CORRELATES AND INCIDENCE OF *PLASMODIUM FALCIPARUM* AMONG HIV INFECTED AND HIV NON- INFECTED CHILDREN BELOW 5 YEARS IN KISUMU COUNTY, KENYA

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MASTER OF SCIENCE

(Epidemiology)

THE JOMO KENYATTA UNIVERSITY OF AGRICULTURE AND TECHNOLOGY

2020

Correlates and incidence of *Plasmodium falciparum* among HIV infected and HIV non- infected children below 5 years in Kisumu County, Kenya

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A thesis submitted in partial fulfillment of the award for the degree of Master of Science in Epidemiology of the Jomo Kenyatta University of Agriculture and Technology

2020

DECLARATION

This thesis is my original work and has not been presented for a degree in any other University

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This thesis has been submitted for examination with our approval as the University Supervisors.

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DEDICATION

This thesis is dedicated to my loving wife, Fridah Cheque and my sons Jaysen Ogony and Jaymon Ogony, without whose inspiration, I would not have made it and achieve this milestone. I would not want to forget my parents, Mr. and Mrs. Ogony for their immense love and support. May the Almighty God in His abundant grace, bless you all.

ACKNOWLEDGMENT

I wish to express my most sincere gratitude to my supervisors, Prof. Simon Karanja and Mr. Henry Kissinger for their continued guidance, patience, encouragement and support in shaping this work and bringing it to successful completion, their close and constant support supervision made this work possible. I extend special thanks to all my Epidemiology class Lecturers and entire School of Public Health JKUAT for moral support and the knowledge imparted, which has been helpful in this research.

I extremely appreciate the profound support of my classmates,you were a good member of our discussion group who illustrated “esprit de corps”.On the same breath, I also thank the entire AMREC community for the support towards this output.

I give thanks to Ethical Review Committee (ERC) of JOOTRH for giving the project proposal a node, likewise Kisumu County Hospital (KCH) ;lead study clinician Lillian Oyucho and lead lab officer Geoffrey Osur and Lumumba sub-county hospital (LSCH) study staffs; Alice Ndege, Dancun ,Claxton and entire clinical team from both hospitals for sacrificially supporting the data collection.

Lastly but not least, I wish to thank all my Godsend friends and mentors especially Rev. Anataka Mugenyi, Prof.Jackson Muhirwe, and Ronald Aswani. I would not wish to forget the musketeers Ben Oyugi and Arthy Yongo, You have been a pillar to lean on during difficult and discouraging moments, may the Almighty God bless you. Not forgetting those who directly or indirectly rendered assistance to me including the ‘Like-minded self-help group’. Above all, I thank the Almighty God who made everything possible for me “Not by power, not by might but by the spirit of the Lord”

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ABBREVIATIONS AND ACRONYMS

ART	Antiretroviral therapy.
CCC	Comprehensive Care Center
CD4	Cluster of differentiation 4.
CDC	Centers for Disease Control and Prevention.
CDH	County Director of Health
CI	Confidence interval.
CIR	Commutative incidence rate
CRF	Case Report Form
CTX	Co-trimoxazole.
DALYs	Disability-adjusted life years.
DOT	Directly observed therapy
ERC	Ethical Review Committee.
GEE	Generalized estimating equations
GLM	Generalized Linear model
HAART	Highly active antiretroviral therapy.
Hb	Hemoglobin
HRP2	Histidine rich protein II
HEU	HIV-exposed uninfected.
HIV	Human immunodeficiency virus.
ICF	Informed consent form.
IEC	Independent Ethics Committee.
IPTpT	Intermittent preventive therapy
JOOTRH	Jaramogi Oginga Odinga Teaching and Referral Hospital
KAP	Knowledge, attitude and practices
KCH	Kisumu County Hospital
LAR	Legally acceptable representative
LScH	Lumumba Sub-County Hospital
MOH	Ministry of Health.
mRDT	Malaria Rapid Diagnostic Test

NASCOP	National AIDS and STI Control Programme
OPD	Outpatient Department
P. f	*Plasmodium falciparum*
PMCT	Prevention of Mother- To- Child Transmission
SBCC	Social Behavior Change Communication
SCHMT	Sub-County Health Management Team.
SID	Subject identification
SP	Sulphadoxine-Pyrimethamine
UNAIDS	United Nations Programme on HIV/AIDS
WHO	World Health Organization.

DEFINITION OF TERMS

Bioavailability	Is a subcategory of absorption and is the fraction (%) of an administered drug that reaches the systemic circulation
Clinical malaria	Asexual parasitemia > 0 AND presence of fever (axillary temperature ≥37.5°C).
Correlate	Variables that has a mutual relationship or connection, in which one affects or depends on another.
Fever	Body temperature above the normal 37◦C degrees Celsius.
HIV negative	Child born of HIV negative mother and or PCR confirmed to be HIV free.
HIV positive	Child born of HIV positive mother and PCR confirmed to be HIV positive.
Incidence	The measure of the probability of occurrence of a given condition in a population within a specified period of time
Oedema	Observable swelling from fluid accumulation in body tissues
Opportunistic infection	Infections that occur more frequently and are more severe in people with weakened immune systems, including people with HIV
Oral medication	Is the process by which drugs are delivered by mouth through the alimentary tract
Pharmacokinetic	The movement of drug into, through, and out of the body (absorption, bioavailability, distribution, metabolism, and excretionof the drug)
prophylaxis	Is the treatment given or action taken to prevent disease

Severe anemia	Documented hemoglobin < 5.0 g/dL with a *P. falciparum* parasitemia > 0 parasites/ul
Standard of care	The degree of care and skill of the average health care provider who practices in the provider's specialty, taking into account the medical knowledge that is available in the field.
Vertical transmission	Passage of a disease-causing agent from mother to baby before or after birth.

ABSTRACT

Globally over 3 billion people are at risk of malaria infection every year. This burden is compounded by the fact that approximately 2-3 million children live with human immunodeficiency virus (HIV) in low and middle income coutries. Malaria and HIV account for a significant amount of morbidity and mortality. Cotrimoxazole prevents opportunistic infections in HIV-infected persons, but its effectiveness in preventing malaria varies especially in children. This cohort study determined the correlates and incidence of *P. falciparum* among HIV positive and negative children < 5 years in Kisumu County. A sample size of 132 was estimated based on methods in Observational Epidemiology. Data analysis was done using Stata version 14. Relative Risk with corresponding 95% CI was used to estimate the strength of association between the independent predictors of malaria. There was a significant difference in the incidence of *P. falciparum* among HIV infected compared to HIV non-infected children (p-value = 0.0030). Symptoms presented such as; Fever RR 0.69 (95%CI: 0.22-2.16), headache RR 1.53 (95%CI: 0.12-19.08),Inability to retain oral medication RR 0.12 (95%C: 0.01-1.92), the number of persons per bed net use where two, RR 5.46 (95%CI: 0.46-64.58), three 2.14 (95%CI: 0.27-17.25) and > three 2.58 (95%CI: 0.27-24.87) were indication to malaria infection. The study concluded that risk factors such as inability to retain oral antimalarial medication, presence of fever and headache were indicative of malaria infection; similarly, caretaker level risk factors such as the individual taking care of the child was also a source of risk to *P.falciparum* infection.The study realized an overall three-month cumulative incidence rate of 17.42%, with a higher proportion (27.27%) of the subject who suffered malaria being HIV negative indicative that Cotrimoxazole offers protection to malaria infection in children below five years. We recommended for policies to emphasise the direct observe therapy at the facility level for malaria treatments with continuous medical education to enhance drug absorption and bioavailability.

CHAPTER ONE

INTRODUCTION

1.1. Background information

Malaria is caused by infection with one or more of the 5 species of parasites within the genus *Plasmodium* and their life cycle (**Figure 1.1)** is almost the same for all the five species that infect humans. Of these, the greatest burden of disease and death is caused by *Plasmodium falciparum*. It is estimated that over 3 billion people are at risk for a new malaria infection every year and that over a million young children die every year from malaria (Guinovart, Navia, Tanner, & Alonso, 2006). The burden of morbidity and lasting damage from clinical yet sub-fatal malaria, especially in children, is incalculable, with hundreds of millions of cases every year. Sub-Saharan Africa suffers disproportionately from these burdens and remains the region at greatest risk(Griffin, Ferguson, & Ghani, 2014)

Gradually as people endure repeated infection, their ability to control the parasite in the bloodstream increases while their inflammatory response is simultaneously blunted, leading to a decreasing severity of disease (Belkaid, Sun, & Bouladoux, 2006). Eventually, depending on the level of infectious pressure, most older children and adults remain asymptomatic with most repeated infections (Marsh & Kinyanjui, 2006) (**Figure 1.2**). While a novel strain of parasite, or other factors such as pregnancy or Human Immunodeficiency Virus (HIV) infection, can alter this hard-won partial immunity, many people in endemic areas likely harbor parasites most of their lives, with parasitemia that are so low they are only occasionally detectable by quality microscopy, and with even fewer clinical episodes. Prolonged, low parasitemia can be characterized by intermittent and unpredictable waves of production of gametocytes, the parasite stage that can infect the mosquito. Gametocytes are never associated with clinical disease. Thus, the primary reservoir of disease is the older child or young adult that is asymptomatic and infective to mosquitoes that will carry the infection to the next, perhaps younger and more susceptible,

host(Laishram *et al.*, 2012)

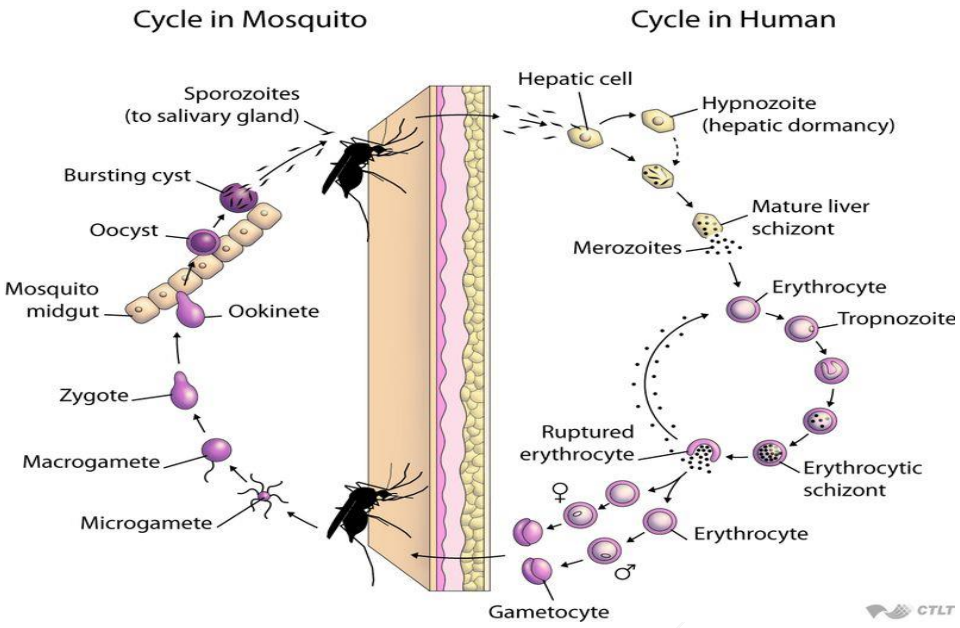

Figure 1.1 *Plasmodium* Life Cycles

On the same note, sub-Saharan Africa suffers from devastating burdens of both HIV and malaria. Approximately 2-3 million children live with HIV in sub-Saharan Africa; about 1500 children are newly infected each day (Prendergast, Tudor-Williams, Jeena, Burchett, & Goulder, 2007). Vertical transmission rates are approximately 12- 40% (De Cock *et al.*, 2000), and down to 2% in the context of optimal Prevention of Mother-To-Child Transmission (PMCT) (Paintsil & Andiman, 2009). HIV-positive children in malaria-endemic areas have an elevated risk of clinical malaria and potentially more severe clinical outcomes compared with HIV-negative children due to compromised immune systems. World Health Organization (WHO) approximates that 3.2 billion people are at risk of malaria globally. Sub-Saharan Africa is disproportionally affected; in 2015, the region had 88% of malaria cases reported and 90% deaths due to malaria.Among the deaths,86% were occurring in children under five years (Unaids & World Health, 2011).That same year, there were approximately 3.4 million children <15 years living with HIV worldwide of which more than 90 % lived in sub-Saharan Africa (Unaids &

World Health, 2011). Malaria and HIV are two infections with overlapping epidemiologic maps that need to be addressed urgently.

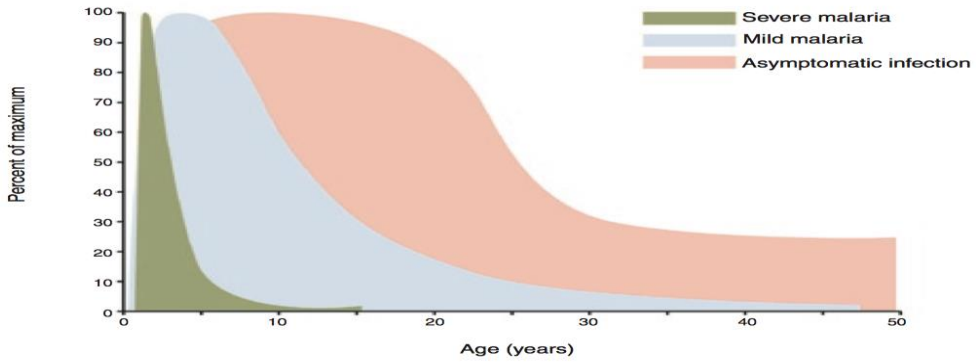

Figure 1.2. A model of the relative age distribution of clinical and asymptomatic malaria in endemic to holoendemic regions

There is an interaction between malaria and HIV infections which causes a global health problem. On the one hand, HIV-related immunodeficiency results in children being more vulnerable to malaria, reducing the efficacy of antimalarial drugs (Ezeamama *et al.,* 2012). This interaction needs to be further investigated in a context where access to Cotrimoxazole prophylaxis and antiretroviral therapy (ART) could have a protective effect against malaria in HIV infected-children(Taylor G Sandison *et al.,* 2011; Unaids & World Health, 2011). Although not defined as an opportunistic disease (World Health, 2004) (Francis X Kyeyune *et al.,* 2014; Francis X. Kyeyune *et al.,* 2014) , a malarial episode may become more serious with HIV influence as reported by many studies mostly conducted in Southern and Eastern Africa (Ezeamama *et al.,* 2012) (Laufer *et al.,* 2006) (DeGennaro & Zeitz, 2009). Before the ART era, Cotrimoxazole (CTX) prophylaxis reduced morbidity and mortality in children with HIV by preventing bacterial infections, diarrhea, malaria, and Pneumocystis jirovecii pneumonia,(C. Chintu *et al.,* 2004). The main objective of this study was to measure the incidence of malaria burden and the correlates in HIV-infected children and uninfected children below 5 years in Kisumu city Kisumu County has a population of 968,909 comprising males (49%) and females (51%) .Children below 15 years constitute 42% of the population, while youth aged 15-24 years

constitute 22% of the population . HIV prevalence in Kisumu is 3.4 times higher than the national prevalence at 19.9% (Wang *et al.,* 2015).The HIV prevalence among women in the county is higher (21.2%) than that of men (18.3%) indicating that women are more vulnerable to HIV infection than men in the County**.** Kisumu County contributed to 9.5% of the total number of people living with HIV in Kenya and is ranked the third-highest nationally. By the end of 2015, a total of 144,303 people were living with HIV in the County with 22% being young people aged 15-24 years and 6% being children under the age of 15 years. The study area has high malaria prevalence (38% in children 0–14 years) and vertical transmission rates of HIV (between 7–15%) in the context of increased uptake of prevention of mother-to-child transmission services)(Kohler *et al., 2014; Thomas et al., 2011)*)

1.2.Statement of the problem.

In 2001, the WHO ranked malaria as the eighth-highest contributor to the global disease burden as reflected in disability-adjusted life years (DALYs), and the second-highest in Africa (Murray *et al.,* 2010). The DALYs attributable to malaria was estimated largely from the effects of *P. falciparum* infection as direct causes of death. Sub-Saharan African children under five years represent 82% of all malaria-related deaths and DALYs.

Malaria is a significant public health problem in Kenya and the leading cause of morbidity and mortality among the children under the age of five years.This population is vulnerable to malaria infection since they have developed minimal immunity to the disease. About 25 million out of the population of 44 million Kenyans are at risk of malaria and account for 30-50% of all outpatient attendance and 20% of all admissions to health facilities.About 170 million estimated working days are lost to malaria each year in; lost days of work, absence from school, expenses for preventive measures, expenses for burial in case of deaths (Packard, 2009). The Kenya malaria survey 2007 showed a prevalence of 17% in children less than 5 years in Kisumu while HIV continues to contribute to high mortality rates, burdening households and straining the national health systems(Diego F Cuadros, Adam J Branscum, & Philip H Crowley, 2011; Jenkins *et al.,* 2015)

Malaria accounts for 2% of global deaths and 2.9% of global DALYs. In the African region of WHO, 9% of deaths and 10.1% of DALYs are attributable to malaria(Lopez & Mathers, 2006). Malaria and HIV interact directionally and synergistically with each other therefore DALYs due to malaria and HIV could be more in high HIV prevalent areas such as Kisumu with high disease burden and comorbidity. Several studies in Africa have addressed the risk of malaria clinical episodes in HIV-infected adults, but little is known concerning overall parasite incidence, regardless of the presence or absence of symptoms in HIV-infected and in HIV non-infected children. This study therefore addressed whether detectable malaria parasitemia and gametocytaemia, occur at increased frequency or intensity in HIV or in non-HIV infected children under five years.

1.3 Justification

The ravages of both the HIV epidemic and the continued intolerable burden of malaria infection pressure are well-publicized. Although animal models exist – and have already been used by some investigators to generate some of the reported preliminary data that was used in hypothesis generation for this study, there is scanty information on the incidence of malaria on HIV infected and the HIV non-infected children below 5 years in Kenya. Based on existing literature, study hypothesized that HIV-infected children are likely to have more incidence, frequency, duration and/or intensity of both symptomatic and asymptomatic parasitemia which could make them potentially virulent reservoirs of malaria infection for the rest of their community. The interactions of HIV and clinical symptomatic malaria have received extensive scrutiny (Hochman & Kim, 2009a, 2009b) "The Impact of HIV and Malaria Coinfection": What is known and suggested venues for further study but there has been little work on asymptomatic malaria in the context of co-infection.

The significance of this study rested in addressing whether detectable malaria parasitemia occurred at increased frequency or intensity in HIV or in non-HIV infected children under 5 years, this could inform the policy-making in addressing the areas of need. The information gleaned from this study will add to the general body of knowledge the association between malaria and HIV in children below 5 yerrs and to would help appropriately design a future study that will pursue additional hypotheses, such as

whether CTX or specific pharmacologic class of Antiretroviral Therapy (ART) in HIV-infected individuals will impact parasite transmissibility to mosquitoes. This could form basis for the nature of care being given to such patients. Taken together, this body of current and proposed work will clarify whether the HIV epidemic are driving additional malaria transmission and or if global health interventions can be more appropriately optimized in areas where both diseases are endemic. The study envisaged to produce key information for policy development at the national level whether to direct or redirect specific measures in given regions in the Republic of Kenya in malaria and HIV case management.

1.4 Research questions

1. What was the incidence of *P. falciparum* infection among HIV infected and HIV non-infected children below 5 years in Kisumu County?
2. What were the child-level factors influencing *P. falciparum* infection among HIV infected and HIV non-infected children below 5 years in Kisumu County?
3. What were the care giver-level factors influencing *P. falciparum* infection among HIV infected and HIV non-infected children below 5 years in Kisumu County?
4. What were the household-level factors influencing *P. falciparum* infection among HIV infected and HIV non-infected children below 5 years in Kisumu County?

1.5 Objectives

To determine the correlates and incidence of *P. falciparum* among HIV infected and HIV-non-infected children below 5 years in Kisumu County, Kenya

1.5.1 Specific objectives

1. To determine the incidence of *P. falciparum* infection among HIV infected and HIV-non-infected children below 5 years in Kisumu County
2. To determine the child-level factors influencing *P. falciparum* infection among HIV infected and HIV non-infected children below 5 years in Kisumu County
3. To determine caregiver-level factors influencing P. falciparum infection among HIV infected and HIV non-infected children below 5 years in Kisumu County

4. To determine the household-level factors influencing *P. falciparum* infection among HIV infected and HIV non-infected children below 5 years in Kisumu County.

1.6 Hypothesis

1.6.1 Null Hypothesis.

There is no significant difference in incidence of *P. falciparum* among HIV infected compared to HIV non-infected children below 5 years in Kisumu County.

1.7 Scope of study

Since the objective was to determine *P. falciparum* (asexual) incidence among HIV infected and HIV non-infected children below 5 years in Kisumu County, Kenya. The study was only able to illustrate the number of new malaria infections as determined by microscopy during the study period amongst the HIV infected subjects and the HIV non-infected. There was no blood kept for any later genetical or molecular analysis or assays of the blood samples collected from the subject to ascertain any drug pharmacokinetic or immunological typing of the subjects.

1.8 Limitations.

This is a prospective cohort tudy in nature and the fact that we only followed the subjects for not more than three months, this limited us in the duration of data and size of data collected hence was not able to experience the different waves of seasonality of malaria occurrences. We also experienced cohort members migrating to different counties or upcountry or change of jobs therefore at times led to delay in scheduled visits. Few experienced challenges in coming back to the clinic as was stipulated/ scheduled even though this did not affect the study outcomes.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

Malaria coinfection is a critical comorbidity in HIV infected individuals. Malaria and HIV account for a significant amount of morbidity and mortality in sub-Saharan Africa with an estimated 22.5 million people living with HIV (Unaids & World Health, 2011) and over 300 to 500 million clinical *Plasmodium falciparum* cases every year. Kisumu County in western Kenya has a high prevalence of malaria and HIV with reports of HIV prevalence ranging from 21 to 44 percent and point prevalence of malaria infection reported at 13 to 42 percent. Frequent and recurrent infections with *P. falciparum* in areas with stable malaria transmission result in a semi-immune state in adults which allows for an increasing proportion of infections to stabilize at variable parasite densities without the severe disease.

HIV-infected adults with decreased CD4 counts (especially those with CD4 counts less than 200) living in areas of stable malaria transmission have an increased incidence of symptomatic malaria infections compared to HIV-uninfected adults and there is evidence of an inverse relationship between the level of parasitemia and CD4 count. Rates of malaria treatment failure have been noted to be higher in HIV-infected persons with the highest rates of failure noted in individuals with CD4 counts less than 200. However, Kamya *et al*. used molecular genotyping in a Ugandan cohort and demonstrated that clinical treatment failure of malaria was actually a result of new infections rather than a recrudescence of the same infection (Moses R. Kamya *et al.,* 2006). The biological basis of these interactions is well established. HIV infection induces cellular depletion and early abnormalities of CD4+ T cells, decreases CD8+ T-cell counts and function (cellular immunity), causes deterioration of specific antigen responses (humoral immunity), and leads to alteration of innate immunity through impairment of cytolytic activity and cytokine production by natural killer cells (Flateau, Le Loup, & Pialoux, 2011).Therefore,

HIV infection affects the immune response to malaria, particularly premunition in adolescents and adults, and pregnancy-specific immunity, leading to different patterns of disease in HIV-infected patients compared with HIV-uninfected patients. Malaria infection leads to CD4 activation and the impaired T cell immunity and loss of antigen-specific memory CD4 cells in HIV-infection (Van Geertruyden *et al.,* 2006) likely causes some loss of the specific disease protective immune response necessary to prevent infection, protect parasitemia persons from developing severe disease, and clear parasitemia with treatment. Though previous studies have not noted an increase in severe or complicated malaria in regions of stable transmission, people living with HIV infection who have no pre-existing immunity to malaria do experience increased disease severity (Laufer *et al.,* 2006).

2.2 Child risk factors to malaria and HIV infections

Children are generally susceptible and vulnerable to malaria (Flateau *et al.,* 2011) and with HIV co-infection they may be at a higher risk of severe malaria infection. Such a co-infection may also retard the age-related acquisition of natural immunity to malaria in children (Orlov *et al.,* 2012) and lead to higher parasite densities thereby increasing the risk of anaemia (Sheet, 2014). Since malaria and HV/AIDS remain health concerns in kisumu county, there is a need for constant monitoring of both diseases in all age groups. Although there have been some reports on malaria in HIV patients in Kisumu, none of them has specifically focused on child specific risk factors influencing the prevalence of malaria in HIV-infected and non infected children. Such data remains very scanty in the country in general. Baseline data on the incidence of malaria in this high risk group of patients is of utmost importance as this will help inform the design of interventions that can reduce the burden of both diseases. The World Health Organization (WHO) recommends placing all infants of HIV infected mothers on co-trimoxazole prophylaxis starting at 6 weeks of age until cessation of breast feeding and exclusion of HIV infection(WHO, 2006). This guideline stems from evidence that co-trimoxazole prophylaxis protects HIV infected children from common opportunistic infections(C

Chintu *et al.*, 2004b), However, there are no studies on the protective efficacy of co-trimoxazole prophylaxis against malaria among HIV exposed.

2.3 Child caretakers level risk factors to malaria infection

Although efficacy of Artemether combined therapy (ACT) is high, there is evidence that non-completion of the full standard regimen will result in treatment failure (Oyakhirome *et al.*, 2007). Taking the full treatment course is not only important for successful elimination of the parasite but also for prevention of resistance development. Previous studies on caretaker adherence to a full treatment course of ACTs have shown varying results, ranging from 39% to 90% (Lemma, Löfgren, & San Sebastian, 2011) Despite the differences observed in adherence rates, the factors found to influence caretaker adherence to antimalarials were similar across the different studies, including caretaker's education level(Lemma *et al.*, 2011), communication with healthcare providers(Conteh, Stevens, & Wiseman, 2007). The 3 day duration of ACT treatments might be one important cause of suboptimal adherence, as was previously shown for choloroquine(Bruxvoort, Goodman, Kachur, & Schellenberg, 2014) .Another factor that is likely to influence adherence, but which is yet to be quantified, is caretaker perception about the drugs used.

2.4 Household level risk factors to malaria infection

Malaria transmission in Kenya varies across climatic seasons, ecological zones, neighboring villages, and even between neighboring households in Kisumu (O'Meara *et al.*, 2008). Households in close proximity to breeding sites have higher mosquito densities and are at increased risk of transmission, usually following a seasonal pattern(Kasasa *et al.*, 2013). However, irrigation, roads and urbanization may create breeding sites that persist throughout the year, diminishing the seasonal effect (Omukunda, Githeko, Ndong'a, Mushinzimana, & Yan, 2012). These environmental risk factors interact with socio-cultural factors at the level of the household, including socioeconomic status, bed net use, and the type of construction of human dwellings (Townes, Mwandama, Mathanga, & Wilson, 2013). These findings suggest that despite high perennial

transmission, there may be important seasonal differences in risk factors and therefore the household activities has a contribution risk to the malaria infection to members

2.5 Theoretical review

Mathematical modeling has been applied to describe the interaction of HIV and malaria infections in sub-Saharan Africa (Diego F. Cuadros, Adam J. Branscum, & Philip H. Crowley, 2011) .Prolonged parasitemia and increased frequency of symptomatic malaria infections in HIV-infected individuals are likely to contribute to malaria transmission. The factors that induce cycling malaria parasites to form gametocytes are incompletely understood. The appearance of gametocytes is enhanced by severe malarial anemia and tissue hypoxia, and there is a possible link between anemia and both the duration of gametocytaemia and mosquito attractiveness (Nacher *et al.,* 2002). HIV-1 exposed or infected Kenyan children had an increased prevalence of severe anemia during *P. falciparum* infection relative to children who were HIV-1 negative (Otieno *et al.,* 2006). The published data in a macaque model shows higher overall parasitemia, and specifically gametocytaemia, in previously SIV-infected macaques than in uninfected controls (Kristin A Trott et al., 2011; Kristin A. Trott et al., 2011). These SIV-induced gametocytes more efficiently infected Anopheles freeborn than did gametocytes from SIV-negative controls.

Mosquitoes can become infected following feeding on patients that lack microscopically detectable sexual stage parasites. With the advent of molecular detection assays, it has become increasingly apparent that microscopy significantly underestimates (submicroscopic) gametocyte carriage that can substantially contribute to transmission (Aâ€• Elbasit, Elbashir, Khalil, Alifrangis, & Giha, 2006; Bousema *et al.,* 2006; Mermin *et al.,* 2006; Shekalaghe *et al.*, 2007). Unfortunately, routine microscopic diagnosis is based on the detection of asexual parasite stages and gametocytes (viewed as clinically irrelevant) are rarely recorded. Elevated HIV plasma viral loads associated with malaria infection and malaria-associated immune suppression likely contribute to the transmission of HIV. (Kwenti, 2018)estimate that an additional 3 million cases of malaria and 65,000

malaria-related deaths annually are due to the impact of HIV. Mathematical model applied to Kisumu district estimated that since 1980, the disease interaction may have been responsible for 8,500 excess HIV infections and 980,000 excess malaria episodes(Abu-Raddad, Patnaik, & Kublin, 2006)

There are many confounders, however, in determining the epidemiologic interaction between HIV and malaria. The antimalarial activities of antiretroviral therapy (especially protease inhibitors) have been reported and studies are ongoing(Skinner-Adams *et al.,* 2012).The symptoms of adverse effects of medications, acute HIV infection, and other opportunistic infections overlap with those of malaria making definitive diagnosis and treatment difficult in malaria-endemic settings (i.e. potential for asymptomatic parasitemia in an HIV-infected person with other cause of acute fever).

Likely the most important confounding factor is the widespread use of CTX prophylaxis in HIV-infected individuals. As an anti-folate similar to sulfadoxine/ pyrimethamine SP, CTX is also an anti-malarial and has been shown to decrease episodes of malaria in both the individuals on this therapy and in their HIV negative household members(Mermin *et al.,* 2004a, 2004b) . Factors associated with gametocytogenesis include single-species infection, parasite density, anemia/reticulocytosis, duration of infection, stress on the parasite population due to host immunity or anti-malarial treatment, and the stage-specificity of the anti-malarial used. Treatment of malaria infection with SP alone results in very high post-treatment gametocyte prevalence that is likely to enhance transmission; treatment with sulphadoxine-pyrimethamine (SP) against resistant infection is followed by the highest gametocytaemia. It is likely that similarly, high gametocytaemia exists in the setting of treatment or prophylaxis with co-trimoxazole and the long-term population effects of widespread co-trimoxazole use on the incidence of malaria infection in individuals and on transmission are not known(Manyando, Njunju, & D'Alessandro, 2013)

2.6 Critics of the existing literature.

The concerns about Cotrimoxazole prophylaxis and malaria treatment and prevention have been harder to address. *In vitro* studies demonstrated cross-resistance between sulfamethoxazole and sulfadoxine and between trimethoprim and pyrimethamine(Iyer, Milhous, Cortese, Kublin, & Plowe, 2001). The initial fear was that widespread implementation of Cotrimoxazole prophylaxis in areas where both HIV and malaria were common would result in selection for antifolate-resistant malaria in the population at large, impairing the efficacy of SP and hastening its demise(González, Ataíde, Naniche, Menéndez, & Mayor, 2012). Less appreciated but more acutely alarming was the possibility that selection for resistant parasites would occur within malaria-infected individuals taking Cotrimoxazole prophylaxis, putting them at increased risk of treatment failure and progression to severe malaria when their malaria was treated with SP(Sridaran et al., 2010).

2.7 Summary

Cotrimoxazole is an antimicrobial drug containing a fixed-dose combination of sulfamethoxazole and trimethoprim. CTX prevents opportunistic infections in HIV-infected or HIV-exposed children, but estimates of the effectiveness in preventing malaria vary (Njama et al., 2003b). It appears to be beneficial for HIV-infected and HIV-exposed as well as HIV-uninfected children. The combination of these drugs produces a synergistic effect against a variety of bacterial and protozoal infections as well as fungal infections. It is recommended for children infected with HIV to be continued until immune recovery is observed on ART. For HIV-exposed uninfected (HEU) children (children born to mothers living with HIV) CTX is recommended from the age of six weeks until they stop breastfeeding and HIV infection is ruled out(Organization, 2016). Randomized clinical trials (RCTs), observational studies and economic analyses have shown that CTX is cost-effective in reducing morbidity and mortality among infants and children living with or exposed to HIV (C Chintu *et al*., 2004a; C. Chintu *et al.,* 2004; Ryan *et al.,* 2008), Estimates of the effectiveness of CTX for preventing malaria, however,

vary widely. For example, the incidence of malaria was reduced by 99% in a clinical trial in Mali but only by 39% in another clinical trial in Uganda (Havig, Skogstad, Kjekshus, & Romøren, 2011; Taylor G. Sandison *et al.*, 2007). Furthermore, the uptake of CTX by national programs has been slow and it continues to be underused (Vitoria, Granich, Banda, Fox, & Gilks, 2010). A major concern with CTX is that its widespread use in high malaria transmission areas may favor cross-resistance to SP, a drug used for intermittent preventive therapy (IPTpT) in pregnant women, for seasonal malaria chemoprophylaxis in children (as SP-AQ) and for intermittent preventive therapy in children (Sridaran *et al.*, 2011). However, it remains to be determined if the presence of antifolate resistant mutants affects the protective efficacy of CTX against malaria**.**

2.8 Research gaps.

In holoendemic or strongly seasonally endemic areas for malaria, the partial immunity in older children and adults develop protects them from clinical episodes while allowing multiple intermittent waves of asymptomatic parasitemia that are occasionally associated with gametocytaemia. It is these semi-immune, asymptomatic individuals that serve as the primary reservoir of disease; only a small proportion of all malaria infections are actually symptomatic, unlike in a naïve population (Bousema *et al.*, 2006). The reported prevalence of malaria parasite infection and of gametocytaemia often depends on the sensitivity of the tools for detection and precent studies with exquisitely sensitive molecular detection indicate that the overall prevalence of parasites in any stage of development, and also of gametocytes, is much higher than previously thought. While the immunosuppression of HIV disease clearly makes the acquisition of clinical malaria episodes more likely, this study evaluated whether infection with HIV leading to the use of CTX may have effects on both the frequency and magnitude of sub-clinical parasitemia.

The incidence of malaria in HIV-infected and HIV uninfected children and the epidemiological impact of extended post-treatment prophylactic effect of artemether lumefanthrine(AL) attributable to protease inhibitors has never been documented in Western Kenya.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Study area

The study was conducted in Kisumu County Hospital and Lumumba sub-county hospitals which are all in Kisumu central sub-county in Kisumu County, Western Kenya. Kisumu County covers an area of 2085.9sqkm. Kisumu has a population of 968,909. (Kenya National Bureau of, 2009). The geographic coordinates of Kisumu include; Latitude: 0°06′07″S. Longitude: 34°45′42″E and elevation above sea level: 1174 m = 3851 ft. The County neighbors Siaya County to the west, Vihiga County to the north, Nandi County to the northeast, Kericho County to the east and Homa Bay County to the southwest (**figure 3.1**). It is one of the eight counties zoned as the malaria-endemic in Western Kenya. Malaria is the leading cause of morbidity and mortality in children below 5 years in Kisumu County. The population in Kisumu is majorly cosmopolitan and is primarily black African. Though the predominant ethnic group is Luo, languages spoken are therefore Luo, Kiswahili, and English. Kisumu county hospital is sitauated in Kisumu central subcounty and it's the biggest County hospital that received all complicated clincal cases across the county and has a bigger CCC department likewise Lumumba sub-county hospital is equally situated in the CBD and has more vibrant CCC department since it is being supported by Family AIDS Care and Education Services (FACES) which is also known for supporting HIV management and focus on vulnerable populations in Kisumu County. Both hospitals serve clients residing in slums, with heaps of garbage and open or busted sewer lines which are breeding areas for mosquito. The dwellings are surrounded by Lake Victoria which is a niche for mosquitoes breeding.

Malaria is holoendemic in this area, and transmission occurs throughout the year. The 'long rainy season' from late March to May produces intense transmission from April to August. The 'short rainy season' from October to December produces another, somewhat less intense, transmission season from November to January and this informs the duration

of three months and the period for this study. Similarly, fishing is one of the major economic activities in Kisumu which is a driver to HIV infection in the county.

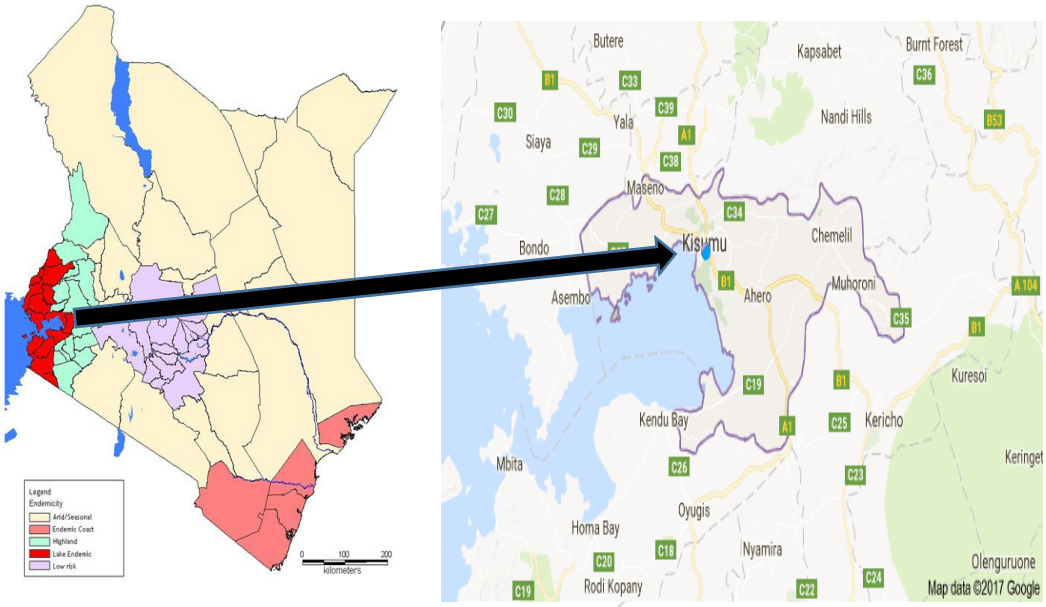

Figure 3.1. Map of Kisumu County indicating the study area

(Source MOH 2006)

3.2 Research design

The study adopted a prospective cohort design. Since this could allow the subjects to be followed up for a period and new cases of malaria were recored for the calculation of incidences.

3.3 Study population

The sample frame was Kisumu County in Kenya, an area endemic for malaria. The study population included male and female children below 5 years old HIV infected as an exposed group and HIV free as an unexposed group from the CCC and the outpatient departments (MCH) respectively and seeking health services in either Kisumu county hospital or Lumumba sub-county hospital.

3.3.1 Sample size determination

The sample size calculation was based on (Kelsey, Kelsey, Whittemore, Evans, & Thompson, 1996). Methods in Observational Epidemiology, 2nd Edition as illustrated below;

$$N_{Kelsey} = \frac{\left(z_{\alpha/2} + z_{\beta}\right)^2 p(1-p)(r+1)}{r(p_0 - p_1)^2}$$

Variable Notations:

P0 Proportion of exposure to disease and q1 = 1-p0

P1 Proportion of unexposed with disease and q2 = 1-p1

r the ratio of population 2 to population 1 (r population 2 to 1 population 1)

$\mathbf{Z_{a/2}}$ Standard normal deviates for a two-tailed test based on alpha level (relates to the confidence interval level).

$\mathbf{\bar{P}}$ The weighted average of P0 and P1 **(P1+rP0)/1+r**

$\mathbf{Z_{\beta}}$ standard normal deviate for a one-tailed test based on beta-level (relates to the power level)

Power (1-beta, % chance of detecting):	80
The ratio of sample size, Unexposed/Exposed:	1
Percent of Unexposed with Outcome:	75
Percent of Exposed to Outcome:	93
Odds Ratio:	4.43
Risk/Prevalence Ratio:	1.24
Risk/Prevalence difference:	0.18

	Kelsey
Sample Size – Exposed	66
Sample Size-None exposed	66
Total sample size:	**132**

3.3.2 Inclusion criteria exclusion criteria

Inclusion criteria	Exclusion criteria
i. A male or female child below 5 years seeking treatment from the Comprehensive Care Clinic (CCC) or Out Patient Department(OPD)/ Mother Child Health (MCH) departments. ii. Malaria Rapid Diagnostic Test (mRDT) negative on the screening date. iii. Willingness and ability the parent or guardian to comply with the study protocol for the duration of the study. iv. Subjects who are confirmed to be HIV infected for the exposed group. v. Subjects who are born of known HIV-negative mothers and are HIV non infected for the unexposed group. vi. Able to give consent and willing to participate in the study and follow up.	i. LAR or parent unwilling or unable to participate in the study including the follow up period. ii. Malaria Rapid Diagnostic Test positive on the screening date. iii. Subjects who are on CTX and are HIV negative (HEI). iv. Subjects who are on any known malaria prophylaxis. v. Any other condition that may result in an unfavorable outcome should the potential subject participate in the study.

3.3.3 Enrolment and study procedures

The study ran for a period of one year from the month of January 2018 to December 2018, each subject was followed up for a period of three months. Recruitment was done from CCC and OPD/MCH where parents of the children were informed about the study and they were asked to volunteer to participate upon consenting. After obtaining a written /signed consent, the subjects were assigned a unique subject identification number (SID) .Vital signs were taken by the triaging study nurse and the participants were then referred to study clinician who took them through; the questionnaire **(Appendix 2)**, took a medical history and performed a physical examination. The subjects were then sent to the hospital laboratory with the laboratory requesistion form for malaria test. Malaria Rapid Diagnostic Test (mRDT) (Paracheck® Pf device, Orchid Biomedical Systems, India) to test for *Plasmodium falciparum*-specific histidine rich protein II (HRP2) was administered by a qualified laboratory officer according to the mRDT job aid **(Appendix 3),** as a screening tool to rule out malaria preexistence. If the mRDT was positive, the

subject had the opportunity to be treated with an anti-malarial according to the current Kenya malaria case management guidelines and was followed up to be recruited after successful completion of treatment.

The RDT negative subjects were recruited in the study and followed up for a period of three months with a fortnight scheduled vist to monitor and capture the incidences of malaria infection.During these scheduled visits, microscopy where slides were stained with Giemsa, and double read (the gold standard for testing of malaria in this protocol) was used where thick and thin slide was prepared and both malaria parasite species and quantification was done according to WHO standards(Organization & Control, 2010) and documented in the CRF, if microscopy was positive for malaria during the subsequent scheduled and or unscheduled visits, the subject was treated with an anti-malarial according to the Kenya malaria case management guidelines(standard of care). Quantification of the parasite was done by a competent laboratory microscopist based on the WHO standards for malaria microscopy reporting. The HIV positive participants were also encouraged to adhere and continue with the CTX and or ART treatment algorithms as advised from the CCC as well as any other medication prescribed by the clinician. Absolutely no personal identifying information was collected, and the subject files and the signed consent document were secured in a lockable metallic box accessed only by the study principle investigator. The summarized study procedures are in **Appendix 4**.

3.4 Sampling techniques and illustrations

Purposive sampling technique was employed to include the HIV exposed group. The entire population of the exposed group was included since that population is quite small. With the implementation and adherence to PMTCT, there was a considerably reduced infection rate in children and thus all the children that were confirmed attending the clinic during the study period were included.

3.5 The instruments.

The instruments of choice in this study were questionnaire and case report forms Case Report Form (CRF). The questionnaire was divided into three sections; Section A collected the subject's (child) level factors information. Section B endeavored to establish the caretaker's level information and section C provided the household level factors. Demographics and socioeconomic data were collected using these tools during once at screening and recruitment. Before the onset of the study,the data collection tools were tested for validity in a different health facility(railway health centre) in kisumu county which was not part of selected facilities for the study.

3.6 Data collection procedures.

A detailed questionnaire was used to interview subjects once they had been recruited and consent given. The questions were answered after a physical examination had been carried out by the qualified clinician. CRF was used to collect clinical information at screening and during the scheduled follow up visits. The clinical information collected included vital signs, and symptoms mainly associated with malaria.

3.7 Data management and analysis.

3.7.1 Data management

The quantitative data from the field was coded and double entered into a computer database designed using MS-Access application. Files Back-up was regularly done to avoid any loss or tampering. Data cleaning and validation were performed in order to achieve a clean dataset that was exported into a Stata version 14 for analysis. All the questionnaires and the CRFs were analyzed.

3.7.2 Data analysis

Data cleaning and validation were performed in order to achieve a clean dataset that was exported from an excel database where the original data was collected into a Stata version 14 for analysis. Analysis was conducted using Stata version 14 statistical software

(StataCorp, 2015). Exploratory data analysis was done at the initial stage to uncover the structure of data and identify outliers or unusual entered values. The threshold for statistical significance was set at $p<0.05$. The study is longitudinal, Risk Ratio (RR) was appropriate. A generalized estimating equations (GEE) model was customized for logistic regression with poison family to report RR with corresponding 95% CI was used to estimate the strength of association between the retained independent predictors of malaria. We fitted a Proportional Cox regression model to obtain the HR.

3.8 Ethical considerations.

Written informed consent for the participation in the study was obtained from the Subject's parents or guardians or LAR. The purpose and the roles of the study subject were explained clearly to the subjects in English, Kiswahili or Dholuo before signing the consent form. Ethical approval was obtained from the Independent Ethical Review Committee (ERC.1B/VOL.1/368) of Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH) **(Appendix 8)** and Board of Post Studies(BPS) of Jomo Kenyatta University of Agriculture and Technology (JKUAT) **(Appendix 6)** .The study was also approved by the county govermenet of Kisumu ,Ministry of Health **(Appendix 7)**

3.9 Dissemination

The findings of this study have been shared with the ministry of health Kisumu county(Kisumu county hospital and Lumumba sub county hospital). The results have also been published with the International Journal of Scientific and Research Publications (IJSRP)

CHAPTER FOUR

RESULTS

4.1 Social and demographic characteristics of the particpants

A total of 132 study participants (n=132) with equal distribution of HIV serostatus, HIV- (n=66) and HIV+ (n=66) were recruited into the study. The overall mean age of the subjects was 2.79±1.07 with males at 2.66 (±1.08) years while the females at 2.91(±1.10) years. The mean age of those who were HIV- was 2.57 (±1.18) years while those who were HIV + were 3.01(±0.95) years. The majority [72 (54.55%)] of the children were aged between 4-5 years,of these, 42(62.69%) were male while 30(46.15%) were females. Majority of the caregivers were at tertary level of education 55(41.67%) followed by secondary level of education at 34(25.76).Most of the caregivers were self employed 71(53.75%) while 39(29.55%) did not have any formal employment. Majority of the caregivers were married 108(81.82%),18(13.64) single while 6(4.54%) were either divorced or Separated or widowed(table 4.1).

Table 4.1 Social and demographic characteristics of the particpants

Variable	Overall n (%)	GENDER Male (n=65) n (%)	Female (n=67) n (%)	HIV STATUS HIV- (n=66) n (%)	HIV+ (n=66) n (%)
Mean Age (Years)	2.79±1.07	2.66±1.08	2.91±1.10	2.57±1.18	3.01±0.95
Age Category:					
[0-1]	5(3.79)	3(4.48)	2(3.08)	5(7.58)	0(0.00)
[1-2]	19(14.39)	9(13.43)	10(15.38)	12(18.18)	7(10.61)
[3-4]	36(27.27)	13(19.40)	23(35.38)	17(25.76)	19(28.79)
Level of Education					
Never	7(5.30)	4(5.97)	3(4.62)	1(1.52)	6(9.09)
Pre-school	3 (1.51)	0(0.00)	2(3.08)	0(0.00)	2(3.03)
Primary	34(25.76)	18(26.87)	16(24.62)	10(15.15)	24(36.36)
Secondary	34(25.76)	16(23.88)	18(27.69)	12(18.18)	22(33.33)
Tertiary	55(41.67)	29(43.28)	26(40.00)	43(65.15)	12(18.18)
Occupation of caregiver					
Employed	22(16.67)	11(16.92)	11(16.42)	10(15.15)	12(18.18)
None	39(29.55)	20(30.77)	19(28.36)	27(40.91)	12(18.18)
Self-employed	71(53.75)	34(52.31)	37(55.22)	29(43.94)	42(63.64)
Marital Status of caregiver					
Married	108(81.82)	51(78.46)	57(85.08)	59(89.39)	49(74.24)
Single	18(13.64)	10(15.38)	8(11.94)	6(9.09)	12(18.18)
Divorced/Separated/widowed	6(4.54)	2(2.99)	3(4.62)	1(1.52)	4(6.06)

4.2 Descriptive analysis of Child level risk factors

The majority of the subjects [106 (80.30%)] were able to retain oral medication, while 23(17.42%) were unable, whereas 3 (2.27%) were reported to have sometimes been able to retain. A relatively high proportion of the children [79 (59.85%)] had a history of fever while 53(40.15%) did not. Out of the total 125 (94.70%), subjects were not on any anti-malarial prophylaxis, while 4(5.3%) were not sure. Most of the antimalarial used were given free from the hospital 60(45.45%), 17(12.88%) bought the drugs from chemists while 10(7.58%) bought the drugs from the hospital whereas 45(34.09%) had never used any antimalarial before. Distribution of the hospital levels where the participants were treated or admitted were; 7(5.30%) went to referral hospitals, 10 (5.58%) went to county hospital, 36 (27.27%) went to sub-county hospitals while 9 (6.82%) went to health

centers, whereas 70(53.03%) had never been treated in any hospital before the study began. The majority of the participants were not school goers 80(60.61%), while 52(39.39%) were school going during the time they were recruited into the study. Majority 71(53.79%) of the children had not been diagnosed with malaria before being recruited into the study, 60(45.45%) had been diagnosed before while 1(0.76%) of the guardians could not remember whether the child had been diagnosed of malaria or not (Table 4.2).

Table 4.2. Descriptive analysis of the child level factors.

VARIABLE		GENDER		HIV STATUS	
	Overall	Male (n=65)	Female (n=67)	HIV- (n=66)	HIV+ (n=66)
	n (%)	n (%)	n (%)	n (%)	n (%)
Retain oral antimalarial Medicine					
Yes	106(80.3)	54(83.08)	52(77.61)	65(98.48)	41(62.12)
No	23(17.42)	11(16.92)	12(17.91)	1(1.52)	32(33.33)
Sometimes	4(3.03)	0(0.00)	4(5.97)	0(0.00)	4(6.07)
History of hospitalization					
No	79(59.85)	40(61.64)	39(58.21)	40(60.61)	39(59.09)
Yes	53(40.15)	25(38.46)	28(41.79)	26(39.39)	27(40.91)
History of fever					
Yes	53(40.15)	38(58.46)	41(61.19)	41(62.12)	38(57.58)
No	79(59.85)	27(41.54)	26(38.81)	25(37.88)	28(42.42)
Level of Hospital [a]					
Referral hospital	7(5.30)	2(3.08)	5(7.46)	3(4.55)	4(6.06)
County hospital	10(5.58)	6(9.23)	4(5.97)	2(3.03)	8(12.12)
Sub County Hospital	36(27.27)	19(29.23)	17(25.37)	20(30.30)	16(24.24)
Health Centre	9(6.82)	5(7.69)	4(5.97)	4(6.06)	5(7.58)
Never been admitted	70(53.03)	33(50.77)	37(55.22)	37(56.06)	33(50.00)
Symptoms Presented					
Abdominal Complications	1(0.76)	1(1.54)	0(0.00)	1(1.52)	0(0.00)
Chronic conditions	1(0.76)	1(1.54)	0(0.00)	0(0.00)	1(1.52)
Common Cold	3(2.27)	1(1.54)	2(2.99)	2(3.03)	1(1.52)
Fever	48(36.36)	27(41.54)	21(31.34)	24(36.36)	24(36.36)
Headache	5(3.79)	2(3.08)	3(4.48)	1(1.52)	4(6.06)
None	73(56.06)	33(50.77)	41(61.20)	38(57.58)	36(4.55)
Duration of Admission					
Never been admitted	71(53.79)	34(52.31)	37(55.22)	34(51.52)	37(56.06)
Less than 1 week	35(26.52)	18(27.69)	17(25.37)	20(30.30)	15(22.73)
Between 2-3 weeks	15(11.36)	7(10.77)	8(11.94)	5(7.58)	10(15.15)
1 month	9(6.82)	4(6.15)	5(7.46)	6(9.09)	3(4.55)
More than 1 month	2(1.52)	2(3.08)	0(0.00)	1(1.52)	1(1.52)
History of malaria infection					
Yes	60(45.45)	32(49.23)	28(41.79)	34(51.52)	60(45.45)
No					
Can't remember	1(0.76)	0(0.00)	1(1.49)	0(0.00)	1(0.76)
Source of antimalarial used					
Bought from chemist	17(12.88)	8(12.31)	9(13.43)	0(0.00)	17(25.76)
Bought from this hospital	10(7.58)	6(9.23)	4(5.97)	3(4.55)	7(10.61)
Given free from this hospital	60(45.45)	30(46.15)	30(44.78)	33(50.00)	27(40.91)
Never been given antimalarial	45(34.09)	21(32.31)	24(35.82)	30(45.45)	15(22.73)

[a] **The level of the hospital where the child was admitted when sick**

4.3 Descriptive analysis of the caregiver level risk factors

The majority of the subjects were being taken care of by their parents [128 (96.97%)], while about 3 (2.27%) were being taken care of by house helps whereas only 1(0.76%) was being taken care of by a relative. High proportion [108(81.82%)] of the caregivers were married, 18(13.64%) were single, 9(3.79%) were either divorced or separated or widowed. Majority 127(96.21%) of the care givers (Mother or Father) were responsible for providing medication to the child if sick, only about 3(2.27%) were given medication by the house help and 2(1.52%) were being given medication by their relatives. A relatively high proportion 55(41.67%) of the caregivers had at least reached tertiary level of education, an equal number of 34 (25.25%) had reached secondary and primary level of education, 7 (5.30%) had never attained any level of education, whereas 3 (1.51%) reached pre-school level. Out of the total number of care givers, 71(53.75%) were self-employed, 39(29.55%) were not employed at all while 22 (16.67%) were formally employed. The majority [65(49.24%)] of the employed guardians reported to work between 8 am -5 pm, 34(25.76%) were working half-day, while the same number 1(0.76%) were working full and half night duty(Table 4.3).

Table 4.3.Descriptive analysis of caregiver level factors

VARIABLES		GENDER		HIV STATUS	
	Overall n (%)	**Male n (%)**	**Female n (%)**	**HIV- n (%)**	**HIV+ n (%)**
Child Caretaker					
House help	3(2.27)	1(1.54)	2(2.99)	1(1.52)	2(3.03)
Mother/Father	128(96.97)	64(98.46)	64(95.52)	65(98.48)	63(95.45)
Relative	1(0.76)	0(0.00)	1(1.49)	0(0.00)	1(1.52)
Marital Status of caregiver					
Married	108(81.82)	51(78.46)	57(85.08)	59(89.39)	49(74.24)
Single	18(13.64)	10(15.38)	8(11.94)	6(9.09)	12(18.18)
Divorced/Separated/widowed	6(4.54)	2(2.99)	3(4.62)	1(1.52)	4(6.06)
Medication giver[b]					
House help	3(2.27)	2(3.08)	1(1.49)	0(0.00)	3(4.55)
Mother/Father	127(96.21)	63(96.92)	64(95.52)	66(100.00)	61(92.42)
Relative	2(1.52)	0(0.00)	2(2.99)	0(0.00)	2(3.03)
Level of Education					
Never	7(5.30)	4(5.97)	3(4.62)	1(1.52)	6(9.09)
Pre-school	3 (1.51)	0(0.00)	2(3.08)	0(0.00)	2(3.03)
Primary	34(25.76)	18(26.87)	16(24.62)	10(15.15)	24(36.36)
Secondary	34(25.76)	16(23.88)	18(27.69)	12(18.18)	22(33.33)
Tertiary	55(41.67)	29(43.28)	26(40.00)	43(65.15)	12(18.18)
Hospital Taker [c]					
Mother	130(98.48)	64(98.46)	66(98.51)	2(3.03)	64(96.97)
Father	2(1.52)	1(1.54)	1(1.49)	0(0.00)	66(100.00)
Occupation of caregiver					
Employed	22(16.67)	11(16.92)	11(16.42)	10(15.15)	12(18.18)
None	39(29.55)	20(30.77)	19(28.36)	27(40.91)	12(18.18)
Self-employed	71(53.75)	34(52.31)	37(55.22)	29(43.94)	42(63.64)
Working Hours					
Day time 8am-5am	65(49.24)	30(46.15)	35(52.24)	42(63.64)	23(34.85)
Day time half day	34(25.76)	17(26.15)	17(25.37)	0(0.00)	34(51.52)
None	31(23.48)	18(27.69)	13(19.40)	24(36.36)	7(10.61)
Night time 8pm-6am	1(0.76)	0(0.00)	1(1.49)	0(0.00)	1(1.52)
Night time half night	1(0.76)	0(0.00)	1(1.49)	0(0.00)	1(1.52)

NA (Not available); statistics omitted due to colinearity. [b] The person giving medication to the child if fell sick. [c] The person who takes the child to the hospital when she/he is sick.

4.4 Descriptive analysis of household-level factors

Out of the total study participants(132), 109 (82.57%) were residing in centers urban areas whereas 22(16.67%) were leaving in rural setups while only one [1 (0.76%)] was residing in what was classified as other residential areas. The majority of the participants [85 (64.39%)] had more than one long-lasting insecticide-treated (LLIN) bed nets, 31 (23.46%) had only one LLIN while 16 (12.12%) did not own LLIN at all. The majority of the participants 68 (51.52%) reported that 3 of them slept under one LLIN, 36(27.27%) shared two per LLIN while 13(9.85%) shared one LLIN for 3 persons. Among the participants, 44(33.33%) of them were residing near waterlogged areas, 86 (65.15%) of them were not residing in waterlogged areas while 2(1.52%) were not sure whether their residential area was waterlogged or not. More participants [66 (50.00%)] were not using any kind of mosquito repellants during the study period, 65 (49.24%) were using mosquito repellants while only 1(0.76%) was not sure. Slightly higher proportion 56(42.42%) reported to be residing in a semi-permanent house with electricity, 52(39.39%) were residing in a permanent house with electricity, 13(9.85%) were residing in a semi-permanent house without electricity while 11(8.33%) were residing in permanent houses without electricity (Table 4.4).

Table 4.4.Descriptive analysis of the household-level factors

VARIABLES		GENDER		HIV STATUS	
	Overall n (%)	Male n (%)	Female n (%)	HIV- n (%)	HIV+ n (%)
Residential area					
Rural area	22(16.67)	10(15.38)	12(17.91)	6(9.09)	16(24.24)
Urban area	109(82.57)	55(84.62)	54(80.60)	60(90.91)	49(74.24)
Other	1(0.76)	0(0.00)	1(1.94)	0(0.00)	1(1.52)
Bed nets available per household					
One	31(23.48)	16(24.62)	15(22.39)	21(31.82)	10(15.15)
More than one	85(64.39)	43(66.15)	42(62.59)	34(51.52)	51(77.27)
None	16(12.12)	6(9.23)	10(14.93)	11(16.67)	5(7.58)
Number of Persons per bednet					
Two	36(27.27)	18(27.69)	18(26.87)	5(7.58)	31(46.97)
Three	68(51.52)	35(53.85)	33(49.25)	39(59.09)	29(43.94)
More than three	13(9.85)	6(9.23)	7(10.45)	11(16.67)	2(3.03)
No bednet	15(11.36)	6(9.23)	9(13.43)	11(16.67)	4(6.06)
Availability of bed nets at the Resident					
Yes	38(28.79)	14(21.54)	24(35.82)	23(34.85)	15(22.73)
No	10(7.57)	5(7.69)	5(7.46)	3(4.55)	7(10.61)
Not sure	84(63.64)	46(70.77)	38(56.72)	40(60.61)	44(66.67)
Presence of waterlogs near residential					
Yes	44(33.33)	18(27.69)	26(38.81)	17(25.76)	27(40.91)
No	86(65.15)	46(70.77)	40(59.70)	49(74.24)	37(56.06)
Not sure	2(1.52)	1(1.54)	1(1.49)	0(0.00)	2(3.03)
Use of mosquito repellants					
Yes	65(49.24)	34(52.31)	31(46.27)	32(48.48)	33(50.00)
No	66(50.00)	30(46.15)	36(53.73)	34(51.52)	32(48.48)
Not sure	1(0.76)	1(1.54)	0(0.00)	0(0.00)	1(1.52)
Nature of Household					
Permanent with electricity	52(39.39)	26(40.0)	26(38.81)	31(46.97)	21(31.82)
Permanent without electricity	11(8.33)	5(7.69)	6(8.96)	1(1.52)	10(15.15)
Semi-permanent with electricity	56(42.42)	27(41.54)	29(43.28)	28(42.42)	28(42.42)
Semi-permanent without electricity	13(9.85)	7(10.77)	6(8.96)	6(9.09)	7(10.61)

4.5 Cumulative Incidence Rate (CIR) and Relative Risk(RR)

The overall three months Commutative Incidence rate (CIR) of malaria was 17.42%.The CIR in HIV non-infected children was 13% while in HIV infected had less CIF (3.7%) in comparison with the control group. Mann-Whitney U test was used to test the null hypothesis that malaria status does not vary with HIV status. This is a test of differences

in medians and it reported a p-value of 0.0030, disproving the null hypothesis (threshold is 0.05). The chi-square test of association between HIV status and Malaria outcome reported Pearson's chi-square p-value=0.003. Therefore, the risk of getting malaria significantly differs across HIV status. The study further showed that the risk of getting malaria infection if one is HIV negative is 0.273 while the risk of getting malaria infection if one is HIV positive is 0.075. The relative risk (RR) was 3.64. Consequently, the risk of getting malaria is almost 4 times higher in the HIV negative subject than HIV positive individuals (Table 4.5).

Table 4.5 Table of Association

	Malaria Status at the end of Observation Period		
HIV Status			**Total**
	0pf/ul n (%)	**>0pf/ul n (%)**	
Negative	48 (72.73%)	18(27.27%)	66(100%)
Positive	61(92.42%)	5(7.58%)	66(100%)
Total	109(82.58%)	23(17.42%)	132(100%)

4.6 Univariate analysis of the child level risk factors

The subjects who HIV negative and were able to retain oral antimalarial medication had RR of 0.12 (95%CI, 0.01-1.92) while the HIV positive subjects had RR of 1.28 (95%CI, 0.17-9.62). The subjects who were not able to retain oral antimalarial medication were used as the reference. The RR for those who had a fever and were HIV negative was 1.22 (95%CI, 0.46-3.25) while those who were HIV positive had 1.10 (95%CI, 1.18-6.61)(Table 4.6).

Table 4. 6 Univariate Analysis of the child level risk factors

Variable	HIV- RR (95% CI)	HIV+ RR (95% CI)
Retain Oral antimalarial		
Medicine		
No	Ref	Ref
Sometimes	N/A	0.00 (0)
Yes	0.12(0.01, 1.92)	1.28(0.17, 9.62)
Antimalarial completion		
Less than a week	0.43(0.11, 1.64)	1.59(0.07, 12.02)
One week	0.85(0.04, 18.88)	0.00(0)
Two weeks	N/A	0.00(0)
More than two weeks	0.00(0)	0.97(0.08, 1.28)
Never used antimalarial	Ref	Ref
History of fever		
No	Ref	Ref
Yes	1.22(0.46, 3.25)	1.10(1.18, 6.61)
Level of Hospitals[a]		
Referral hospital	1.35(0.06, 8.80)	0.00(0)
County hospital	2.70(0.05, 9.03)	2.21(0.15, 3.36)
Sub County Hospital	0.48(0.10, 2.31)	1.03(0.08, 3.35)
Health Centre	8.10(0.08, 10.193)	3.87(0.22, 7.64)
Never been admitted	Ref	Ref
Symptoms Presented		
Abdominal complications	0.00(0)	N/A
Chronic conditions	N/A	0.00(0)
Common Cold	1.85(0.23, 4.45)	0.00(0)
Fever	0.77(0.26, 2.25)	2.06(0.34, 3.78)
Headache	3.69(0.47, 8.89)	0.00(0)
Never presented any	Ref	Ref
Duration of Admission		
1 month	0.00(0)	0.00(0)
Between 2-3 weeks	2.56(0.68, 9.61)	0.00(0)
Less than 1 week	1.49(0.54, 4.10)	3.60(0.60, 6.00)
More than 1 month	0.00(0)	0.00(0)
Never been admitted	Ref	Ref
History of malaria infection		
Yes	1(0)	0.07(0.01, 0.85)
Never	1.67(0.65, 4.31)	0.05(0.00, 0.57)
Cannot remember	Ref	Ref

[a] The level of the hospital where the child was taken for treatment.

4.7 Multivariate analysis of the child level risk factors

The subjects who had a fever and were HIV negative had RR 0.10 (95%CI, 0.01-1.24) while those who were HIV positive had RR 3.2 (95%CI,0.39-8.98). The subjects who had a headache and were HIV negative had RR 0.16 (95%CI,0.01-4.93) whereas those who were HIV positive had RR 8.14 (95%CI,0.36-17-32)(Table 4.7).

Table 4. 7: Multivariate analysis of the child level risk factors

Child-level Risk Factors	HIV- RR (95% CI)	HIV+ RR (95% CI)
Source of Antimalarial used		
Bought from the chemists	N/A	3.70(0.28, 9.12)
Bought from this hospital	3.03(0.27, 5.86)	2.20(0.15, 12.11)
Given free from this hospital	2.19(0.59, 3.10)	12.40(0.85, 30.56)
Never been given antimalarial	Ref	Ref
Level of Hospital		
Referral hospital	0.00(0)	0.00(0)
County hospital	0.00(0)	0.00(0)
Sub County Hospital	0.00(0)	0.00(0)
Health Centre	0.00(0)	0.00(0)
Never been admitted	Ref	Ref
History of hospitalization		
No	Ref	Ref
Yes	0.00(0)	10.20(0.53, 28.13)
Symptoms Presented		
Abdominal complications	0.00(0)	N/A
Chronic conditions	N/A	1.00(0)
Common Cold	0.31(0.01, 12.09)	N/A
Fever	0.10(0.01, 1.24)	3.20(0.39, 8.98)
Headache	0.16(0.01, 4.93)	8.14(0.36, 17.32)
None	Ref	Ref
Retain Oral Medicine		
No	Ref	Ref
Sometimes	N/A	0.00(0)
Yes	0.57(0.03, 1.99)	0.33(0.05, 2.37)

4.8 Univariate analysis of caregiver level risk factors

Caregivers who had reached tertiary levels of education and were taking care of HIV negative subjects had RR 0.21 (95%CI,0.03-1.65) of getting malaria while those who were HIV positive had RR 13.0 (95%CI,8.90-18.67) of getting malaria(Table 4.8).

Table 4. 8: Univariate analysis of the caregiver level risk factors

Variable	HIV- Relative Risk (95% CI)	HIV+ Relative Risk (95% CI)
Child Caretaker		
House help	Ref	Ref
Mother/Father	0.26(0.03, 1.97)	0.00(0)
Relative	N/A	1(0)
Marital Status of the caregiver		
Married	0.25(0.03, 1.92)	0.00(0)
Other	Ref	Ref
Single	0.33(0.03, 3.68)	1(0)
Divorced /Separated	3.82(0.51, 8.73)	N/A
Widowed	N/A	0.00(0)
Medication giver [b]		
House help	Ref	Ref
Mother/Father	N/A	0.00(0)
Relative	N/A	1(0)
Level of Education		
Never	Ref	Ref
Pre-school	N/A	1(0)
Primary	0.60(0.07, 4.98)	0.04(0)
Secondary	0.17(0.01, 1.84)	1(0)
Tertiary	0.21(0.03, 1.65)	13.00(8.90,18.67)
Hospital Taker [c]		
Father	Ref	Ref
Mother	1(0)	0.00(0)
Occupation of caregiver		
Employed	1.01(0.67, 3.82)	1(0.06, 5.99)
None	Ref	Ref
Self-employed	0.81(0.30, 2.25)	0.86(0.09, 8.24)
Working Hours		
Day time 8am-5am	1.49(0.53, 4.17)	0.61(0.06, 6.72)
Day time half day	N/A	0.41(0.04,4.54)
None	Ref	Ref

[b] the individual who usually give the medication to the child as advised by the clinician.[c] the individual who usually takes the child to the hospital if the child falls sick

4.9 Multivariate analysis of the caregiver level risk factor

Among the caretakers who reached a primary level of education and were taking care of the HIV negative children had RR 0.60 (95%CI 0.07-4.98) while those who took care of the HIV positive had RR 1.3 (95%CI,1.13-6.56). Those who reached the tertiary level of education and were taking care of HIV negative children had RR 0.20 (95%CI,0.02-1.52) whereas those taking care of HIV positive children had RR 6.30 (95%CI,0.24-15.61).The

subjects who were being taken care of by their parents and were HIV negative had RR 0.19(95%CI,0.02-1.52) while those who were being taken care of by their parents and were HIV positive had RR 3.3(95%CI.0.66-25.18) (Table 4.9).

Table 4. 9. Multivariate analysis of the caregiver level risk factor

Risk Factors	HIV- Relative Risk (95% CI)	HIV+ Relative Risk (95% CI)
Level of Education		
Never	Ref	Ref
Pre-school	N/A	1.00(0)
Primary	0.60(0.07, 1.98)	1.30(0.13, 2.56)
Secondary	0.17(0.01, 1.84)	1.00(0)
Tertiary	0.20(0.02, 1.52)	6.30(0.24, 13.61)
Child Caretaker		
House help	Ref	Ref
Mother/Father	0.19(0.02, 1.52)	3.30(0.66, 5.18)
Relative	N/A	2.30(0.12, 4.17)

4.10 Univariate analysis of the household-level risk factors

The subjects who confirmed the availability of mosquito nets and were HIV negative had RR 0.87(95%CI, 0.32-2.32). The subjects who were not living near waterlogged areas and were HIV negative had RR 1.21(95%CI,0.40-3.69) while those who were HIV positive had RR 0.11(95%CI,0.01-1.19)(Table 4.10).

Table 4. 10 Univariate analyses of the household-level risk factors

Variable	HIV- RR (95% CI)	HIV+ RR (95% CI)
Residence		
Rural area	2.86(0.94, 8.68)	0.00(0)
Urban area	1(0)	0.00(0)
Other	Ref	Ref
Bed nets available per household		
One	1.57(0.32, 7.79)	0.00(0)
More than one	1.62(0.35, 7.38)	0.00(0)
None	Ref	Ref
Number of persons per bednet.		
Two	3.30(0.55, 19.75)	0.00(0)
Three	1.41(0.31, 6.44)	0.00(0)
More than three	1.50(0.25, 8.98)	0.000(0)
No bednet use	Ref	Ref
Availability of bed nets at the Residential		
Yes	0.87(0.32, 2.32)	8.80(0.92, 14.60)
No	0.00(0)	6.29(0.39, 10.49)
Not sure	Ref	Ref
Presence of Waterlogs near residential		
Yes	1(0)	0.15(0.01, 3.59)
No	1.21(0.40, 3.69)	0.11(0.01,1.19)
Not sure	Ref	Ref
Use of Mosquito Repellants		
Yes	1(0)	6.6(0.01,10.03)
No	1.48(0.57, 3.81)	0.00(0)
Not sure	Ref	Ref
Nature of the House		
Permanent with electricity	0.58(0.06, 5.75)	1.00(0)
Permanent without electricity	0.00(0)	0.00(0)
Semi-permanent with electricity	0.80(0.08, 7.93)	0.00(0)
Semi-permanent without electricity	Ref	Ref

4.11 Multivariate analysis of household-level risk factors

The number of people per one-bed net varied, two people under a one-bed net and with an HIV negative child had RR 3.52 (95%CI, 0.59-21.18) while HIV positive children have RR 6.63 (95%CI, 0.99-8.13). Three people under the one-bed net with an HIV

negative child have an RR 1.41(95%CI, 0.31-6.46) whereas HIV positive child has an RR 10.94 (95%CI, 0.55-54.11)(Table 4.11).

Table 4. 11: Multivariate analysis of household-level risk factors

Risk Factors	HIV- Relative Risk (95% CI)	HIV+ Relative Risk(95% CI)
Number of persons per bednet.		
Two	3.52(0.59, 5.18)	6.63(0.99, 8.13)
Three	1.41(0.31, 6.46)	10.94(0.55, 24.11)
More than three	1.57(0.26, 9.36)	6.90(0.23, 13.57)
N/A	Ref	Ref
Use of Mosquito Repellants		
Yes	0.64(0.25, 1.66)	0.21(0.02, 1.90)
No	N/A	0.65(0)
Not sure	Ref	Ref

4.12 Relative Risk of the selected risk factors

Fever had RR=0.69 (95%CI; 0.22-2.16), headache RR=1.53 (95%CI; 0.12-19.08) and retention of oral medicine had RR=0.12 (95%CI; 0.01-1.92) of suffering from malaria infection. For the number of persons sleeping under a bednet, two had RR=5.46 (95%CI; 0.46-64.58), three RR=2.14 (95%CI; 0.27-24.87) and >three RR=2.58 (95%CI: 0.27-24.87) of suffering from malaria infection. (Table 4.12).

Table 4. 12 Calculations of Relative Risk of the selected risk factors

Risk Factors	HIV- RR (95% CI)	HIV+ RR (95% CI)
Child Caretaker		
House help	Ref	Ref
Mother/Father	0.00(0)	2.31(0.33, 4.95)
Relative	N/A	4.60(0)
Symptoms Presented		
Abdominal complications	0.00(0)	N/A
Chronic conditions	N/A	0.00(0
Common Cold	0.00(0)	0.00(0)
Headache	1.53(0.12, 2.08)	0.00(0)
Fever	0.69(0.22, 2.16)	1.28(0.17, 2.62)
None	Ref	Ref
Retain oral medicine		
No	Ref	Ref
Sometimes	N/A	0.00(0)
Yes	0.12(0.01, 1.92)	0.19(0.02, 1.89)
Number of Persons Sleeping under one bednet		
Two	5.46(0.46, 10.58)	5.35(0.36, 8.99)
Three	2.14(0.27, 7.25)	2.37(0.66, 5.36)
> three	2.58(0.27, 4.87)	5.13(0.53, 9.51)
None	Ref	Ref

NA (Not Available) statistics omitted due to collinearity

4.13 Cox proportional Hazard Ratios.

Children who were taken care of by their parents had HR=2.44(95%CI; 0.27-22.19) while those who presented with fever had HR=1.37(95%CI; 0.38-5.34) times of getting malaria infection, those who experienced headache were HR 4.27 (95%CI; 0.30-5.04) times at risk of getting malaria (Table 4.13.).

Table 4. 13: Cox proportional Hazard Ratios

Overall Risk Factors	HIV- Hazard Ratios (95% CI)	HIV+ Hazard Ratios (95% IC)
The ability of the child to retain oral Medicine		
No	Ref	Ref
Sometimes	1.00(0)	N/A
Yes	1.00(0)	0.00(0)
Symptoms Presented		
Abdominal complications	N/A	N/A
Chronic conditions	N/A	N/A
Common Cold	1.00(0)	N/A
Fever	1.37(0.38, 3.34)	0.00(0)
Headache	4.27(0.30, 5.04)	N/A
None	Ref	Ref
Child Caretaker		
House help	Ref	Ref
Mother/Father	2.44(0.27, 4.19)	1.00(0)
Relative	N/A	N/A
Number of people Sleeping Under one bednet		
Two	0.32(0.02, 1.39)	1.00(0)
Three	0.24(0.02, 1.53)	N/A
More than three	0.20(0.01, 0.73)	1.00(0)
None	Ref	Ref

CHAPTER FIVE

DISCUSSION, CONCLUSIONS, AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Incidence *P. falciparum* infection

Study done by (Harouna *et al.*, 2015) in Abidjan, Côte d'Ivoire realized a high incidence rate of malaria (18.3/100 CY) that was strongly reduced in children on cotrimoxazole alone or combined with ART when adjusting for severe immunodeficiency, our study realized an overall cumulative incidence of 17.42%, and is in agreemenet with this study ,the CIR was greater in HIV negative children (13%) than in HIV positive children (3.7%).This finding is suggesting that CTX is prodiving protection to malaria infection and this concoincides with the findings of a cohort study done in Kampala Uganda to estiamate the protective efficacy of trimethoprim-sulfamethoxazole (TMP/SMX) prophylaxis and ITNs on the incidence of malaria ,they concluded that combined use of TMP/SMX prophylaxis and insecticide-treated bed nets was associated with a dramatic reduction in malaria incidence among HIV-infected children (Moses R Kamya *et al., 2007)*. Prospective cohort study done by (Harouna et al., 2015) to determine effect of cotrimoxazole prophylaxis on the incidence of malaria in HIV-infected children in Abidjan, Côte d'Ivoire also concluded that CTX should be provided as widely and as durably as possible in all children, as recommended by WHO (Organization, 2016). Likewise, the provision of insecticide-treated bed-nets could reduce the incidence of malaria even further in children under five, who are more sussceptical to malaria infection. These interventions will be helpful in reaching the sixth millennium development goals to improve child health(United, 2013).

5.1.2 Child level risk factors associated with *P.falciparum* infection

Risk factor analysis performed for this study identified a number of variables that, alone or in unison, would affect a child's risk of malaria.It is essential to achieve effective antimalarial drug concentrations for sufficient time to ensure high cure rates. According to WHO, Artemisinin-combination therapies (ACTs) (first-line treatment of malaria) exhibit excellent efficacy and the potential to minimize the development of drug resistance. Studies were done to determine the increased risk of early vomiting among infants and young children treated with Dihydroartemisinin-Piperaquine compared with AL for uncomplicated malaria, the ACTs appeared to be well-tolerated and with rare toxicities (Nosten & White, 2007),(Ratcliff *et al.,* 2007),(Yeka *et al.,* 2008),(Leonardi, Gilvary, White, & Nosten, 2001). Early vomiting reduces the effectiveness of ACT antimalarial therapies because of reduced drug absorption and children below the age of 18 months were found to be at risk of vomiting (Creek *et al.,* 2010). In our study, although 106(80.3%) of the study subjects were able to retain oral antimalarial, about 23 (17.42%) were not able to retain oral ACT. Those who were able to retain oral medication were 0.12 times RR=0.12 (95%CI; 0.08-1.92) less likely to get malaria infection as compared to those who were able to retain oral medication.

A study was done in Kenyan (Mutanda *et al.,* 2014), concluded that fever is a sensitive indicator of clinical malaria in children <5 years. Adding a headache to fever as a screening symptom for *P.falciparum* infection increases the sensitivity of detection at the cost of decreased specificity. Guidelines for the treatment of malaria in Kenya say the first symptoms of malaria are nonspecific and similar to those of a minor systemic viral illness (Zurovac *et al.,* 2004).In this study 48(36.36%) experienced fever, 5 (3.79%) experienced headache, The study showed that those who had headache were 1.53 times [RR=1.53:95%CI; 0.12-19.08] more likely to have malaria compared to those who experienced fever [RR=0.69:95%CI; 0.12-1.92].

5.1.3 Child caretakers risk factors associated with *P.falciparum* infection

The study by (Birhanu, Yihdego, & Yewhalaw, 2017) suggested that knowledge alone is not sufficient enough to drive LLIN to use and care-seeking towards malaria prevention strategy. In their study, caretakers recognized malaria mostly by chills fever and headache. Our study, even though a majority had reached a tertiary level of education, the subjects who were being taken care of by their parents were 2.4 times [HR=2.44:95%CI; 0.27-22.19] at risk of developing malaria than their counterparts. Another study by (Njama *et al.,* 2003a) in determining malaria-related knowledge, attitude and practices (KAP) reported mosquitoes and/or malaria as the cause of fever. Higher levels of education for the caregiver were associated with positive malaria-related KAP. Their independent predictors of malaria incidence were also similar to the risk factors in our study.

5.1.4 House hold level risk factors associated with *P. falciparum* infection

Long-lasting insecticidal nets (LLINs) are effective interventions for reducing the burden of malaria (Clark *et al.*, 2016). According to PMI operation Plan FY 2018, LLINs are defined as one net per two people. In this study, although the results are not statistically significant, we realized that two people sleeping under one LLIN were 5.46 times [(RR=5.46; 95%CI; 0.46-64.58)], at risk of getting malaria than if they were three [(RR=2.14:95%CI; 0.27-17.25)] per bed net. The recommended ration of two persons per bed net could be effective for two adults; this could be impracticable for children since they could roll towards the bed net edge exposing the child to a mosquito bite. Previous studies show that large-scale, free net distribution campaigns reduce inequities in household net ownership (Kulkarni *et al.*, 2010), ,(Larson *et al.*, 2014),(Noor, Amin, Akhwale, & Snow, 2007),(Bernard *et al.*, 2009). Socioeconomic factors, such as household wealth and education, have also been identified as consistent and important predictors of mosquito net acquisition (Thwing *et al*., 2008),(Clark *et al.*, 2016),(Noor, Omumbo, Amin, Zurovac, & Snow, 2006).

5.2. Conclusion

The study found a three-month cumulative incidence rate of malaria was 17.42%, with a higher proportion (27.27%) of the subject who suffered *P.falciparum* being HIV negative compared to HIV positive (7.58%). There was a relatively weak inverse relationship (Cramer's V of -0.2596) between HIV status and malaria outcome consequently higher number of subjects who had malaria were HIV negative ,therefore CTX prophylaxis reduces the incidence of clinical malaria in HIV infected individuals protects against malaria and CTX may have a role for malaria prophylaxis in specific HIV negative target groups henece the CTX prophylaxis was protective against the incidence of malaria in HIV-infected children. Thus, these drugs should be provided as widely and durably as possible in all HIV-infected children <5 years of age.

Child level risk factors such as inability to retain oral antimalarial medication, presence of fever and headache were indicative of malaria infection.

Children who were taken care of by their parents were also more prone to *P.falciparum* infection. Lastly, the use of long-lasting insecticide-treated nets as house level factors showed that the ratio of persons to one net directly affected infection with *P.falciparum*. Children should be protected from direct contact with the bednet walls when they are sleeping to prevent mosquito bites.

5.3. Recommendations

- Cotrimoxazole prophylaxis is protective against malaria when associated with ART in HIV-infected children.Guidlines should be revised to contain the use of CTX for management of malaria and should be included in the prophylaxis guidelines.
- We recommend policies should be created to emphasize the Direct observe therapy (DOT) at the facility level with continuous health education to the caregivers to enhance drug absorption and bioavailability.
- There is still need to consistently emphasize to the health care workers to give health talks to the patient or the child's caregivers or via the use of quality strategic social behavior change communications (SBCC) which are essential in malaria

prevention and treatment to ensure the knowledge for taking care of the child is universal.

- There is also a need to promote and encourage or follow up on the availability and proper use of the LLINs. The package of ANC in addition to the free LLINs should include baby cots to ensure the children are protected from mosquito bites

5.4. Recommendation for further Research work:

1. More research including molecular typing and pharmacokinetics is needed to establish the protection that the children who are on HARRT have against malaria infection in the population of Kisumu County.
2. The effects of ART and Cotrimoxazole on susceptibility to malaria parasitemia and fever should be studied in a range of endemic settings.
3. We also need more information about pharmacokinetic interactions between antimalarial and antiretroviral and about the implications of widespread Cotrimoxazole use in areas of high malaria prevalence.

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APPENDICES

Appendix I: Informed consent form (English version)

Study title: Correlates and Incidence of *P.falciparum* among HIV infected and HIV-free Children below 5 years in Kisumu County, Kenya**.**

Version Number: 00 Date.03 Apr 2017.

Age: Children less than 5 years (confirm with the clinic book)

Participant number…….....

(Insert subject ID here)

THIS DOCUMENT SHOULD BE GIVEN TO THE PARTICIPANT IN THE FORM THAT IT IS IN, WITHOUT OMITTING ANY SECTION. THE CONTENTS OF THIS DOCUMENT SHOULD BE EXPLAINED TO THE PARTICIPANT ORALLY!

RESEACHER (NAME); JACK OUKO OGONY DATE……

Introduction

You are being asked for consent to take part in a clinical research study titled 'Correlates and Incidence of *P.falciparum* among HIV Infected and HIV non infected Children below 5 years in Kisumu County'.

(A copy of this sheet will be given to you as a parent or guardian

1. **What does giving consent for this study mean?**

Giving consent means that you have volunteered to participate in the research study in your area of residence. You are free to decide whether you want to participate in the study or not. Therefore, take the time to read and understand these instructions. You can also discuss with family, friends and even your healthcare workers who serve you. You can ask us any questions if there is anything you do not understand or if you need further explanation.

2. **Why is this study being carried outdone?**

The research study that we are asking your consent to participate in is being conducted so as to get more information on correlates and incidence of malaria infection among HIV infected and HIV non-infected in children below 5 years. Malaria is a significant public health problem in Kenya. The most vulnerable to the disease include children below 5 years, people living with HIV and pregnant women.

3. **How many people will participate?**

Children below 5 years male or female will be enrolled in this study.132 participants will be enrolled in the study, which is 66 HIV infected and 66 non-infected cases.

4. **Who can participate in this research study**?

The following requirements must be fulfilled for someone to participate in this research study :(i) Be able to comply with the requirements of this research study (ii) Be a male or female below 5 years (ii) parent/guardian be willing to give written informed consent. You will not be allowed to participate if; (i) A child in care, by protection services such as governmental as required by the law (ii) You are participating in any drug study (iii) as declared by the study clinician.

5. **Who will I contact to answer any questions regarding this study?**

If you want to contact someone or if you have any questions regarding your rights in this research study, you can contact the Principal Investigators Jack Ogony P.O.Box.7394-40100 Kisumu, Tel +254723107953, Prof. Simon Karanja Tel +254726424669, or Mr. Henry Kissinger Tel +254723440110 both of JKUAT.

6. **What does this study involve?**

You will be asked several questions about yourself and your child such as medical history, residence, and age before the clinician send you to the laboratory for lab investigations, after reviewing your malaria test result you will be asked if you can participate in this study today. This study will be explained to you and also request to give consent to continue with the research study. Results from the lab will be given as soon as they are available and you will not take extra time in the facility.

7. What are the risks expected if you participate in this research study?

Your child may feel a little pain when blood is being drawn from your finger during the malaria testing.

8. What payments will be involved in this research study?

You will not be given any direct payments for allowing your child to participate in this research study, however, the transport allowance of 100 will be given to the subject parents during the scheduled visits.

9. Are there any benefits from participation in this study?

If the results will show that you have an infection, you will be treated with the relevant medication. The findings of this study will be of significance to the persons in the study area and to the international community as far as malaria and HIV coinfection is a concern.

10. What will be done with the information that I will provide?

The information will be collected for the purpose of ;(1) Publishing the results of this research study, (2) Providing it as part of research to other companies, universities for the purposes of better understanding the relationship between malaria and HIV coinfection, (3)Using it to plan for further research or for management of malaria and HIV. (These will not include any information that directly identifies you)

If you accept your child to participate in this research study, please write your name and sign together with the date here below, or put your fingerprint.

I agree that this study has been explained to me. I agree to participate. And I know who to communicate with in case I have questions in the future.

Participant number……

Finger print if the participant is unable to write

I accept to participate in this research study;

Participant's parent signature.....Date.....

Participant's parent name.....

I confirm that I have conducted this consenting process according to laid down procedures.

Signature of person providing consent;

.....Date.....

Name of person providing consent;

.....Date……...

If the participant is unable to read or write, his/her witness must sign this for him or her

Signature of participant's Witness;

…….....Date.....

Name of participant's witness;

Appendix 1A: Informed Consent Form (Kiswahili version)

Kichwa cha Utafiti: Mahusiano na Matukio ya *P.falciparum* kati ya watoto chini ya miaka 5 walioambukizwa HIV na wale bila HIV katika Jimbo la Kisumu, Kenya.

Nambari ya Toleo: 00 **Tarehe.03 Aprili 2017.**

Umri: Watoto chini ya miaka 5 (kuthibitisha na kitabu cha kliniki)

Nambari ya Mshiriki ....
(Andika Kitambulisho cha mhusika hapa chini)

HATI HII NI LAZIMA LIPEANWE KWA MSHIRIKI KATIKA HALI ILIYOKO, BILA KUACHA SEHEMU YOYOTE. YALIYOKO KATIKA HATI NI LAZIMA YAFAFANULIWE KWA MSHIRIKI KWA MDOMO!

MCHUNGUZI (JINA); JACK OUKO OGONY TAREHE .....

Utangulizi

Unaombwa kuidhinisha kushiriki katika utafiti wa kliniki unaoitwa Mahusiano na Matukio ya *P.falciparum* kati ya watoto chini ya miaka 5 walioambukizwa HIV na wale bila HIV katika Jimbo la Kisumu, Kenya.

(Nakala ya karatasi hii utapewa kama mzazi au mlezi)

1. Kutoa idhini kwa utafiti huu inamaanisha nini?

Kutoa idhini ina maana kwamba umejitolea kushiriki katika utafiti katika eneo lako la kuishi. Wewe uko huru kuamua kama unataka kushiriki katika utafiti au la. Kwa hiyo, chukua muda wako wa kusoma na kuelewa maelekezo haya. Unaweza pia kujadiliana na familia, marafiki na hata wafanyakazi wako wa afya ambao wanakuhudumia. Unaweza kutuuliza swali lolote ikiwa kuna kitu ambacho hauelewi au unahitaji ufafanuzi zaidi.

2. Kwa nini utafiti huu unafanywa?

Uchunguzi wa utafiti ambao tunaomba idhini yako kushiriki unafanywa ili kupata habari zaidi juu ya mahusiano na matukio ya maambukizo ya malaria kati ya watoto chini ya miaka 5 walioambukizwa HIV na wasioambukizwa HIV. Malaria ni shida muhimu ya afya ya umma nchini Kenya. Wale walioathiriwa na ugonjwa huu ni pamoja na watoto chini ya miaka 5, watu wanaoishi na HIV na wanawake wajawazito.

3. Ni watu wangapi watashiriki?

Watoto chini ya miaka 5 wa kiume au wa kike wataandikishwa katika utafiti huu. Washiriki 132 wataandikishwa katika utafiti huu, hii ni kumaanisha 66 walioambukizwa HIV na 66 wasioambukizwa.

4. Ni nani anayeweza kushiriki katika utafiti huu?

Mahitaji yafuatayo yanapaswa kutimizwa kwa mtu kushiriki katika utafiti huu:

(i) Kuwa na uwezo wa kuzingatia mahitaji ya utafiti huu

(ii) Kuwa mwanamume au mwanamke chini ya miaka 5

(iii) Mzazi /mlezi awe tayari kutoa idhini ya kuarifiwa lililoandikwa.

Huwezi kuruhusiwa kushiriki kama;

(i) Mtoto aliye katika huduma , kwa huduma za ulinzi kama vile za kiserikali kama inavyotakiwa na sheria

(ii) Unahusika katika utafiti wowote wa madawa

(iii) kama ilivyoelezwa na daktari wa utafiti.

5. Ni nani nitawasiliana naye kujibu maswali yoyote kuhusu utafiti huu?

Ikiwa unataka kuwasiliana na mtu au una maswali yoyote kuhusu haki zako katika utafiti huu, unaweza kuwasiliana na Mtafiti Mkuu Jack Ogony, Sanduku La Posta 7394-40100 Kisumu, Simu +254723107953, Prof. Simon Karanja, Simu +254726424669, au Henry Kissinger, Simu +254723440110 wa JKUAT.

6. Utafiti huu unahusisha nini?

Utaulizwa maswali kadhaa kuhusu wewe mwenyewe na mtoto wako kama vile historia ya matibabu, makazi na umri kabla ya daktari akutume kwenye maabara kwa uchunguzi wa maabara, baada ya kuchunguza matokeo yako ya malaria utaulizwa ikiwa unaweza kushiriki katika utafiti huu leo.

Utafiti huu utafafanuliwa kwako na pia kuombwa kutoa idhini ya kuendelea na utafiti. Matokeo kutoka kwa maabara yatapeanwa haraka mara tu yatapatikana na huwezi kuchukua muda zaidi katika kituo hicho.

7. Je! Ni hatari zipi zinazotarajiwa ikiwa unashiriki katika utafiti huu?

Mtoto wako anaweza kuhisi maumivu kidogo wakati damu linachukuliwa kutoka kwenye kidole wakati wa kupima malaria.

8. Ni malipo gani yatahusishwa katika utafiti huu?

Hautapewa malipo yoyote ya moja kwa moja kwa kuruhusu mtoto wako kushiriki katika utafiti huu, hata hivyo malipo ya usafiri ya shilingi 100 litapewa wazazi wa wahusika wakati wa ziara zilizopangwa.

9. Kuna faida yoyote kutokana na kushiriki katika utafiti huu?

Ikiwa matokeo yataonyesha kuwa una maambukizi yoyote, utatibiwa na dawa husika. Matokeo ya utafiti huu yatakuwa muhimu kwa watu katika eneo la utafiti na kwa jumuiya ya kimataifa kama vile maambukizi ya malaria na HIV yanahusishwa.

10 . Ni nini kitakachofanyika kwa habari ambayo nitatoa?

Habari zitakusanywa kwa lengo la:

(1) Kuchapisha matokeo ya utafiti huu,

(2) Kulitoa kama sehemu ya utafiti kwa makampuni mengine, vyuo vikuu kwa madhumuni ya kuelewa vizuri uhusiano kati ya malaria na HIV,

(3) Kulitumia kuandaa utafiti zaidi au usimamizi wa malaria na HIV. (Hizi hazitajumuisha habari zozote zinazokutaja moja kwa moja).

Ikiwa unakubali mtoto wako kushiriki katika utafiti huu, tafadhali andika jina lako na saini pamoja na tarehe hapa chini, au tia alama ya kidole chako.

Nakubali kwamba utafiti huu umefafanuliwa kwangu. Nakubali kushiriki. Na ninajua ni nani wakuwasiliana naye ikiwa nina maswali wakati ujao.

Nambari ya mshiriki .....

Alama ya kidole ikiwa mshiriki hawezi kuandika

Nakubali kushiriki katika utafiti huu;

Saini ya mzazi wa mshiriki ..... .Tarehe.....

Jina la mzazi wa mshiriki ....

Ninathibitisha kwamba nimefanya mchakato huu wa idhini kulingana na taratibu zilizowekwa.

Saini ya mtu anayetoaidhini;.....Tarehe.....

Jina la mtu anayetoa idhini; .....

Ikiwa mshiriki hawezi kusoma au kuandika, shahidi wake lazima asaini hapa kwa Saini ya Shahidi

wamshiriki;.....Tarehe.....

Jina la shahidi wa mshiriki;.....

Appendix 1B: Informed Consent Form (Dholuo version)

Nonro: Tudruok gi bet mar *P.falciparum* kuom nyithindo ma hikgi tin ne higa bi 5 man kod kute ayaki gi maongego ei aluora mar Kisumu kaonti.

Namba mar andiko: 00 Tarik.03 Apr 2017.

Higa: nyithindo ma hikgi tin ne higa abich (kaka ondiki e bug klinik)

Namba nonro mar jachiwre……….

(Ndik namba mar jachwre ka)

OBOKENI ONEGO OSOM NE JACHIWRE KAKA ONDIKENI MA ONGE WEYO BATHE MORO AMORA.GIGO MONDIKI E OBOKENI ONEGO OLER NE JACHIWRE KOD DHOK!

NYING JATELO MAR NONRO; JACK OUKO OGONY TARIK……...

Chakruok

Ikwayi ka inyalo yie bedo achiel kuom jochiwre enonro mar ngeyo ka nitie tudruok gi bet mar *P.falciparum* (malaria) kuom nyithindo ma hikgi tin ne higa abich (5) man kod kute ayaki gi maongego ei aluora mar Kisumu kaonti

(Obokeni ibiro miyi kaka janyuol kata kaka jarit mar nyathi

Chiwruok e nonro ni nyiso nang'o?

Yie bedo jachiwre e nonro nyiso ni in achiel kuom jogo mibiro timgo nonro e gweng maidakie. In thuolo mar bedo e nonro kata weyo. Kuom mano, Kaw thuoloni makende mondo isom kendo iwinj andiko e obokeni. Bende inyalo lalori gi anyuola, osiepe kata jogo machiwoni thieth. Oyieni penjowa gima ok owinjore e obokeni maler mondo oleri matut.

1. **Nonroni itimo nang'o?**

Nonro mawakwayi ni ichiwrieni itimo mondo oyud tudruok mantie ekind midhusi mar malaria kuom nyithindo ma hikgi tin ne abich man gi kute mag ayaki to kod mago maonge kod kute mag ayaki. Ma en nikuop nyithindo matindo gi mine mapek eman gi ohinga matin mar dhaw gi tuochegi e dendgi.

2. **Ji adi mabiro bedo e nonroni?**

Nyithindo ma yawuoyi gi manyiri ma hikgi tin ne higa abich ma jokenya ibiro mi thuolo mondo ochiwre e nonroni. Jochiwre 132 ibiro mi thuolo, 66 man gi kute mag ayaki to kog 66 maonge kod kute mag ayaki.

3. **Ng'awa manyalo chiwre enonroni?**

Magi emadwarore mondo omi omiyi thuolo mar chiruwk e nonro ni: (i) Nyaka ibedni inyalo rito gigo midwaro enonro ndalo duto (ii) wuoyi kata nyako ma hike tin ne higni abich.(iii) Janyuol/Jarit moyie keto koke kata sei e oboke mar chiwruok. Ok bi yieni chiwri kaponi: (a) Nyathi mayudo thieth kendo irito gi chik kata migepe mag sirkal. (b) Ka isechiure e nonro mar yath mar malaria sani. (c) Kaka ong'adi gi jachiw thieth e nonroni.

4. **Ng'ano ma anyalo wuoyogo ka an gi penjo ewi nonroni?**

Kidwaro tudri gi ngato kata in gi penjo ewi ratiro mari e nonroni, inyalo tudri gi jatend nonro ma en Jack Ogony P.O.Box.7394-40100 Kisumu, Namba simbe +254723107953, Ngire. Simon Karanja namba simbe +254726424669, kata Henry Kissinger namba simbe +254723440110 mawuok JKUAT.

5. **Nonroni dwaro ang'o?**

Ibiro penji penjo mathoth kuomi gi nyathini kata nyithindi machalo kaka; historia mar ngimani, kar dakni kod hiki kapok daktari oori epimi eod pim. Bang' neno dwoko mari, ibiro kwayi mondo ichiwri enonroni kawuono. Ibiro lerni ma kendo nokwayi mondo iyie idhi nyime e nonroni. Dwoko mar pim ibiro miyi mapiyo kaka nyalore kendo on nikaw kindeni mang'eny e osiptal ka.

6. **Hinyruok mage manyalo wuok kuom chiwruok e nonroni?**

Nyathini nyalo winjo lit mana matin Sama igolone remo e lith lwete sach pimo malaria kata ka igolone remo mar pimo tuo moro amora

7. **Chudo mage mantie e nonroni?**

Ok bi chuli kuom yie ni nyathini ochiwre enonroni, kata kamano ibiro chiw omenda maromo siling 100 mar yore wuoth e limbe mochiki e ndalo mag nonro.

8. **Be nitie ber mora amora kuom chiwruok enonroni?**

Ka duoko mag pim biro nyiso ni in gi tuo mora amora, to ibiro thiedhi gi yedhe makare. Duoko mar nonroni bende biro bedo maber ne jochiwre makar dak motime nonro kendo ne ji duto kaluore gi tudruok manie tuo mar malaria kod ayaki kanyakla.

9. **Ango ma ibiro tim kod weche ma abiro chiwo?**

Weche mibiro choki ewi nonroni notigo kuom: (1) Ndiko ayanga duoko mar nonro ni. (2) Chiwo kaka nonro oyudo ne migepe mamoko machalo kaka mbalariany mondo okel ler mantie e kind tuo mar malaria kod ayaki kuom nyithindo m hikgi tin ne abich. ((3) Tiyo kode e pango nonro mamoko kata kuom rito jogo man gi tuo mar malaria kod kute ayaki. (Maok noriw weche mayangi kaka jachiwre)

Ka iyie chiwo nyathini mondo odonj e nonroni, wakwayi mondo indik nyingi kendo iket sei gi tarik pinyka kata iket koki.

Ayie ni nonro ni oselerna. Kendo ayie mar chiwra. Ang'eyo ng'ama atudra godo ka an kod penjo.

Namba jachiwre…….

Kogno mar jachiwre kaok **onyal ndiko**

Ayie chiwra e nonroni;

Sei mar janyuol/jarit jachiwre…… Tarik……

Nying janyuol/jarit jachiwre……

Asingora ni aselero nonro ni ne jachwre kaka dwarore

Sei mar jaler nonro……..…Tarik……..……

Nying jaler nonro……..

Ka jachiwre ok nyala somo kata ndiko, janeno ne nyaka ket sei.

Sei mar janeno……. Tarik……..……

Nying janeno……

Appendix II: Questionnaire

This study seeks to determine the correlates and incidence of *P.falciparum* among HIV infected and HIV-free children below 5 years in Kisumu County, Kenya

Please answer the questions as honestly as possible. Your responses will be treated with a high level of confidentiality.

INSTRUCTIONS

1. Please answer the questions in the order they appear in the questionnaire.
2. Check the box that shows your best answer to each question.
3. There are no right or wrong answers. Please be as truthful as you can.
4. Your answers will be completely confidential. No one but the research team can know how you answered questions.
6. Please do not skip any question instead seek for clarification of what you do not understand.
7. You can stop filling out the questionnaire at any time you wish.

PARTICIPANT IDENTIFICATION……..

QUESTIONNARE ADMISION DATE……

SECTION A: CHILD INFORMATION

1. What is the age of your child?

   ☐ Below 1 yrs. ☐ Between 2-3 yrs ☐ Between 3-5 yrs.

   ☐ Above 5 yes

2. Does your child normally retain oral medicine on administration?

   ☐ Yes ☐ No ☐ Sometimes

3. What is the gender of your child?

   ☐ Male ☐ Female ☐ Other

4. Is your child on any known malaria prophylaxis

☐ Yes ☐ No ☐ Not sure

5. Has your child ever been treated with antimalarial

☐ Yes ☐ No ☐ Not sure

6. Where did you get the antimalarial that you gave your child?

☐ Given free from this hospital ☐ bought from the chemists

☐ bought from this hospital ☐ did not manage ☐ Not applicable

7. Is the child going to school?

☐ Yes ☐ No ☐ N/A

8. How long ago did the child complete antimalarial medication

☐ less than a week ☐ one week ☐ two weeks ☐ More than two weeks

9. Did the drug(s) help the child?

☐ Yes ☐ No ☐ Not sure ☐ Not applicable

10. Has your child ever been admitted?

☐ Yes ☐ No ☐ Not sure ☐ Not applicable

11. Which level of the hospital was your child admitted?

☐ Health Centre ☐ Sub County hospital ☐ County hospital

☐ referral hospital

12. Can you think of some of the symptoms that you/your child presented with to warrant admission?

☐ Fever ☐ Headache ☐ Abdominal Complications

☐ Inflammation skin infections ☐ Common cold

☐ Chronic conditions: Specify: _____ ☐ Others_____

13. For how long did your child remain admitted in the hospital?

☐ Less than 1 week ☐ between 2-3 weeks ☐ 1 month ☐ More than 1 month

SECTION B: SUBJECT'S PARENT/CARETAKER'S INFORMATION.

1. What gender is the parent/guardian of the child?

   ☐ Male ☐ Female ☐ Other

2. Who normally takes care of the child on day today? **(tick the appropriate)**

   ☐ Mother/Father ☐ House help ☐ Relative

3. Has your child developed a fever in the last two weeks?

   ☐ Yes ☐ No ☐ NA

4. What is your marital status:

   ☐ Single ☐ Married ☐ other .specify----------

5. Who normally gives the medications if the child is sick? **(tick the appropriate)**

   ☐ Mother/Father ☐ House help ☐ Relative

6. What is the highest level of education you have attained?

   ☐ Never ☐ Pre- school ☐ Primary ☐ Secondary

   ☐ Tertiary +

7. Who normally takes the child to the hospital if she/he falls sick?**(tick the appropriate)**

   ☐ Mother ☐ Father ☐ House help

8. How many are you in your household**(Insert the numbers in the box)**

   ☐ Male ☐ Female

9. Are you employed or self-employed?

   ☐ Employed ☐ Self-employed ☐ None

10. Has your child ever been admitted?

    ☐ Yes ☐ No ☐ Not sure ☐ Not applicable

11. What are your working hours?

    ☐ Day time 8am -5am. ☐ Day time half day ☐ Night time 8pm -6am

    ☐ Night time half night.

SECTION B: HOUSEHOLD INFORMATION

1. Where do you stay?

   ☐ Rural area ☐ Urban area ☐ Other_____

2. How many bed nets do you have at home?

   ☐ None ☐ One ☐ More than one

3. Do you sleep in one bed with this child?

   ☐ Yes ☐ No ☐ NA ☐ other specify…….

4. How many people sleep under a one-bed net in your household

   ☐ Two ☐ Three ☐ More than three ☐ not applicable

5. Do you sleep under the same bed net with this child (ren)?

   ☐ No ☐ Yes ☐ NA

6. How many residential houses do you have in your compound or the compound where you stay?

   ☐ Just one ☐ between 2-3 ☐ above 4. ☐ Not sure

7. Are all residential houses in your compound or the compound where you stay have bed nets?

   ☐ Yes ☐ No ☐ Not sure

8. Do you have any water logs around your house?

   ☐ Yes ☐ No ☐ Not sure

9. Do you use mosquito repellants or spray your house/compound with the repellants?

   ☐ Yes ☐ No ☐ Not sure

10. Has your child ever been diagnosed with malaria before?

    ☐ Yes ☐ Never ☐ Can't remember

11. What is the nature of your house?

    ☐ Permanent house with electricity ☐ Permanent without electricity

☐ Semi-permanent with electricity ☐ Semi-permanent without electricity

☐ None specify……

QUESTIONNAIRE ADMINISTERED BY;

Name……..

Signature……. Date……

'THANK YOU FOR YOUR CO-OPERATION AND ACCEPTING TO PARTICIPATE IN THIS STUDY'

Appendix III: mRDT Job Aid

How To Do the Rapid Test for Malaria

Collect:

a. **NEW unopened** test packet
b. **NEW unopened** spirit swab
c. **NEW unopened** lancet
d. **NEW** pair of disposable gloves
e. Buffer
f. Timer


Disposable gloves

Spirit swab

Lancet

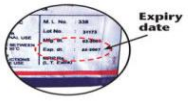
Test packet


Timer


Buffer

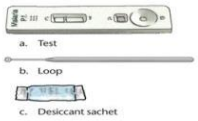
READ THESE INSTRUCTIONS CAREFULLY BEFORE YOU BEGIN.

1. Check the expiry date on the test packet.



2. Put on the gloves. Use new gloves for each patient

3. Open the packet and remove:



4. Write the patient's name on the test.

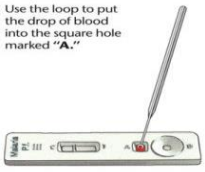
5. Open the alcohol swab. Grasp the 4th finger on the patient's left hand. Clean the finger with the spirit swab. Allow the finger to dry before pricking.

6. Open the lancet. Prick patient's finger to get a drop of blood.

7. Discard the lancet in the Sharps Box immediately after pricking finger. **Do not set the lancet down before discarding it.**

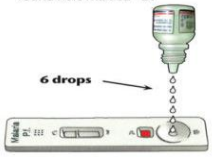
8. Use the loop to collect the drop of blood.

9. Use the loop to put the drop of blood into the square hole marked **"A."**



10. Discard the loop in the Sharps Box.

11. Put six (6) drops of buffer into the round hole marked **"B."**



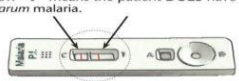
12. Wait **15 minutes** after adding buffer.

13. Read test results. (**NOTE: Do Not** read the test sooner than **15 minutes** after adding the buffer. You may get **FALSE** results.)

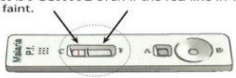
14. How to read the test results:

POSITIVE

One red line in window **"C" AND** one red line in window **"T"** means the patient **DOES** have *falciparum* malaria.

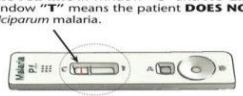


The test is **POSITIVE** even if the red line in window **"T"** is faint.



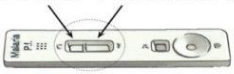
NEGATIVE

One red line in window **"C"** and **NO LINE** in window **"T"** means the patient **DOES NOT** have *falciparum* malaria.



INVALID RESULT

NO LINE in window **"C"** means the test is damaged.



A line in window **"T"** and **NO LINE** in window **"C"** also means the test is damaged. Results are **INVALID**.

If no line appears in window "C," repeat the test using a **NEW unopened** test packet and a **NEW unopened** lancet.

15. Dispose of the gloves, spirit swab, desiccant sachet and packaging in a non-sharps waste container.

16. Record the test results in your CHW register. Dispose of cassette in non-sharps waste container

NOTE: Each test can be used **ONLY ONE TIME.** Do not try to use the test more than once.

TDR
WORLD HEALTH ORGANIZATION
USAID FROM THE AMERICAN PEOPLE
QUALITY ASSURANCE PROJECT

Appendix IV: Summary of the study procedures

			Month1	Month 2	Month 3
Study procedure	**Blood assay volume**	**Screening**	**Visit 1**	**Visit 2**	**Visit 3**
Eligibility evaluation		X			
Informed consent		X			
Demographics		X			
Vital signs		X	X	X	X
Other medical treatments		X	X	X	X
mRDT	0.1ml	X			
Blood smear	0.1ml		X	X	X
Hematology [x]					

1. Hematology[x] include Hb, hematocrit and will be done as guided by the clinical presentation of the subject
2. 'X' indicates one sapling per visit.
3. Complete physical exam on Day 0, Targeted physical on all subsequent day

Appendix V : Kisumu County MoH Approval

Jack Ouko Ogony,
Jomo Kenyatta University of Agriculture and Technology.
(JKUAT).
P.O.Box 7394-40100,
Kisumu.
+254723107953.
13/09/2017.

The Director,
Department of Health,
Kisumu County Government ,
P.O.Box 721-40100,
Kisumu.

Approved
COUNTY DIRECTOR OF HEALTH KISUMU
13/9/17

Dear Sir/Madam,

RE: REQUISITION FOR PERMISION TO CARRY OUT RESEARCH IN KISUMU COUNTY HOPITAL.

I am a student pursuing Masters of Science in Epidemiology from JKUAT admission number **TM306-C012-0863/2016** in the Kisumu CBD campus.

I hereby submit my request to allow me collect data from Kisumu county hospital which is the study area. My study title is '**Correlates and Incidence of *P.falciparum* among HIV infected and HIV non- infected Children below 5 years in Kisumu County, Kenya**' .It is a three month study which will begin upon your permission .The study has been approved by the ERC of Jaramogi Oginga Odinga Teaching and Referral Hospital, the approval is attached **(Ref:ERC.1B/VOL.I/368).**

I therefore write to seek your kind approval to be allowed to carry out the study within the Kisumu county hospital in this reference. Of interest is *P.falciparum* among HIV infected and HIV non-infected Children below 5 years as indicated in the protocol.The sample size is 132 both from OPD and CCC departments' .Thanks in advance for your kind assistance.

Thanks you.

Yours faithfully.

Jack Ogony.

COUNTY DIRECTOR OF HEALTH KISUMU

Received on 14/09/017

Appendix VI : BPS Approval Letter

JOMO KENYATTA UNIVERSITY
OF
AGRICULTURE AND TECHNOLOGY
DIRECTOR, BOARD OF POSTGRADUATE STUDIES

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Email: director@bps.jkuat.ac.ke

TEL: 254-067-52711/52181-4
FAX: 254-067-52164/52030
TEL: 254-067-52711/52181-4
FAX: 254-067-52164/52030

REF: BPS/TM306-C012-0863/2016 **5th FEBRUARY 2018**

OGONY OUKO JACK
C/o SPH – KISUMU CBD
JKUAT

Dear, Mr. Ogony,

RE: APPROVAL OF MSc. RESEARCH PROPOSAL AND SUPERVISORS

Kindly note that your research proposal entitled: "**correlates and incidence of P. falciparum among HIV infected and HIV non-infected children below 5 years in Kisumu County, Kenya**" has been approved. The following are your approved supervisors:-

1. Prof. Karanja Simon
2. Mr. Henry Kissinger Ochieng Athiany

Yours sincerely,

PROF. MATHEW KINYANJUI
DIRECTOR, BOARD OF POSTGRADUATE STUDIES

Copy: Dean, SPH

Appendix VII: Kisumu County Hospital Approval Letter

Jack Ouko Ogony,
Jomo Kenyatta University of Agriculture and Technology.
(JKUAT).
P.O.Box 7394-40100,
Kisumu.
+254723107953.
15/09/2017.

The Medical Superintendent,
Kisumu County Hospital,
P.O.Box 1818-40100.
Kisumu.

Dear Sir/Madam,

RE: REQUISITION FOR PERMISION TO CARRY OUT RESEARCH IN KISUMU COUNTY HOPITAL.

I am a student pursuing Masters of Science in Epidemiology from JKUAT admission number **TM306-C012-0863/2016** in the Kisumu CBD campus.

I hereby submit my request to allow me collect data from Kisumu county hospital which is the study area. My study title is '**Correlates and Incidence of *P.falciparum* among HIV infected and HIV non- infected Children below 5 years in Kisumu County, Kenya'** .It is a three month study which will begin upon your permission .The study has been approved by the ERC of JOOTRH **(Ref:ERC.1B/VOL.I/368)** and County Director of Health ,attached.

I therefore write to seek your kind approval to be allowed to carry out the study within the Kisumu county hospital in this reference. Of interest is *P.falciparum* among HIV infected and HIV non-infected Children below 5 years as indicated in the protocol **(copy provided).**The sample size is 132 both from OPD and CCC departments' .Thanks in advance for your kind assistance.

Thanks you.

Yours faithfully.

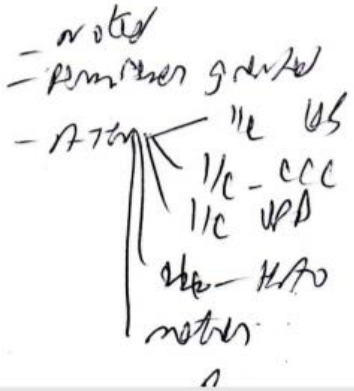
Jack Ogony.

CC

Laboratory department i/c

CCC department i/c

OPD Department i/c



Appendix VIII : ERC Approval

MINISTRY OF HEALTH

Telegrams: "MEDICAL", Kisumu
Telephone: 057-2020801/2020803/2020321
Fax: 057-2024337
E-mail: ercjootrh@gmail.com
When replying please quote

JARAMOGI OGINGA ODINGA TEACHING & REFERRAL HOSPITAL
P.O. BOX 849
KISUMU

4th September, 2017

Ref: ERC.1B/VOL.I/368

Date .....

Ogony Ouko Jack,
Reg. TM306-C012-0863/2016,
JKUAT.

Dear Jack,

RE: REQUEST FOR ETHICAL APPROVAL TO UNDERTAKE A STUDY ENTITLED: *"CORRELATES AND INCIDENCE OF P.FALCIPARUM AMONG HIV INFECTED AND HIV NON-INFECTED CHILDREN BELOW 5 YEARS IN KISUMU COUNTY, KENYA"*

The JOOTRH ERC reviewed your protocol in a meeting held on 6th July, 2017. Issues were raised by reviewers which you satisfactorily addressed. You are therefore, permitted to commence your study immediately. Note that this approval is granted for a period of one year (4th September, 2017 to 3rd September , 2018). If it is necessary to proceed with this research beyond the approved period, you will be required to apply for further extension to the committee.

Also note that you will be required to notify the committee of any protocol amendment(s), serious or unexpected outcomes related to the conduct of the study or termination for any reason.

In case the study site is JOOTRH, kindly report to the Chief Executive Officer before commencement of data collection.

Finally, note that you will also be required to share the findings of the study in both hard and soft copies upon completion.

The JOOTRH ERC takes this opportunity to thank you for choosing the institution and wishes you the best in your endeavours.

Yours sincerely,

JOOTRH ETHICS & REVIEW COMMITTEE
P. O. Box 849 - 40100
KISUMU

WILBRODA N. MAKUNDA
For: **SECRETARY – ERC,**
JOOTRH.

Appendix IX: Screening Case Report Form.

1.9 INFORMED CONSENT

Has parent/guardian of the subject provided the written informed consent? Yes ☐ No ☐

If yes, Initial Informed Consent Date and time: |__|__| |__|__|__| |__|__|__|__| *Time:* |__|__|*:*|__|__|*hr*

dd *mmm* *yyyy*

If No, exclude from the study

Has a copy of signed informed consent been given to the subject's parent/guardian?

Yes ☐ No ☐ If No explain _____

DEMOGRAPHIC DATA.

Subject's initials I___I___I___I Gender: Male ☐ Female ☐

Date of birth known? Yes ☐ No ☐ Yes, Date: |__|__| |__|__|__| |__|__|__|__|

dd *mmm* *yyyy*

Subject's Age: Year(s) ____ Months _____

If NO, Kindly check and confirm with the clinic book. If not carried on this day, remind the mother to bring the book in the next visit.

VITAL SIGNS AND ANTHROPOMETRY

Axillary Temperature: |__|__|.|__| ^{o}C

Vitals Taken by: _____ Date: |__|__| |__|__|__| |__|__|__|__| Time: |__|__||__|__|

Initials *dd* *mmm* *yyyy*

24hr

(kindly repeat Vitals if above/Below Normals)

REPEAT VITAL SIGNS

Vitals Taken by: _____ Date: |__|__| |__|__|__| |__|__|__|__|

Time: |__|__||__|__|

Initials	*dd*	*mmm*	*yyyy*	*24hr*

MEDICAL HISTORY & PHYSICAL EXAMINATION

Take comprehensive history and perform physical examination and record in the progress notes provided then transfer information appropriately in the sections provided below.

OTHER MEDICAL TREATMENT: REMINDER!!

(Confirm the HIV status of the subject from the questionnaire)

1. Is the subject currently on ART? YES ☐ NO ☐,
   If yes indicate the latest CD4 and viral load results

   CD4_____ , Viral Load _____._____copies

2. Is the subject currently on CTX treatments YES ☐ NO ☐
   Indicate other treament apart from CTX if

PHYSICAL EXAMINATION

Perform a complete physical examination and record the findings in the section below.

Please document all abnormal pathological findings as medical condition or disease

LAMBARÉNÉ ORGAN DYSFUNCTION SCORE (LODS)

Date of evaluation: |__|__| |__|__|__| |__|__|__|__| Time: |__|__|.|__|__|hr

Perform the LODS and score appropriately below.

Calculation of LODS: Sum of Prostration, Coma and Deep Breathing where NO= 0, YES=1

	YES	NO
Prostration	☐	☐
Coma		
Deep Breathing	☐	☐

Total LODS score: _____

ADVERSE EVENTS: REMINDER!

Has the subject experienced any adverse event whether elicited or reported spontaneously by the subject from the time the informed consent was signed?

Yes ☐ No ☐

INCLUSION CRITERIA

All must be **YES** for inclusion in the study.

		YES	NO
1.	A male or female child of 5 years and below	☐	☐
2.	mRDT negative for malaria parasites at the screening	☐	☐
3.	Availability of the child's parent/guardian and their willingness to provide written informed consent according to local practice.	☐	☐

4.	Willingness and ability to comply with the study protocol for the duration of the study.	☐	☐

EXCLUSION CRITERIA

All must be **NO** for inclusion in the study

		YES	**NO**
1.	Results indicating either microscopy or mRDT positive of malaria parasites	☐	☐
2.	LAR or parent unwilling or unable to participate in the study including the follow up period	☐	☐
3.	Participation in any investigational drug study prior to screening OR on any known malaria prophylaxis.	☐	☐
4.	other condition that may result in an unfavorable outcome should the potential subject participate in the study	☐	☐

Is the subject eligible to continue screening?

Yes ☐ No ☐

If yes please complete the screening lab request section below:

SCREENING LAB REQUEST SECTION

☐ RDT

☐ HB (if necessary)

Other Laboratory Test

☐ Specify _____

Lab ordered by _____ Date _____ Time _____ hrs

Initials *dd/mmm/yyyy*

Specimen Collected by: _____ Date _____ Time _____hrs

Initials *dd/mmm/yyyy*

If specimen not collected, state reason: _____

ELIGIBILITY CHECK BY INVESTIGATOR

Is the subject eligible to continue being included into the study based on the above clinical information, inclusion and exclusion criteria? YES ☐ NO ☐

If YES, assign the study arm. Study arm: _____

If NO, is the subject a screening failure? YES ☐ NO ☐ NA ☐

If YES, state reason for screening failure: _____

INVESTIGATOR SIGNATURE

I confirm that I have reviewed the data in these screening documents for this subject. All information entered by myself or my colleagues is, to the best of my knowledge, complete and accurate, as of the date below.

Investigator's name: _____

VITAL SIGNS AND ANTHROPOMETRY

Axillary Temperature: |__|__|.|__| ^{o}C

Vitals Taken by: _____ Date: |__|__| |__|__|__| |__|__|__|__|

Time: |__|__||__|__|

Initials *dd mmm yyyy 24hr*

(Kindly repeat Vitals if above/Below Normal)

REPEAT VITAL SIGNS

Check box if not applicable ☐

Axillary Temperature: |__|__|.|__| ^{o}C Pulse: |__|__|__| b/min

Vitals Taken by: _____ Date: |__|__| |__|__|__| |__|__|__|__|

Time: |__|__||__|__|

Initials *dd* *mmm* *yyyy* *24hr*

MEDICAL HISTORY & PHYSICAL EXAMINATION

Take comprehensive history and perform physical examination and record in the progress notes provided then transfer information appropriately in the sections provided below.

SIGNS AND SYMPTOMS OF CURRENT ILLNESS

Sign/Symptom	YES	NO	NOT DONE	Start Date	End Date	Ongoing	
						YES	NO
Headache				__|__|__|__|__|__|__	__|__|__|__|__|__|__		
Chest pain				__|__|__|__|__|__|__	__|__|__|__|__|__|__		
Vomiting				__|__|__|__|__|__|__	__|__|__|__|__|__|__		
Nausea				__|__|__|__|__|__|__	__|__|__|__|__|__|__		
Chills				__|__|__|__|__|__|__	__|__|__|__|__|__|__		
Dizziness				__|__|__|__|__|__|__	__|__|__|__|__|__|__		
Abdominal pain				__|__|__|__|__|__|__	__|__|__|__|__|__|__		
Fatigue				__|__|__|__|__|__|__	__|__|__|__|__|__|__		

Diarrhea				|__|__||__|__|__||__|__|	|__|__||__|__|__||__|__|__|		
Fever				|__|__||__|__|__||__|__|	|__|__||__|__|__||__|__|__|		
Sign/symptom	**YES**	**NO**	**NOT DONE**	**START DATE**	**END DATE**	**Ongoing**	**YES NO**
Coma				|__|__||__|__|__||__|__|	|__|__||__|__|__||__|__|__|		
Seizures				|__|__||__|__|__||__|__|	|__|__||__|__|__||__|__|__|		
Prostration				|__|__||__|__|__||__|__|	|__|__||__|__|__||__|__|__|		
Other; specify				|__|__||__|__|__||__|__|	|__|__||__|__|__||__|__|__|		

OTHER MEDICAL TREATMENT: REMINDER!!

(Confirm the HIV status of the subject from the questionnaire)

3. Is the subject currently on ART? YES ☐ NO ☐,
If yes indicate the latest CD4 and viral load results

CD4_____ , Viral Load _____._____copies

PHYSICAL EXAMINATION

Perform a complete physical examination and record the findings in the section below.

Critical elements that must be completed prior to inclusion include assessment of cardiovascular and respiratory status, peripheral assessment of volume status, evaluation for meningism and assessment of the Lambaréné organ Dysfunction score (LODS).

Please document all abnormal pathological findings as a medical condition or disease

LAMBARÉNÉ ORGAN DYSFUNCTION SCORE (LODS)

Date of evaluation: |__|__| |__|__|__| |__|__|__|__| Time: |__|__|·|__|__|hr.

Perform the LODS and score appropriately below.

Calculation of LODS: Sum of Prostration, Coma and Deep Breathing where NO= 0, YES=1

	YES	NO
Prostration	☐	☐
Coma		
Deep Breathing	☐	☐

Total LODS score: _____

SYSTEM	Normal	Abnormal	If abnormal, please specify	Not done
Respiratory	☐	☐		☐
Cardiovascular	☐	☐		☐
Peripheral volume status	☐	☐		☐
Meningitis	☐	☐		☐
Hydration status	☐	☐	*indicate % dehydration*	☐

Allergy	☐	☐		☐
HEENT	☐	☐		☐
Gastrointestinal	☐	☐		☐
Urogenital	☐	☐		☐
Musculoskeletal	☐	☐		☐
Dermatological	☐	☐		☐
Hematological	☐	☐		☐
SYSTEM	**Normal**	**Abnormal**	**If abnormal, please specify**	**Checkbox**
Endocrine	☐	☐		☐
Neurological	☐	☐		☐
Psychiatric	☐	☐		☐
Other *(specify)*	☐	☐		☐

CLINICAL SIGNS & SYMPTOMS OF SEVERE MALARIA

Asses for the clinical signs and symptoms of severe malaria and complete the following sections as appropriate:

1. **Cerebral Malaria:** Present ☐ Absent ☐ Not done ☐
   If present, Blantyre Coma Scale: _____
2. **Unarousable Coma:** Present ☐ Absent ☐ Not done ☐
   If present, Blantyre Coma Scale: _____
3. **Repeated generalized seizure:** Present ☐ Absent ☐ Not done ☐
   If present, length (duration in minutes):_____minutes
   Nature (type):_____
   Number of episodes: _____

4. **Repeated focal seizure** Present ☐ Absent ☐ Not done ☐

If present, length (duration in minutes):_____minutes

Nature (type):_____

Number of episodes: _____

5. **Severe Anemia:** Present ☐ Absent ☐ Not done ☐

If present, Lab ID;_____

Haemoglobin (Hb): |__|__|.|__| g/dL

Hematocrit: |__|__|.|__|%

MCV: |__|__|.|__| f

6. **Acidemia:** Present ☐ Absent ☐ Not done ☐

Comment:_____

7. **Hypaerlactatemia:** Present ☐ Absent ☐ Not done ☐

Comment:_____

8. **Circulatory collapse or shock:** Present ☐ Absent ☐ Not done ☐

Comment:_____

9. **Hyperparasitemia:** Present ☐ Absent ☐ Not done ☐

If present: _____ Parasites per µL

10. **Hypogylcaemia:** Present ☐ Absent ☐ Not done ☐

Comment:_____

11. **Jaundice:** Present ☐ Absent ☐ Not done ☐

Comment:_____

12. **Acute renal failure:** Present ☐ Absent ☐ Not done ☐

Comment:_____

13. **Haemoglobinuria:** Present ☐ Absent ☐ Not done ☐

Comment:_____

14. **Respiratory distress:** Present ☐ Absent ☐ Not done ☐

Comment:_____

15. **Pulmonary Oedema:** Present ☐ Absent ☐ Not done ☐

Comment: _____

16. **Spontaneous bleeding:** Present ☐ Absent ☐ Not done ☐

Comment: _____

17. **Disseminated Intravascular**

Coagulopathy: Present ☐ Absent ☐ Not done ☐

Comment: _____

18. **Severe Vomiting:** Present ☐ Absent ☐ Not done ☐

Comment: _____

19. **Prostration:** Present ☐ Absent ☐ Not done ☐

Comment: _____

ADVERSE EVENTS: REMINDER!

Has the subject experienced any adverse event whether elicited or reported spontaneously by the subject from the time the informed consent was signed?

Yes ☐ No ☐

Is the subject eligible to continue with the study?

Yes ☐ No ☐

If yes please complete appropriate lab request section:

LAB REQUEST SECTION

☐ MBF

☐ HB (if necessary)

Other Laboratory Test

☐ Specify _____

Lab ordered by _____ Date _____ Time _____ hrs

Initials *dd/mmm/yyyy*

Specimen Collected by: _____ Date _____ Time _____hrs

Initials *dd/mmm/yyyy*

If specimen not collected, state reason: _____

ELIGIBILITY CHECK BY INVESTIGATOR

Is the subject eligible to continue being in the study based on the above clinical information? YES ☐ NO ☐ If NO, state reason: _____