewise, 128 (76.7%) lived in an area less than 5 kilometers away from the nearest health institution, 29 (17.4%) lived 6-10 kilometers away and 10 (6.0%) lived more than 10 kilometers away.

The means of transportation to the nearest health facility for 301 (89.3%) of the patients was traveling on foot. The rest traveled either by car (4.2 %), by using horse / mule back (3.0 %) or by cart (2.7%) (Table 3).

Table 2 The socio-economic status of the falciparum malaria patients from three health institutions in Hadya zone, Southern Ethiopia, 2003 (n = 337).

Variables	Frequency (No.)	(%)
Current living condition		
Alone	27	(8.0)
With family	298	(88.4)
Other	12	(3.6)
Source of income for living		
Self	139	(41.2)
Relatives	135	(40.1)
Spouse	46	(13.6)
Other	17	(5.1)
Average Family Income (Birr per month) (n = 41)		
<100	17	(41.5)
100-250	9	(21.95)
251-500	9	(21.95)
>500	6	(14.6)
Occupation		
Farmer	130	(38.6)
Merchant and government employee	27	(8.1)
Student	101	(30.0)
House wife	44	(13.1)
Other**	35	(10.5)
Literacy Status		
No formal education	113	(33.6)
Elementary School	116	(34.4)
Secondary school and above	108	(32.1)

** Includes daily laborers, soldiers or jobless

Table 3 Accessible health institutions, distance and means of transportation to the current and the nearest health institution among *falciparum* malaria patients from three health institutions in Hadya Zone, Southern Ethiopia, 2003.

Variable	Frequency (No.)	(%)
Accessible Health Institutions (n= 337)		
Hosanna Health Center	149	(44.2)
Shone Health Center	130	(38.6)
Hosanna Hospital	58	(17.2)
Distance from home to the current health inst. (n = 219)		
0-5 km	55	(25.1)
6-10 km	43	(19.6)
> 10 km	121	(55.3)
Distance from home to the nearest health inst. (n =167)		
0-5 Km	128	(76.7)
6-10 Km	29	(17.4)
>10 Km	10	(6.0)
Means of transportation to nearest health inst. (n= 337)		
On foot	301	(89.3)
By car	14	(4.2)
On horse/mule back	13	(3.9)
By cart	9	(2.7)

5.4. HIV sero-prevalence

The HIV sero-status assessment revealed that 4.2 % (14 out of 337) of the *P. falciparum* malaria patients were sero-positive for ELISA HIV test. Though the proportion of HIV positive male patients (4.7 %) was higher than the proportion of females (2.9 %), there was no statistically significant difference between the two groups in terms of seropositivety. In the same way the proportion of seropositives among the patients in the age group 25-34 years (5.8 %) was higher in relative terms than the proportion of seropositives among patients in the age group 15-24 years (2.8%). And the proportion of seropositives in urban setting (7.4%) was also higher compared to the proportion of seropositives in the rural setting (3.3%), however these differences were not statistically significant. No statistically significant association was also found for HIV seropositivety with religion, ethnicity, occupation and literacy status of the patient (Table 4).

The HIV sero-prevalence rate was higher among those not living with family (10.3%), than those living together with family (3.4%), and in those with monthly income >250 Birr (13.3%) than those with lower income (3.8%) in comparison with the seropositivety rate among those who did not report their income (3.7 %). Yet these differences also were not statistically significant (Table 4).

Table 4 Socio-demographic and socio-economic variables and their association with HIV serostatus among *P. falciparum* malaria patients from three health Institutions in Hadya Zone, Southern Ethiopia, 2003 (n = 337)

Variable	HIV status		Odds Ratio	Adjusted OR
	Positive No (%)	Negative No (%)	(95 % CI)	(95 % CI)
Sex				
Male	11 (4.7)	222 (95.3)	1.67 (0.42,7.80)	2.91 (0.61,13.96)
Female*	3 (2.9)	101 (97.1)	1	1
Age				
15-24*	5 (2.8)	176 (97.2)	1	1
25-34	9 (5.8)	147 (94.2)	2.16 (0.64,7.57)	1.34 (0.32,5.54)
Marital Status				
Married	9 (5.8)	145 (94.2)	2.21 (0.66,7.76)	1.81 (0.41,7.96)
Single ,widowed & Divorced *	5 (2.7)	178 (97.3)	1	1
Address				
Rural*	9 (3.3)	260 (96.7)	1	1
Urban	5 (7.4)	63 (92.6)	2.29 (0.64,7.83)	1.77 (0.38,8.33)
Duration lived in the area				
0-10	4 (8.2)	45 (91.8)	2.47 (0.62,9.18)	---
11-20 & above*	10 (3.5)	278 (96.5)	1	
Religion				
Protestant *	10 (7.7)	245 (92.3)	1	1
Orthodox	2 (6.1)	31 (93.9)	1.58 (0.0,8.24)	0.36 (0.03,3.81)
Others	2 (4.1)	47 (95.9)	1.04 (0.24,4.6)	0.57 (0.09,3.61)
Ethnic group				
Hadya*	8 (3.1)	252 (96.9)	1	1
Kambata	2 (5.7)	33 (94.3)	1.91 (0.0,10.36)	2.55 (0.45,14.49)
Other	4 (9.5)	38 (90.5)	3.32 (0.79,12.97)	4.31 (0.72,25.93)
Occupation				
Farmer	6 (4.6)	124 (95.4)	1.20 (0.36,3.93)	1.04 (0.22,4.97)
Other*	8 (3.9)	199 (96.1)	1	1
Literacy Status				
No formal education	7 (6.2)	106 (93.8)	1.36 (0.36,5.61)	1.44 (0.43,4.82)
Elementary School	2 (1.7)	114 (98.3)	0.36 (0.03,2.28)	0.38 (0.07,2.02)
Secondary School and above*	5 (4.6)	103 (95.4)	1	1
Current Living Condition				
With family*	10 (3.4)	288 (96.6)	1	1
Other	4 (10.3)	35 (89.7)	3.29 (0.83,12.27)	3.41 (0.98,11.96)
Income				
<250	1 (3.8)	25 (96.2)	1.04 (0.14,7.71)	1.17 (0.14,9.59)
> 250	2 (13.3)	13 (86.7)	3.99 (0.55,22.36)	3.08 (0.59,15.99)
None*	11(3.7)	285 (96.3)	1	1

* Reference groups used for comparison.

5.5. Reported symptoms of AIDS and HIV related risk factors

5.5.1. Reported symptoms of AIDS

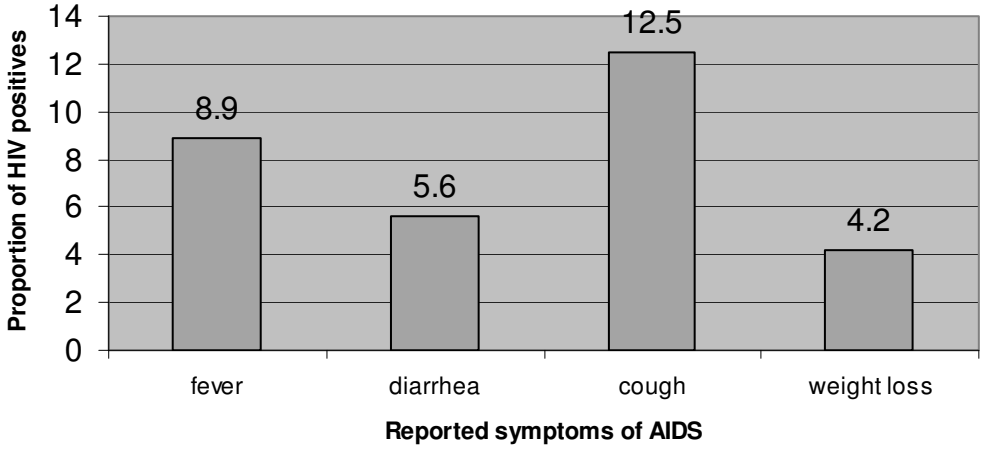
Among the respondents 91 (27.0%) reported prolonged fever in the last one year, out of whom only 2 (2.2%) had it for more than three weeks. Diarrhea in the last one year was reported by 21(6.2%) of the patients. But only one person had it for more than a month. Cough was also reported by 26 (7.7%) of the patients. Of these only three (11.5%) had it for more than one month. Presence of weight loss in the past one year was reported by 52 (15.4%) of the patients, and only four (7.7%) had lost >10% of their body weight (Table 5).

The respective proportion of seropositivety was higher among those who reported to have had prolonged fever, diarrhea, cough, and weight loss in the last one year (Figure 1), than those who reported not to have these symptoms.

Table 5 Symptoms of AIDS among *P.falciparum* malaria patients from three health institutions in Hadya Zone, Southern Ethiopia, 2003.

Variables	Frequency	(%)
Prolonged fever (n = 337)	91	(27.0)
Duration of fever (n = 91)		
<1 week	73	(80.2)
1-2 week	11	(12.1)
2-3 week	5	(5.5)
>3 week	2	(2.2)
Diarrhea (n = 337)	21	(6.2)
Duration of diarrhea (n = 21)		
<1 month	20	(95.2)
>1 month	1	(4.8)
Cough (n = 337)	26	(7.7)
Duration of cough (n = 26)		
<1 month	23	(88.5)
>1 month	3	(11.5)
Weight loss (n = 337)	52	(15.4)
Extent of weight loss (n = 52)		
<10%	48	(92.3)
>10%	4	(7.7)

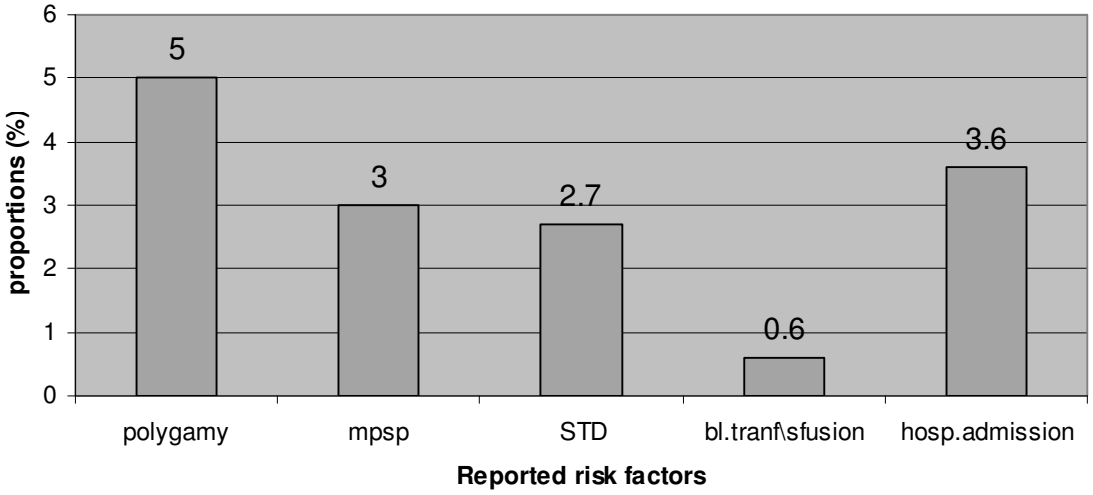
Figure 1. Proportion of serppositives among P.falciparum malaria patients presenting with symptoms of AIDS, Hadya Zone, Southern Ethiopia, 2003.



5.5.2. HIV Related Risk Factors.

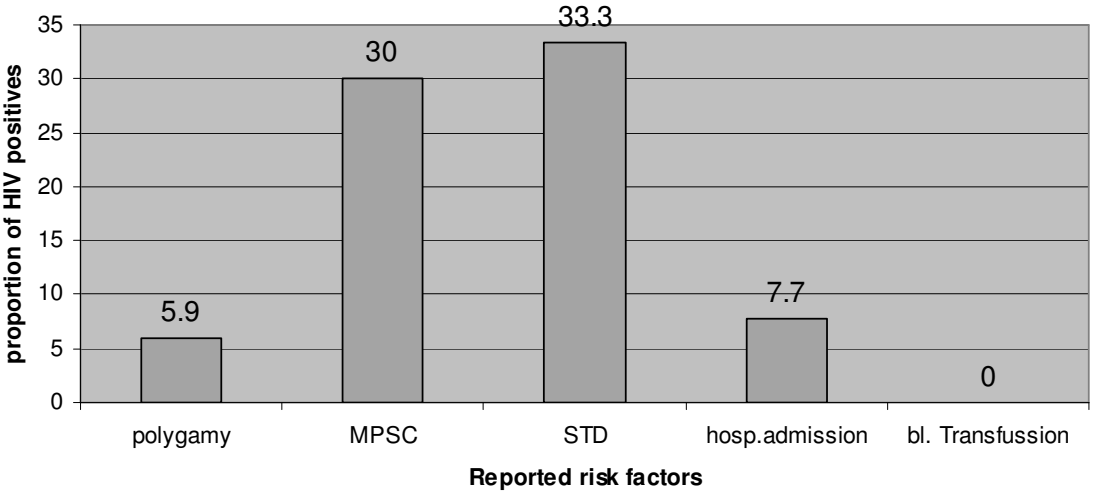
Of all the respondents 17 (5.0%) claimed that they were engaged in a polygamous marriage, 7 (2.1%) had extra marital non commercial sex partners and 3 (0.9%) had extra marital commercial sexual partners (Figure 2). Though 212 (62.9%) of the respondents have heard about STDs and 9 (2.7%) reported to have an episode of STD in the last one year. Twelve (3.6%) had history of hospital admission in the last 10 years due to various reasons and 2 (0.6%) had blood transfusion in the same reference time. The most common cause of admission for these patients with past history of hospitalization was labor and delivery 4 (33.4%), followed by injury 2 (16.8 %). The other reasons for admission were appendectomy, dermatologic problems, hypertension, malaria, typhoid fever and unknown diagnoses. Each of these was responsible for single admissions.

Figure 2. HIV related risk factors among P.falciparum malaria patients in Hadya Zone, Southern Ethiopia, 2003.



The proportion of HIV seropositives was found to be proportionally larger among those who reported to have multiple partner sexual contacts (MPSC) and history of STDs in the last one year (Figure 3).

Figure 3. Proportion of HIV positives among P.falciparum malaria who reported to have HIV related risk factors, Hadya Zone, Southern Ethiopia, 2003.



5.6. Reported symptoms and occurrence of malaria

Majority 272 (80.7%) of the respondents claimed to know or to have heard of the occurrence of malaria in their area and 325 (96.4%) reported that they know at least one symptom of the disease. Among those who reported to know the symptoms of malaria (n=325), most 287 (88.3%) reported three or more symptoms of malaria, 27 (8.3%) reported only two symptoms and 11 (3.4%) reported only one symptom. The most frequently reported symptoms were fever (88.6%) followed by rigors (80.0%), headache (80.0%), chills (76.6%), back ache (65.2%) and joint pain (57.2%). Only 26 (8%) mentioned other symptoms like poor appetite and extreme weakness (Table 6).

Among those who claimed the occurrence of malaria in their respective areas (n=325), 291 (89.5%) claimed that they preferred to seek treatment for malaria for themselves and their family from health center, clinic or malaria control center. Twenty four (7.4%) prefer to go to pharmacy (drug shop) by themselves and the rest 3.1% prefer to go to a traditional healer. The reasons mentioned for preferring the respective sources were effectiveness of treatment for 232 (69.4%), followed by nearness to home (11.0 %), low cost of treatment (10.1%), and short waiting time (4.2%). The rest eight (2.4%) gave reasons like parent's or husband's decision (Table 6).

Table 6 Knowledge of symptoms of malaria and treatment seeking behavior among falciparum malaria patients from three health institutions in Hadya Zone, Southern Ethiopia, 2003. (n = 325)

Variable	Frequency	(%)
Heard about malaria in the area (n = 337)		
Yes	272	(80.7)
No	65	(19.3)
Knew main symptoms of malaria (n = 325)		
Only one	11	(3.4)
Only two	27	(8.3)
Three and more	287	(88.3)
Reported Symptoms of malaria (n = 325)		
Fever	288	(88.6)
Chills	249	(76.6)
Rigor	260	(80.0)
Headache	260	(80.0)
Backache	212	(65.2)
Joint pain	186	(57.2)
Other	26	(8.0)
Seek treatment for malaria usually from (n = 325)		
Health center/clinic and malaria control center	291	(89.5)
Traditional healers	10	(3.1)
Pharmacy	24	(7.4)
Reasons for preferring this source (n = 325)		
Treatment is effective	232	(69.4)
Nearness to home	37	(11.0)
Low cost of treatment	34	(10.1)
Short waiting time	14	(4.2)
Other	8	(2.4)

5.7. Knowledge of Malaria Transmission, Prevention and Outcome

Only 162 (48.1%) of the respondents claimed that malaria could be transmitted from an infected person to a healthy person. The rest 175 (52.0%) claimed that either malaria can not be transmitted from person to person or they had no idea at all. Among those who claimed that malaria is transmissible (n=162), 145 (90.0%) reported mosquito bite as a means of transmission followed by respiratory route (15.0%), and bodily contact (9.0%). The remaining 33 (20.0%) reported that malaria can be transmitted through various ways like flies, and dirty water (Table 7).

About 80% (272) of study subjects reported that malaria is preventable. Out of them 204 (75.0%) reported just one method of prevention, 39 (14.0%) reported two methods and the remaining 30 (11.0%) reported three or more preventive methods. The most frequently mentioned method of prevention was taking tablets (71.0%) followed by environmental sanitation (47.0%), insecticide sprays (19.0%) and bed nets (10.0%). The remaining (9.0%) reported various other methods like traditional cotton clothes, smoke and good diet. When asked "what will happen if a malaria patient is left untreated?" majority of the respondents, reported death (88.4%) as an out come. Some reported debility (5.3%) as an out come and the remaining 2.4 % reported chronicity and self-cure (Table 7).

Table 7 Knowledge about malaria transmission, preventive methods and out come among *falciparum* malaria patients from three health institutions in Hadya Zone, Southern Ethiopia, 2003.

Variables	Frequency	(%)
Malaria transmissible? (n = 337)		
Yes	162	(48.1)
No	175	(52.0)
Means of Transmission (n = 162)		
Mosquito bite	145	(90.0)
Bodily contact	14	(9.0)
Respiratory route	25	(15.0)
Other*	33	(20.0)
Is malaria preventable? (n = 337)		
Yes	272	(80.7)
No	65	(19.3)
Mentioned methods of malaria prevention (n = 272)		
Only one	204	(75.0)
Only two	39	(14.0)
Three and more	30	(11.0)
Preventive Methods (n = 272)		
Take tablets	192	(71.0)
Insecticide spray	53	(19.0)
Environmental Sanitation	90	(47.0)
Bed Nets(ITN)	20	(10.0)
Other	24	(9.0)
Reported Outcome of Untreated Malaria(n = 337)		
Death	298	(88.4)
Debility	18	(5.3)
Self cure	2	(0.6)
Chronicity	6	(1.8)
I do not Know	13	(3.9)

* Such as flies and dry water

5.8. Presence of Recent Malaria Illness and treatment seeking behavior.

Among the respondents 149 (44.2%) reported that they had at least one episode of malaria in the last one year excluding this one. Of them 59 (39.6%) had three or more attacks, 41 (27.6%) had two attacks and 49 (32.9%) had only one attack of malaria. The majority, 85 (57.0%), had their last malaria infection in the past six months time, 42 (28.0%) 6 -11 months back, 13 (9.0%) one year back and 9 (6.0%) do not remember the time they had the last attack of malaria. The last episode was diagnosed symptomatically in 106 (71.0%) of the cases; only 43 (29.0%) were microscopically confirmed through blood film examination (Table 8).

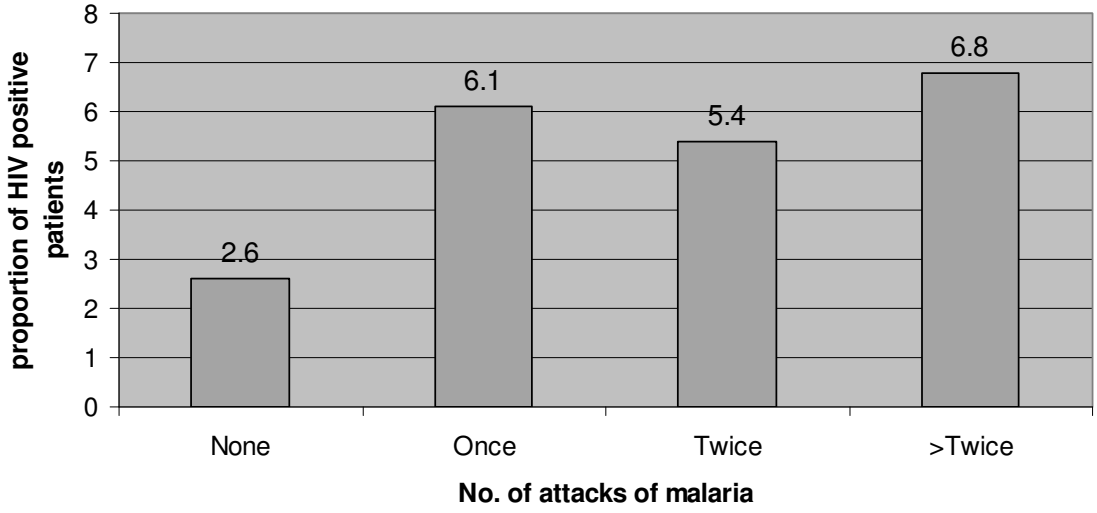
Though 33 (22.0%) could not remember the duration of illness for the last episode, 63 (42.0 %) claimed that they were ill for less than one week, 37 (25.0 %) for 1-2 weeks and 16 (11.0 %) for more than two weeks. Among the 149 patients who claimed to have past history of malaria, 137 (92.0%) were treated for the illness and the rest 12 (8.5%) were not. The most frequently used sources of treatment for malaria were health institutions for 111 (81.0%), followed by pharmacy for 23.4 %. All treated patients (100%) were given tablets during treatment. Twelve (8.8 %) were given injections in addition during treatment and only one person received intravenous treatment (Table 8). Of those who received treatment (n = 137), 134 (97.8 %) said that they were cured from their illness.

Table 8 Recent infections due to malaria in the last one year, treatment types and outcomes among *falciparum* malaria patients in Hadya Zone, Southern Ethiopia, 2003.

Variables	Frequency	(%)
Had malaria in the last one year (n = 337)		
No	188	(55.8)
Yes	149	(44.2)
No of episodes in last one year(n = 149)		
Once	49	(32.9)
Twice	41	(27.6)
More than twice	59	(39.6)
Last episode of malaria (n = 149)		
Just one year back	13	(9.00
6-11 months back	42	(28.00
< 6 months	85	(57.0)
I do not remember	9	(6.0)
Diagnoses (n = 149)		
Symptomatically	106	(71.0)
Laboratory	43	(29.0)
Duration of Illness (n = 149)		
< 1 week	63	(42.0)
1-2 weeks	37	(25.0)
>2 weeks	16	(11.0)
Do not remember	33	(22.0)
Took Treatment (n = 149)		
Yes	137	(92.0)
No	12	(8.5)
Source of Treatment (n = 137)		
Health institution	111	(81.0)
Pharmacy	32	(23.4)
Traditional healers	1	(0.7)
Type of treatment (n = 137)		
Tablets	137	(100.0)
Injections	12	(8.8)

The proportion of HIV sero-positives among the patients who reported to have various levels of attacks is presented in Figure 4. The results show that the average proportion of sero-positive individuals among who reported to have malaria infection (6.1%) in the last one year was more than those who did not (2.6%).

Figure 4. Proportion of HIV seropositives among P.falciparum malaria patients among those who reprted to have attecks of malaria in the last one year, Hadya Zone, Southern Ethiopia,2003.



5.9. Symptoms of current Malaria illness and Treatment Types Sought

5.9.1. Symptoms of Malaria

Most of the patients (86.7%) reported at least one symptom of malaria at the time of arrival to the respective health institution. Majority of them (86.0%) had three or more symptoms of malaria, where as the remaining had either two or one symptom (Table 9). The most frequently reported symptoms were fever (90.4%) followed by headache (83.9%), chills (83.2%), rigors (77.1%), joint pain (76.0%) and body ache (57.2 %).

The majority, 231 (69.5%), of the patients had not taken any treatment for the current illness prior their arrival to the current health institution, where as 106 (31.5%) had already taken some sort of treatment prior to arrival. Among those who already took treatment, 53 (50.0%) took treatments from health institutions, 40 (37.7%) under went self-treatment and the rest 13 (12.3%) took treatment from other sources including traditional practitioners (Table 9).

Table 9 Symptoms of malaria and treatment sought before coming to health institutions among *P. falciparum* patients in three health Institutions in Hadya Zone, Southern Ethiopia, 2003. (n = 337)

Variable (n = 292)	Frequency	(%)
Symptoms of malaria (n = 292)		
One	29	(9.9)
Two	12	(4.1)
Three and more	251	(86.0)
Frequently mentioned symptoms (n = 292)		
Fever	264	(90.4)
Chills	243	(83.2)
Rigors	225	(77.1)
Head ache	245	(83.9)
Joint pain	222	(76.0)
Body ache	167	(57.2)
Took Treatment		
Yes	106	(31.5)
No	231	(68.5)
Source of treatment (n = 106)		
Health institution	53	(50.0)
Self treatment	40	(37.7)
Other	13	(12.3)

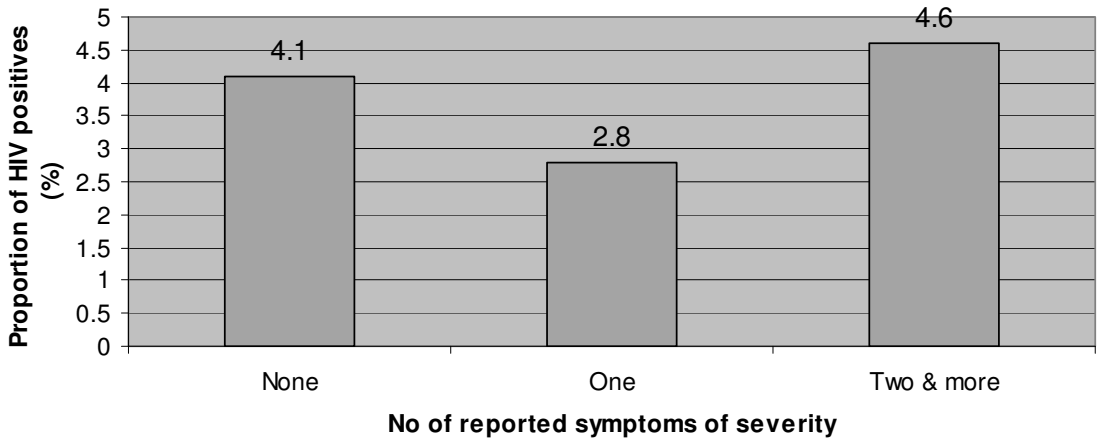
5.9.2. Symptoms of Severe Complicated Malaria

Among all the patients included in the study, almost half 167 (49.6%) of them reported to have at least one severe symptom of malaria. Out of them (n = 167), most 111 (66.5%) reported three symptoms, 21.6% reported one symptom and the remaining 12.0% reported two symptoms. The most frequently reported symptoms of severity were cerebral manifestations (76.7%), followed by persistent vomiting (35.3%), dark urine (21.6%), inability to eat or drink (18.0%), and prostration (16.8%) (Table 10). The HIV positivety rates versus the number of reported symptoms of severe malaria are presented in Figure 5.

Table 10 Symptoms of severe complicated malaria among P.falciparum Malaria patients from three health institutions in Hadya Zone, Southern Ethiopia, 2003. (n = 337)

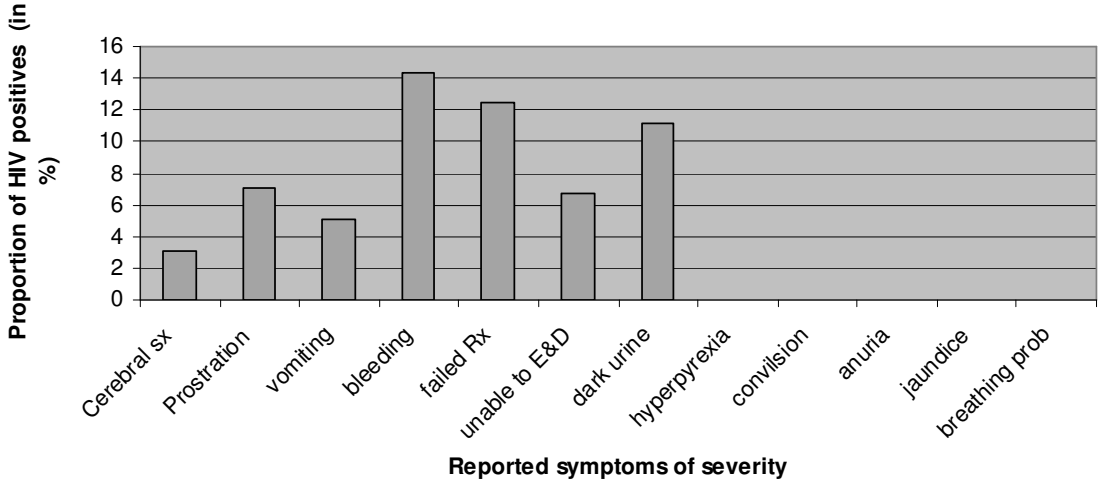
Variables	Frequency	(%)
Frequently mentioned symptoms (n = 167)		
Cerebral manifestations	128	(76.7)
Persistent vomiting	59	(35.3)
Dark urine	36	(21.6)
Unable to eat or drink	30	(18.0)
Prostration	28	(16.8)
Hyperpyrexia	14	(8.4)
Convulsions	9	(5.4)
No response to treatment For three day	8	(4.8)
Spontaneous bleeding	7	(4.2)
Breathing difficulty	4	(2.4)
No urine(in 24 hrs)	2	(1.2)
Yellowish eyes	2	(1.2)

Figure 5. Proportion of HIV seropositives among P.falciparum malaria patients who reported to have symptoms of severity (expressed in number of symptoms), Hadya Zone, Southern Ethiopia, 2003.



Patients who reported certain symptoms like cerebral manifestations, convulsions, no urine output, jaundice, breathing difficulty and hyper pyrexia were either all HIV negative or have very low HIV prevalence than those who did not reported to have these symptoms (Figure 6).

Figure 6. Proportion of HIV positives among P.falciparum malaria patients who reported to have symptoms pf severity (expressed in reported symptoms), Hadya Zone, Southern Ethiopia, 2003.



5.10. Physical Signs of malaria and HIV/AIDS Illnesses.

The most frequently detected physical findings among the patients were pallor (44.8%), splenomegally (19.9%) and hepatomegally (7.4%). Accordingly only 62 (18.4%) of the patients had physical evidences for severe malaria. Among those who had severity signs (n = 62), 44 (71.0%) had only one sign, 16.1% had only two and 12.9% had three or more signs. The most frequently observed severity signs were prostration (29%), cerebral manifestations (25.8%) and hyperpyrexia (5%). Based on the clinical data 62 (18.4%) of the patients were diagnosed to have severe complicated malaria (Table 11).

Almost all of the patients on whom the important physical findings were not detected, were also negative for HIV test (Annex V). The proportion of HIV seropositive individuals among those with severe malaria (4.8%) was similar with those with no severity signs (4.0%). But the proportion of sero-positives was more among those with two and more signs (8.3%) than those with one sign (2.3%) and those who do not have any (4.3%) (Figure 7).

In the same way all the patients who presented with severity signs of cerebral malaria and prostration were negative for HIV tests and also majority of those who presented with hyperparasitaemia and other symptoms of severity were also HIV negative (Annex V).

Figure 7. Proportion of HIV seropositives among P>falciparum malaria patients with different signs of severity, Hadya Zone, Southern Ethiopia, 2003

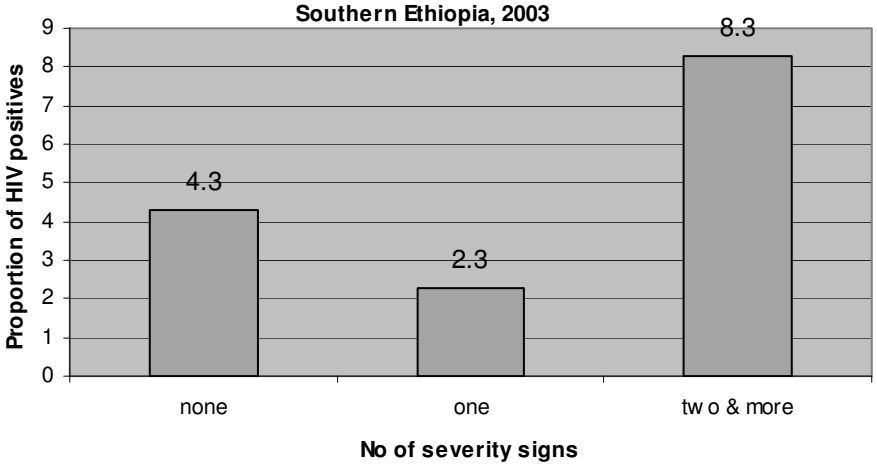


Table 11 Physical signs of malaria among *falciparum* malaria patients from health institutions in Hadya Zone, Southern Ethiopia, 2003.

Variables	Frequency	(%)
Physical findings (n = 337)	151	(44.8)
Pallor		
Jaundice	10	(3.0)
Sub conjuctival hemorrhage	7	(2.1)
Oral candidacies	1	(0.3)
Hepatomegally	25	(7.4)
Herpes Zoster	1	(0.3)
Splenomegally	67	(19.9)
Petichea	4	(1.2)
Peripheral Edema	2	(0.6)
Signs of severeity (n = 62)		
One	44	(71.0)
Two	10	(16.1)
Three or more	8	(12.9)
Signs (n = 62)		
Prostration	18	(29.0)
Cerebral manifestations	16	(25.8)
Hyper parasitemia	17	(5.0)
Other	18	(29.0)
Type of patient (n = 337)		
Uncomplicated Malaria	275	(81.6)
Severe Complicated Malaria	62	(18.4)

5.11. Malaria Species Identified and Parasitic Load

Majority 327 (97.0%) of the patents had pure *P. falciparum* malaria infection and the rest 10 (3.0%) had mixed *P. falciparum* and *P.vivax* malaria infection (Figure 8). The *P. falciparum* parasitic load of the patients as is detected by blood film microscopy revealed that most 159 (47.2%) had parasitic load "+++", 21.1% had "++++", 16.6% had "++" and 13.6% had "+". Only 1.5% had "+++++" (Figure 9).

Figure 8. Species of malaria detected by blood film microscopy among P.falciparum malaria patients in Hadya Zone, Southern Ethiopia, 2003.

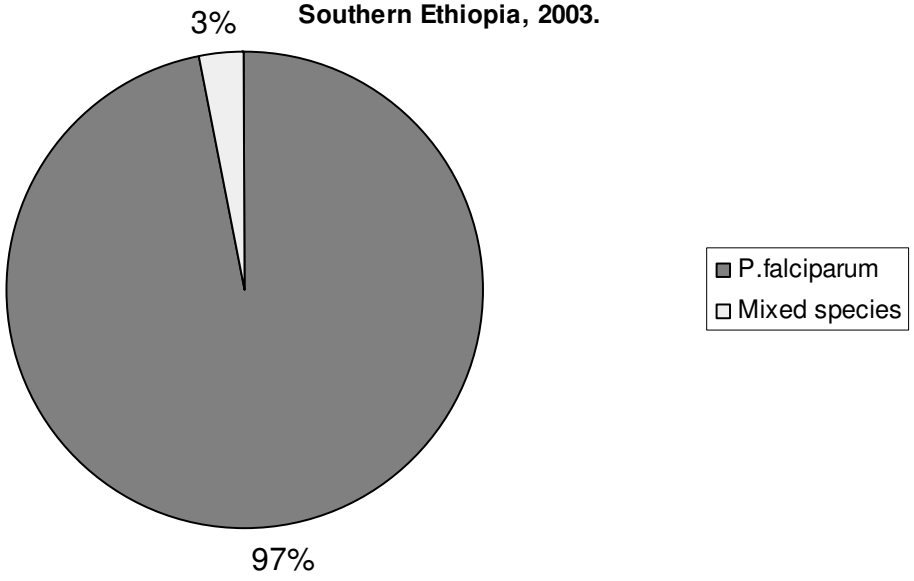
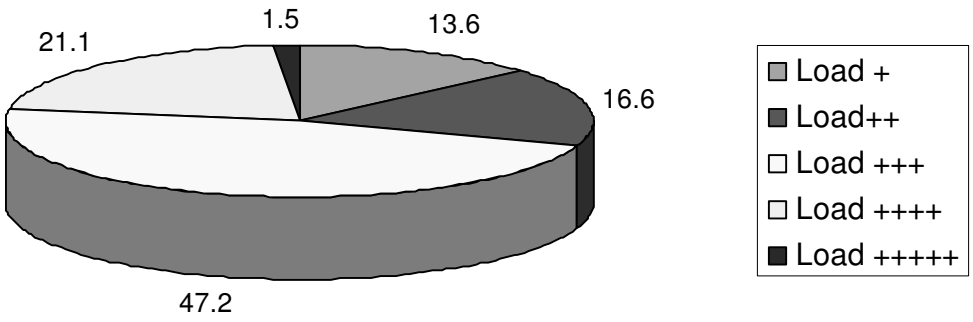
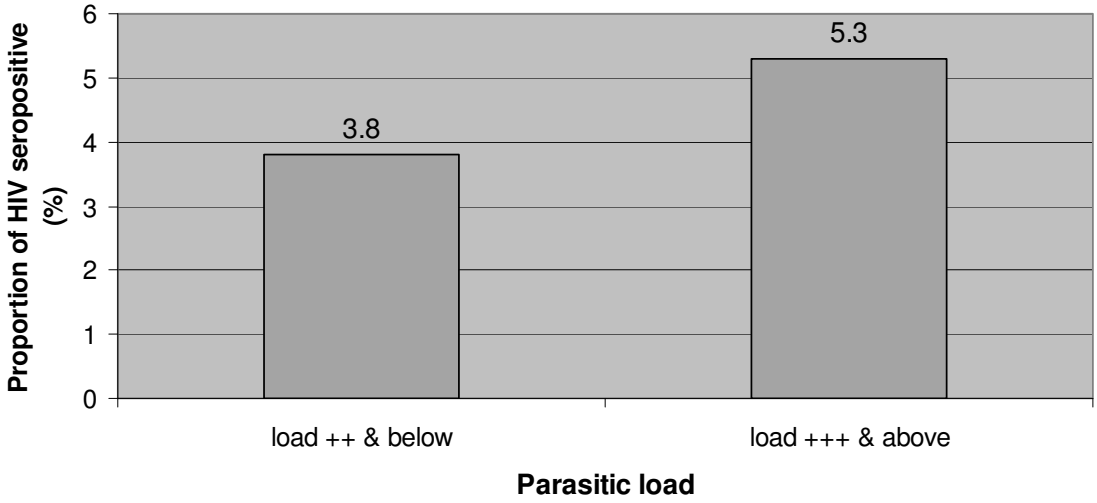


Figure 9. Parasitic load of malaria parasites detected by blood film examination among P. falciparum malaria patients, Hadya zone, Southern Ethiopia, 2003.



It was noted that those patients (n = 10) who presented with mixed *P. falciparum* infection and *P.vivax* were all HIV negative and the proportion of HIV positive individuals was higher among those with high parasitic loads (5.3%) than those with relatively lower parastaemic limits (3.8%)(Figure 10).

Figure 10. Proportion of HIV sroposirtives among P. falciparum malaria patients with various levels of parasitemia, Hadya Zone, Southern Ethiopia, 2003.



6. DISCUSSION

There has been no published study, at the time this study was conducted, in Ethiopia done to asses the magnitude of malaria and HIV co-infection. Most of the studies are from other African countries mainly Eastern and South Eastern Africa (1).

The determination of malaria HIV co-infection rate is important because there are hypotheses and even study reports on the possible association between the two infections (1, 7, 8). If this is the case, knowing the magnitude of the problem will have many practical implications especially in countries where both diseases are leading causes of morbidity and mortality. For example, the decision to integrate or not to integrate resources against HIV and malaria, as was for TB and HIV, will depend on sound evidence. Assessment of the knowledge and attitude and practice of patients towards malaria and HIV related risk factors also will help in planning intervention activities for the prevention of these problems in the community. The study also serves as a baseline and comparative data for similar future studies.

A season of peak malaria transmission was selected to maximize the number of *P. falciparum* positive malaria patients to be included in the study. For similar reasons of maximizing the HIV prevalence rate of study subjects, the study was done among those patients in the age group 15-34 years, as this is the age group characterized by peak HIV prevalence in the country (18).

In this study the magnitude of HIV seroprevalence among *P. falciparum* malaria patients was 4.2%. This prevalence is relatively lower than the 2001 MOH report of HIV seroprevalence in the same zone, in Hosanna town (5.9%) (18, 20). This slight difference could be explained by the fact that, the current study includes more rural residents (79.8%), or is due to the fact that all of the women included in the later are sexually engaged pregnant women making them more vulnerable than the population in the current study of whom more than half were single, or it could be part of the national decline in HIV prevalence.

Prevalence studies in different population groups in the country revealed that HIV prevalence rates differ among different sub groups of the population. Reports have noted that there is a significantly increased HIV seropositivety rate among registered TB patients (33, 34, 35) when compared to the rate in the general population. The HIV seropositivety rate for adult TB patients in health institutions in southern Ethiopia including Hosanna hospital in the year 2002 was 19.4 % (36). In the current study we do not find such higher rates. This may indicate absence of relationship between HIV and malaria at least like the strong relationship that was found between TB and HIV, though the study methods used were similar.

In another study done in Butajira (southern Ethiopia) in the year 2000, the seroprevalence of HIV was 3.2% among ANC attendees and 1.4% among the general population (37). The current rate is higher, which could be explained by a difference in geographic location and in socio-demographic characteristics of the two study groups.

In a cross-sectional study in Zimbabwe, the prevalence of both malaria and HIV was 5.9% and it was significantly higher in males (10.8%) than in females (3.7 %) and the study concluded that there is no association between malaria and HIV (38). The respective rate and conclusion of the current study is in agreement with this Zimbabwean study and other similar African studies (1, 39). How ever the study design in the current study is cross-sectional and seroprevalence rate was not assessed for comparative groups with no malaria infection but with similar characteristics. These options were not entertained because longitudinal studies would take more time and the resources available for the study.

The HIV seroprevalence in the current study was more for males than females. This is not in agreement with the different national reports where more females are affected (40, 41). Possible explanation is the proportionally more male patients being included in the study. This is because males most of the time are working outside, staying outside longer and late than the women during the seasons of major farm activities, which coincides with major seasons of malaria transmission and then are prone to malaria infection than the females (14). The Zimbabwean study also demonstrated a higher rate of HIV-malaria co-infection among the males than the females (38).

There was no evidence to support the association between the presence of reported symptoms and an observed sign of AIDS versus HIV seropositivety. This is not in line with the already existing data reported in the literature. An explanation is that most of the

seropositive patients were picked up in this study were in the early stages of the disease, so that they were negative for signs and symptoms related to the syndrome. The number of cases with symptoms and signs of AIDS were few in this study to draw any valid conclusion based on tests of statistical significance.

About 80 % of the patients reported that either they knew or had heard of the occurrence of malaria in their area of residence. This is an indication that the respective areas selected for the study are malarious and known to have malaria transmission. The majority (96.6 %) of the patients reported at least one symptom of malaria; fever was the most frequently reported (88.6 %) symptom of malaria. These findings are in agreement with the studies done in Butajirra, Southern Ethiopia in 1999 and in Central Ethiopia in 1993 (42,43).

Many of the patients (89.5%) claimed that they prefer to seek treatment for malaria for themselves or for their families either from health center; clinic or malaria control center. The most frequently mentioned reason for preferring these mentioned sources of treatment was effectiveness of treatment (69.4%). In the central Ethiopian study (1993), the most frequently sought sources of ant-malaria was drug shops (57 %) followed by government clinics (46.3%) (43). The difference could be explained by a relatively better access and improved treatment-seeking behavior of the current population in the study area. In the same study the most frequently mentioned reason for preferring the mentioned sources of treatment was effectiveness of treatment (83.3 %).

More than half (52.0 %) of the respondents reported that malaria can not be transmitted from infected person to healthy ones or they have no idea about it at all. Only 48 % reported malaria to be transmissible. This finding is in agreement with the Butajirra study (43.7%) by *Wakgarii et al*. But it is much lower than the rate in the central Ethiopian study where 74 % reported malaria to be transmitted. This difference could be attributed to the lack in knowledge about sources of malaria infection among the study population. Among those who knew that malaria is transmitted, 90 % reported mosquito bite as a means of transmission. This is relatively a very high figure compared to the central Ethiopian study where only 4.5% reported this method of transmission and the Southern Ethiopian Study (Butajirra) where 66 % reported the mode of transmission to the bite of infective mosquitoes. This shows the presence of a better knowledge in the method of HIV transmission.

Over 80% of the patients in this study reported that malaria is preventable. This is in agreement with the south Ethiopian study (42), where 85.7% reported malaria to be preventable. But the finding is much higher from that of the central Ethiopian study where only 10.3 % thought malaria preventable. This could be explained by a better knowledge on malaria prevention among the southern population. The most frequently mentioned method of prevention was tablet chemoprophylaxis (71 %) which is in agreement with the two studies as well, where the majority reported the same method as a preventive tool.

The knowledge of ITN was very low (10 %) in the study area which is similar to the Butajirra study (13 %). Nobody mentioned bed nets in the Central Ethiopian study. This could be due to the time gap, since ITN's have started to be widely promoted only recently.

More than 88 % admitted that the outcome of malaria, if left untreated, to be death. A similar figure (85 %) was reported by the central Ethiopian study which shows that the illness is considered as an important disease with fatal outcome by the population.

A little bit less than half of the patients reported that they had at least one malarial attack in the last one year excluding the current one. This is due to the fact that the area being malarious, people have infections frequently. In more than half of the patients the last attacks of malaria occurred in the last six months. This could be explained by the fact that the major seasons of malaria transmission overlapped with this interval. Most of these last attacks of malaria were diagnosed symptomatically; only 19 % were microscopically confirmed. Considering the fact that most (about 80 %) of the patients are from rural setting, where the clinics either do not have laboratory facilities or laboratory professionals to perform the procedure, the trend is to treat patients symptomatically according to the national guidelines (15).

The majority (>90 %) of cases reported that they were treated for this last attack and the most frequently used places of treatment were heath institutions (81 %). These findings are in agreement with the treatment seeking behaviors of current episodes mentioned

earlier. All (100 %) of the treated patients reported that they were given tablets. Only 8.8 % were given injections in addition. This could suggest that this last attack of malaria most probably was not severe malaria, except the one individual who reported to have received IV fluids in addition. These findings are similar with the Central Ethiopian study where the rate of treatments with tables and injections were 98 % and 28 % respectively.
In this study it was observed that the number of attacks of malaria in the past one year were similar among those with seropositivety and seronegative patients. These findings are in agreement with the Zimbabwean study (38), where no association was noted between presence of malaria and HIV infection. But the later study did not asses the past attacks and conclusions were drawn from the currently present symptoms of malaria. In other cohort studies the rate ratios (RR) of non severe malaria did not show statistically significant difference between HIVSP and HIV SN groups. (1)

Though statistical analysis was not performed due to smaller rates, the HIV seropositivety rate was low in those who had the symptoms of severity. In a prospective cohort study done in Zimbabwe (22), after adjusting for confounders, the risk of developing severe complicated malaria was significantly more in HIV seropositive than HIV seronegative patients. In two other studies done in urban Burundi and Zambia (1) among admitted adults with severe malaria, CFR was more than twice as high in the HIVSP compared to the HIVSN groups. The observed difference could be explained by the differences in study designs employed (cohort versus cross sectional), and the study groups (hospital admitted) included as well as relatively small sample size in the latter two studies.

There were also, certain interesting observations made from the study. Those patients who reported to have cerebral manifestation and convulsion were all HIV negative unlike those patients who did not report to have these symptoms. The same observations were also noted regarding the physical signs. Those patients who presented with cerebral manifestations of severity were all HIV negative. In a study done in African children with symptomatic HIV infection, these children were found to be 'protected' against cerebral malaria (6). This has been attributed to lower levels of TNF in HIV infected children. TNF is reported to have a potentiating effect on the endothelial adherence and clogging of microcirculation by parasitized red cells. In an animal study using mice, murine AIDS was found to confer protection against the severity of neurological manifestations of experimental cerebral malaria and this protection was higher with longer duration of immunodeficiency. IL-10 from splenic cells was shown to play a crucial role in this protection (6).

Though relatively larger proportion of hyreparasitemic patients was HIV positive, no statistically sound association was noted between parasitic load and of patients and HIV seropositivety. Many different studies done in Africa also noted no statistically different finding in peripheral parasitemia among HIV seronegative and seropositive groups of malaria patients (1).

7. STRENGTHS AND LIMITATIONS OF THE STUDY

7.1. Strengths of the study

- The study is one of the few contributions in the area of investigations assessing the relationship between HIV and malaria in the country.

- Behavioral, clinical and laboratory data were collected from the subjects included in the study.

- As to the data quality, the use of a standardized questionnaire, pretests done before the data collection and the training of and practical sessions for data collectors, the use of control tools during data collection (including the laboratory methods) will make it internally valid.

7.2. Limitations of the study.

- The nature of the study being cross sectional, is not the best type of study to establish presence or absence of a cause effect association or relationship between two diseases. In such cases longitudinal analytic study types are preferred.

- This is an institutional study and the selection of the health institutions to be included in the study was based on the criteria set and was not an arbitrary random selection. This would create selection bias and affect the representative-ness of the study subjects.

- Due to very smaller rates of HIV seroprevalence, statistical tests for significance of associations were not performed which could have helped to draw more valued conclusions.

8. CONCLUSIONS AND RECOMMENDATIONS

8.1. CONCLUSIONS

From this study, the following conclusions could be drawn,

- The prevalence of HIV in the study subjects was similar to the figures of HIV prevalence in Ethiopia for the rural population and with the findings of ANC sentinel reports in the same area.

- Though studies like this one were used to verify associations between HIV and certain diseases like TB, no evidence of association between HIV and malaria was found, since this study design may not be an appropriate one to investigate the possibly existing association between these two diseases.

- Overall the study population has a better knowledge on the occurrence, means of transmission and prevention of malaria as well as in treatment seeking behaviors. Except that they had certain misconceptions and deficiencies in the knowledge that malaria could be transmitted from person to person and the modes of malaria transmission

8.2. RECOMMENDATINS

- Further studies should be done in the area with a relatively improved study designs and methodologies, which employ follow up for out comes of treatment and case fatality rates of cases and control groups. Most of the studies that drew conclusions that there are associations between HIV and malaria are cohort studies.

- Appropriate messages on malaria transmission and prevention methods including ITN promotion should be provided.

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10. ANNEXES

ANNEX 1

Questionnaire for the assessment of HIV & malaria co-infection among health Institution visitors in Hadya zone, southern Ethiopia.

(Interview includes confirmed malaria patients in the age group15-34 years)

1-Patient code number……

2-Health institution ……..

3-Date of interview ……...

4-Name of interviewer …….

5-Name of supervisor……

Introduction

My name is _____. I am working as a data collector for a research being conducted by Addis Ababa University, Department of Community Health, in collaboration with Southern Nations Nationalities and Peoples Region –Health Bureau and Hadya Zone Health Department. We interview confirmed *P.falciparum* malaria patients in selected health institutions in Hadya Zone to find about social back ground and medical situation of these patients that would help in identifying possible new dimensions in the management of such patients as well as for further planning and study purposes. I kindly request you to participate in the interview. Your kind participation will be of very much help for better understanding of the disease in the Zone as well as for the

region. And as a result, the large majority who suffer from the disease will also be beneficial.

I am going to ask you some personal questions pertaining to the above issues in which all your answers will be kept completely confidential. Your name will never be written in this form, and will never be used in connection with any of the information you tell me. You do not have to answer any question that you do not want to answer. You may end this interview at any time you want to. However, your honest answers to these questions will help us better understand the social back ground and clinical characteristics of malaria patients in the Zone. We would greatly appreciate your help in responding to this survey.

Thank you!

There fore are you willing to participate in the interview?	1.Yes	If yes, continue with the interview
	2.No	If no, stop the interview

Parts included in this Questionnaire.

Introduction and informed consent form

Part I Socio demographic characteristics of the respondents

Part II Questions related to malaria

Part III Questions related to sexual history

Part IV Clinical information

Part I. Socio demographic characteristics of the respondent

Roll no.	Questions	Answers	Code	Skip to
101	Sex of the respondent	1. Male 2. Female		
102	Age (how old were you at your last birth day?)	1. _____ (In years) 2. I don't know 3. No response		
103	What is your current marital status?	1. Married 2. Single 3. Widowed 4. Divorced 5. No response		
104	Where is your current place of residence?	1. Urban 2. Rural 3. No response		
105	Distance from your place of residence to the current health institution?	_____ (In kilometers)		
106	Distance from your current place of residence to the nearest health institution? (If it is different from the current one)	_____ (in kilometers)		
107	Mode of transport to the nearest health institution	1. By foot 2. By bus 3. By horse back 4. By cart 5. Do not know 6. No response		
108	How long did you live in the area? (intermittently/ permanently)	1. <one year 2. 1-5 years 3. 6-10 years 4. 11-15 years 5. >15 years 6. Since birth		
109	Educational status. What is the highest level of educational status you have completed?	1. Not able to read and write. 2. Only read and write. 3. Elementary school (grade1-6) 4. Secondary school (grade 7-12) 5. Higher education (Grade 12 +) 6. No response		

110	What is your religion?	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5. Others (specify)_____		
111	What is your ethnic group?	1. Hadya 2. Kambata 3. Amhara 4. Guraghe 5. Siltie 6. Oromo 7. Others (specify)_____		
112	What is your occupation?	1. Farmer 2. Merchant 3. Government employee 4. Student 5. House wife 6. Daily laborer 7. Soldier 8. No job 9. Others (Specify)_____		
113	What is your current living condition?	1. Alone 2. With family 3. With friends 4. On the street 5. Others (Specify)_____		
114	What is your main current source of income?	1. Self 2. Relatives 3. Spouse 4. Friends 5. Others_____		
115	What is your average family income per month?	_____ (in Birr)		

Part II. Questions about knowledge attitude and practice related to malaria and Treatment seeking behavior.

Roll No	Question	Answer	Code	Skip to
201	Have you ever had malaria in your area?	1.Yes 2. No		
202	What are the main symptoms of malaria? (More than one response is possible).	1. Fever 2. Chills 3. Shivering 4. Head ache 5. Back ache 6. Joint ache 7. I do not know 8. others (specify)_____		
203	Where do you and your family go to seek treatment for malaria?	1. Traditional healer 2. Health center/ clinic 3. Pharmacy (Drug shop) 4. Malaria Control labs 5. Others (specify)_____		
204	Why do you prefer these sources? (More than one response is possible).	1. Treatment is effective 2. Low cost of drugs 3. Short waiting time 4. Closeness to home 5. Others (specify)_____		
205	What is the outcome of malaria if not treated early?	1. Death 2. Debility 3. Self cure 4. Chronicity 5. I do not know 6. Others (specify)…….		
206	Is malaria a transmissible disease?	1. Yes 2. No 3. I don't know		
207	How is malaria transmitted from person to person?	1. Through mosquito bite. 2. Through bodily contact with patients		

		3. Via respiratory route 4. By flies 5. Others (specify)____ 6. I do not know		
208	Is malaria a preventable disease?	1. Yes 2. No 3. I do not know		
209	If yes, what kind of methods you know to prevent malaria?	1. Take tablets 2. House hold spray with insecticides 3. Environmental sanitation 4. Use of mosquito net(bed net) 5. Use local cotton sheets 6. Smoke from burning leaves and animal products (cow dung) 7. I do not know 8. Others (specify)____		
210	Have you had malaria in the last one year	1. Yes 2. No 3. No response		
211	If yes how many episodes did you have? (Number of times)	1. One episode 2. Two episodes 3. More than two 4. Don't remember		
212	When was the last time you had malaria during the last year?	1. One year back 2. 9-11 months back 3. 6-8 months back 4. 3-5 months back 5. <3 months back		
213	How did you know that you had malaria?	1. I know the symptoms 2. Laboratory diagnoses 3. By traditional healer		

214	For how many days were you sick during this last episode?	_____ (In days)		
215	Did you seek any medical treatment for this last episode of malaria?	1. Yes 2. No 3. No response		
216	From where?	1. Traditional healer 2. Health center/ clinic 3. Pharmacy (Drug shop) 4. Malaria Control labs 5. Others (specify)_____		

Part III. Questions related to HIV/AIDS related high risk behaviors.

Roll No	Questions	Answers	Code	Skip To
301	If currently married, a) For men, Do you have more than one wife?	1. Yes 2. No 3. No response		
	b) For women, Does your husband have other wives?	1. Yes 2. No 3. No response		
302	Have you had sex with a non commercial sexual partner in the last one year?	1. Yes 2. No 3. No response		
303	Have you had sex with commercial sex worker during the last one year?	1. Yes 2. No 3. No response		
304	Have you ever heard of disease that can be transmitted through sexual intercourse?	1. Yes 2. No 3. Do not know 4. No response		
305	Have you had genital ulcer during the past one year?	1. Yes 2. No 3. Do not know 4. No response		
306	Have you had genital discharge during the last one year?	1. Yes 2. No 3. Do not know		

		4. No response		
307	Did you have history of blood transfusion during the last one year?	1. Yes 2. No 3. No response		
308	Have you ever had history of hospitalization due to any illness in the last ten years?	1. Yes 2. No 3. No response		
309	If yes specify the type of illness/illnesses that resulted in your hospitalization.	1. _____ 2. _____ 3. _____		

Part IV. Clinical Information of Patients.

Roll No	Questions (Medical History)	Answers	Code	Skip to
401	Do you currently have any of these?	1. Fever 2. Chills 3. Shivering 4. Head ache 5. Joint ache 6. Generalized ache		
402	Have you taken any drug for your current illness before arrival to this institution?	1. Yes 2. No 3. Don't know		
403	If yes from where?	1. Traditional healers 2. Health institution 3. Self Medication 4. Pharmacy		
404	Do you have any of the following? (can be more than one option)	1. Altered Consciousness (confusion, sleepy, drowsy, coma) 2. Not able to drink or feed 3. Frequent and persistent vomiting		

		4. Convulsions (or recent history of convulsion) 5. Inability to sit or stand up 6. No urine out put in the last 24 hours 7. Spontaneous bleeding (gum bleeding, epistaxes, hematemesis, mellena) 8. Yellowish discoloration of eyes 9. Dark urine 10. Difficult breathing 11. Failure to respond to treatment 2-3 days 12. Hyper pyrexia (T^o $\geq 38^oC$)		
405	Did you have had history of fever in the last one year?	1. Yes 2. No 3. No response		
406	If yes what was the duration?	1. For less than one week 2. For 1-2 weeks 3. for 2-3 weeks 4. For >3 weeks 5. Do not know		
407	Have you had diarrhea in the last one year?	1. Yes 2. No 3. No response.		
408	If yes for how long?	1. < 1 month 2. > 1 month 3. Do not know		
409	Have you had history of cough in the last one year?	1. Yes 2. No 3. Don't know		
420	If yes, for how long?	1. <1month 2. >1month 3. Do not know		

421	Did you lost significant body weight during the last six months?	1. Yes 2. No 3. Don't know 4. No response		
422	If yes, what was the maximum body weight lost?	1. Less than 10% of the body weight. 2. Greater or equal to 10% of the body weight 3. Not measured		

ANNEX II

Check list of physical signs and laboratory data to be filled for the patients under the study.

Part I. Check list of Physical Signs.

Roll No	Type of Examination	Findings	Code	Skip to
501	Pallor (check conjunctiva)	1. Present 2. Absent		
502	Jaundice (Check sclera)	1. Present 2. Absent		
503	Sub conjunctival hemorrhage	1. Present 2. Absent		
504	Check for generalized lymph adenopathy	1. Present 2. Absent 3. Others (specify)_____		
505	Check for oral candidiasis. (Look for oral mucosa)	1. Present 2. Absent 3. Others (specify)_____		
506	Herpes Zoster? (Look for lesion or scar)	1. Present 2. Absent 3. Others (specify)_____		
507	Splenomegally (Palpate the abdomen)	1. Present 2. Absent 3. Others (specify)_____		
508	Hepatomegally (Palpate the abdomen)	1. Present 2. Absent 3. Others (specify)_____		

509	Peripheral edema (Check the musculo-skeletal System)	1. Present 2. Absent		
510	Peticheae (check the integumentary system)	1. Present 2. Absent		
511	Glasgow Comma Scale (For patients with impaired consciousness)	1. 3-5 2. 5-9 3. 9-12 4. >12		
512	Type of patient based on the clinical data	1. Uncomplicated malaria 2. Severe Complicated Malaria (SCM)		
513	If SCM indicate which one the patient fulfills as a severity criteria.	1. Comma 2. Severe Anemia 3. Jaundice 4. Prostration 5. Hyper parasitemia 6. Other (specify)_____		

Part II. Laboratory Results

Roll No	Types of investigation done for the patient	Result	Code	Skip to
601	Blood microscopy (species of malaria identified)	1. P.falciparum 2. Mixed species		
602	Parasitic load	1. + 2. ++ 3. +++ 4. ++++ 5. +++++		
603	Sero status of the patient	1. Positive 2. Negative		

ANNEX III

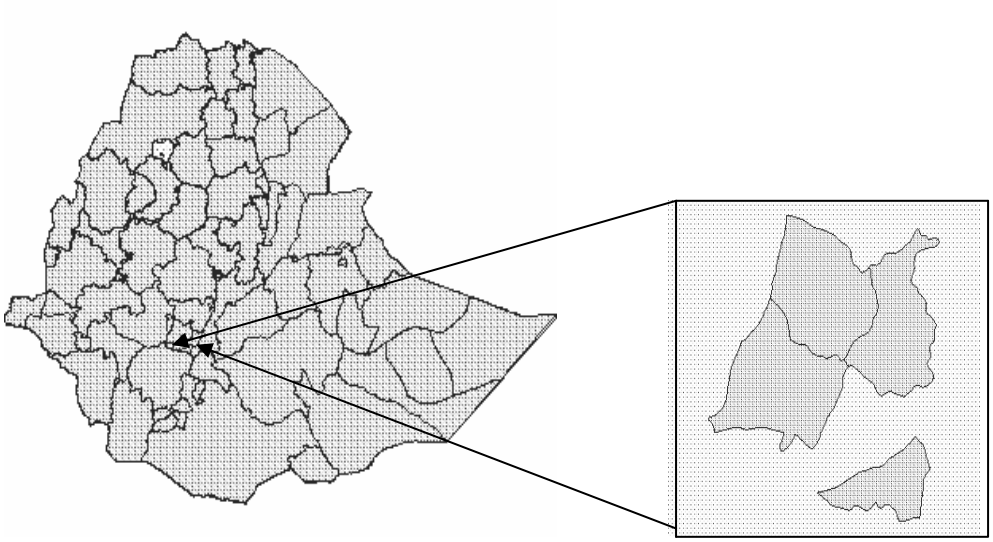
ELISA WORK SHEET

Manufactory Date ____
Expiration Date _____
Principle _____ Batch No. _____

0	1	2	3	4	5	6	7	8	9	10	11	12
A												
B												
C												
D												
E												
F												
G												
H												

Cut of value _____ # of positives
Lower Limit _____ # of negatives Signature _____
Upper Limit _____ # indeterminate Date Tested _____

ANNEX IV. MAP OF THE STUDY AREA, HADYA ZONE, 2001/02.



Map of Ethiopia showing the different Zones

Map of Hadya Zone showing the different Woredas in the zone

ANNEX V BAR CHARTS

Chart I .Proportion of HIV positives and HIV negative patients among P.falciparum malaria patients who presented with physical findings of malaria and AIDS,Hadya Zone,Southern Ethiopia,2003

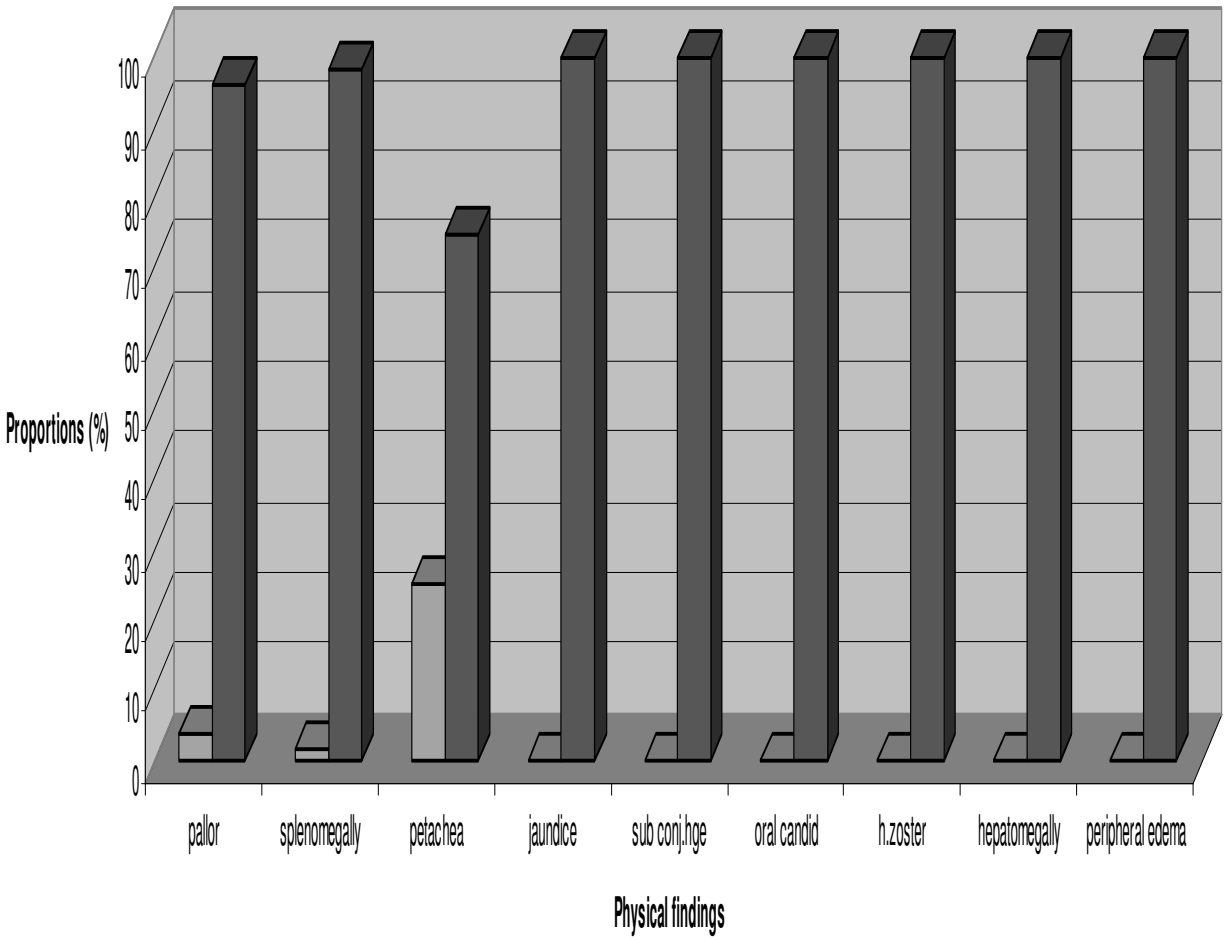


Chart II. Proportion of HIV seropositives and seronegatives among P. falciparum malaria patients presenting with different signs of sever malaria, Hadya Zone, Southern Ethiopia, 2003