COMPARISON OF CAPILLARY AND VENOUS BLOOD IN DETECTION OF MALARIA PARASITEMIA AMONG CHILDREN ATTENDING SELECTED HEALTH FACILITIES IN IBADAN, OYO STATE

BY

OBIEKE STELLA EZIAFAKEGO

(MB;BS DELSU)

MATRIC NUMBER: 211192

A DISSERTATION SUBMITTED TO THE DEPARTMENT OF EPIDEMIOLOGY AND MEDICAL STATISTICS, FACULTY OF PUBLIC HEALTH, COLLEGE OF MEDICINE, UNIVERSITY OF IBADAN IN PARTIAL FULLFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTER OF SCIENCE IN CLINICAL EPIDEMIOLOGY

JANUARY 2021

ATTESTATION

I declare that the work in the thesis entitled — "**Comparison of Capillary and Venous blood in Detection of Malaria Parasitemia among Children Attending Selected Health Facilities in Ibadan.**" was carried by me in the Department of Epidemiology and Medical Statistics, Faculty of Public Health, university of Ibadan under the Supervision of Professor IkeOluwapo O. Ajayi and Dr Eniola A. Bamgboye. The information derived from the literature has been duly acknowledged in the text and a list of references provided. No part of this thesis was previously presented for another degree or diploma at any university.

_____

Obieke Stella Eziafakego

MB;BS (DELSU)

CERTIFICATION

I certify that this project — **Comparison of Capillary and Venous Blood in detection of Malaria Parasitemia among Children attending Selected Health Facilities in Ibadan** was carried out by OBIEKE Stella in partial fulfillment for the award of Masters of science in Clinical Epidemiology, department of Epidemiology and Medical Statistics, Faculty of Public Health, University of Ibadan, Nigeria.

_____

Professor IkeOluwapo O. Ajayi

MB;BS, MCI.Sc, MPH, Ph.D, MD, FMCGP, FWACP, Cert. Field Epid. Cert M& E

_____

Dr Eniola. A Bamgboye

MB;BS, MSc, FWACP, Cert. Clin.Epid.

DEDICATION

This work is dedicated to Almighty God, the Creator and the Author of life for the privilege of witnessing the end of this programme.

ACKNOWLEDGEMENTS

My gratitude to God is infinite. I wish to express my heartily and sincere gratitude to my supervisors, Prof. IkeOluwapo Ajayi, Dr. E.A. Bamgboye and Prof C. Falade co-supervisor under whose tutelage, guidance and tolerance I was able to produce this work. May God almighty grant them great reward.

I appreciate several individuals who played important roles in preparing me for what I am today, Prof. G.O. Okagbare, Dr Ibiyemi Umuago, Dr Kaunda Ibebuike and Rev Fr James Urien for all their prayers, support and encouragement. To my parent and siblings especially my twin sister Mrs. Linda Ajeigbe to whom I will forever remain loyal.

I am grateful for the supports Prof C Falade rendered in the course of my research, for allowing me use her private laboratory and instruments as well as her staffs for their supports, especially Mrs Akinyele Abimbola, the microbiologist who made lots of sacrifice to ensure timely reporting of the slides despite the COVID-19 lockdown. To my course mate Dr Mrs Ajetumobi, thank you for every encouraging words and teachings.

Lastly, to my darling husband Engr. Omogbolade Adepitan, for his undiluted love, support and encouragement to pursue this degree and my sons, Emmanuel and Joshua whom were both conceived during the course of the program for their cooperation.

I will forever remain grateful to you all.

ABSTRACT

Malaria is a life-threatening disease caused by parasites that are transmitted to people through bite of infected female Anopheles mosquitoes. In order to eradicate the disease and avoid complications that may arise from severe infection, there is need to improve in management. Current diagnostic method requires testing blood samples which are commonly prepared using capillary or venous blood. However, it is unclear whether capillary or venous blood samples provide better diagnostic performance among children in Nigeria. This study aimed at comparing capillary and venous blood using RDT and microscopy in detection of malaria parasitemia in children attending selected health facilities in Ibadan, Oyo State, Nigeria.

A comparative cross-sectional study was conducted from November 2019 to June 2020 among 286 children, ages 6 months to 15 years old recruited by convenience from two selected Local Government Areas in Ibadan. A pre-tested structured interviewer administered questionnaire was used to collect information on the social demographic characteristics, information on child's health, malaria management and laboratory investigation results. Both venous and capillary blood samples were taken from the same child, and were examined using rapid diagnostic test and microscopy of stained thick and thin blood films. Descriptive statistics such as frequency, percentage, were used to summarize categorical variables while mean, standard deviation and range were used for continuous variables. Measures of performance such as Sensitivity, specificity, predictive value were used to determine validity; measure of accuracy, Chi-square was used to test significance in differences in performance of RDT and microscopy using capillary and venous blood. Factors associated with parasitaemia using both blood samples for RDT and microscopy was also examined. Level of significance was set at 5%.

Mean age of the children was 5.7 ± 3.9 S.D, 178(62.2%) of the 286 enrolled were males. One hundred and two presented with fever and 21 patients have used antimalarial drug two weeks prior to presentation. Using capillary blood, 76 (26.6%) were positive for RDT and 88 (30.8%) for Microscopy (x^2=250.38, p= < 0.001). From the venous blood, 76 (26.6%) were positive for

RDT and 92 (32.2%) for microscopy (x^2=256.08, p=<0.001.). Comparing capillary and venous blood when used for RDT, both gave the same proportion of parasitemia (n=76; 26.6%). Comparing capillary and venous blood when used for microscopy, venous blood gave a higher proportion of parasitaemia (n=92; 32.2%) than capillary blood (n= 88, 30.8%) [x^2=132.02, P=<0.001). The sensitivity, specificity, NPV and PPV of RDT using capillary blood with microscopy as gold standard were 93.4%. 71.5%, 88.1%, and 82.9% respectively. The sensitivity, specificity, NPV and PPV of RDT using venous blood with microscopy as gold standard were 94.8%, 71.7%, 87.7%, and 86.8 % respectively. Accuracy for RDT using capillary blood or venous blood was 86.8% and 87.5% respectively. Having a high temperature was the only factor associated with parasitemia positivity for both capillary and venous blood when used for RDT and microscopy. (p<0.05).

This study showed significant difference in malaria parasite detection between capillary and venous blood using microscopy while malaria detection between venous and capillary using RDT were similar. However, microscopy was more sensitive than RDT in both venous and capillary blood. Therefore, the use of capillary blood is advised for detection of malaria in children, a material which can be easily obtained by less invasive methods, for both RDT and microscopy.

Key words: Malaria parasitemia, Capillary blood, Venous blood, RDT, Sensitivity, Specificity, Accuracy

TABLE OF CONTENTS

LIST OF TABLES

LIST OF APPENDICES

LIST OF ACRONYMS

ACT	Artemisinin Based Combination Therapy
CAP	Capillary

FMOH	Federal Ministry Of Health
LGA	Local Government Area
ITN	Insecticide Treated Bed Net
MP	Malarial Parasitaemia
MPD	Mean Parasite Density
mRDT	Malaria Rapid Diagnostic Test
NMCP	National Malaria Control Program
NPV	Negative Predictive Value
PHC	Primary Health Centre
PPV	Positive Predictive Value
P	Plasmodium
SMOH	State Ministry of Health
SN	Sensitivity
SP	Specificity
UNICEF	United Nations Children Education fund
VEN	Venous
W.H.O	World Health Organization

DEFINITION OF TERMS/OPERATIONAL DEFINITION

Malaria parasitaemia: This refers to the presence of at least one asexual parasite in the blood film of the study participant.

A blood smear is declared negative if no asexual parasite were seen after examining 100 high power microscopic fields and no asexual parasites were found.

Fever will be defined as axillary body temperature ≥ 37.50C and measured using digital clinical thermometer.

Parasite density: Refers to the number of parasites per microlitre of blood, taking the putative mean number of leucocytes per microlitre of blood as 8000 expressed as: Parasite density = Parasite count × 8000 / Number of WBC counted

Fever: Fever is defined as axillary body temperature ≥ 37.5oC and measured using digital clinical thermometer.

Anaemia: Anaemia is defined as haemoglobin < 11g/dl. Haemoglobin normal range for under five children is 11-13g/dl

Sensitivity: The probability that a test correctly classifies people with pre-clinical disease as positive or the ability of a test to detect a disease when it is present.

Specificity: The probability that the test classifies as negative people who are not diseased or the ability of a test to indicate non-disease when disease is absent.

Positive Predictive value: is the probability that subjects with a positive screening test truly have the disease.

Negative Predictive value: is the probability that subjects with a negative screening test truly do not have the disease.

Prevalence: is the number of disease cases present in a particular population at a given time.i.e measures of disease that allow us to determine a person's likelihood of having a disease.

CHAPTER ONE

INTRODUCTION

1.1 Background of study

Malaria is a life threatening disease caused by parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes.(WHO 2020).It is a mosquito-borne disease caused by protozoan parasites of genus plasmodium and five species are reported for their infections in humans; *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae,* and recently *Plasmodium knowles*. (Shapiro,*et al*., 2013). *Plasmodium spps* differs in instances of asymptomatic and clinical malaria, and the degree of parasitaemia may influence the pathological and biochemical presentations of individuals presenting with either of these condition. (Ojurongbe, *et al.,*2011)

Globally*, P. falciparum* accounted for 99.7% of estimated malaria cases in the WHO African region, 50% in the WHO South-East Asian region, 71% in the Eastern Mediterranean and 65% in the Western Pacific. Malaria is major health problem, responsible for approximately 217 million cases of malaria and 435,000 deaths in 2017 and increased to 228 million cases in 2018 with a total of 405,000 deaths worldwide, mostly children in the African region. (CDC2018). Nigeria has the greatest prevalence of malaria infection and accounts a quarter of all malaria cases in the WHO African region. (WHO 2013) Estimate shows that nearly 60% of the cases of clinical malaria and 700,000 to 1.3 million deaths attributable to malaria (over 90%) occurred in sub-Saharan Africa. (WHO 2013)

Early malaria diagnosis is among the most important malaria control strategies, a policy that was adopted by the Nigerian National Malaria Program in 2011.The diagnosis of malaria is based on both clinical symptoms and signs, and parasitological tests are light microscopy and

immunochromatographic rapid diagnostic tests (RDTs). (Falade, Ajayi, *et.al*., 2016). Microscopy of Giemsa-stained blood smears remains the gold standard for confirmation of malaria diagnosis. Samples can be prepared in two blood film, the thin blood film which allows species identification and the thick blood film under microscopy have appearance of parasite that is more distorted, it allows larger volume of blood and it's eleven times more sensitive than the thin film. Therefore, picking up low level of infection is easier on the thick film. Thus, microscopy has numerous advantages which include: Identification and quantitation of the causative organism, economical and reliable diagnostic method. (Falade, Ajayi *et al*., 2016)

Rapid Diagnostic Tests (RDTs) are based on the detection of antigens derived from malaria parasites in lysed blood, using immuno-chromatographic methods. Currently, high-quality RDTs have become available and are now the preferred option for many national malaria control programs, including Nigeria (FMOH. 2011), because of their simplicity and speed in yielding reliable results. Histidine-rich protein II (HRP2) based RDTs are the preferred options for tropical areas, where *Plasmodium falciparum* is responsible for >95% of malaria infections. This method is increasingly in use for diagnosis of malaria parasite due to the fact that it is rapid, easy to use and does not require much training or special equipment (McMorrow, *et al*., 2011). In detection of Malaria, the threshold of rapid diagnostic tests is in the range of 1000 parasites/microliters of blood (commercial kits can range from about 0.002% to 0.1% parasitemia) while compared with thick film microscopy threshold of malaria detection is less about 5 parasites/microliter.(Richard, David, *et al*.,2006).

According to World Health Organization (WHO), an estimate of 276 million of rapid diagnostic tests (RDTs) were sold globally in 2017, of which RDTs (66%) detected *P. falciparum* only and were supplied to sub-Saharan Africa. In Sub-Sahara Africa, RDTs are becoming increasingly the most used method to test for malaria diagnosis among suspected

malaria patients in public health facilities. In 2017, an estimated 75% of malaria tests were conducted using rapid diagnostic tests, up from 40% in 2010. (WHO 2018)

Malaria diagnosis involves identification of malaria parasites in the blood of an infected individual, this blood can be taken through various blood vessels in the body and the common method of blood collection is through capillary and venous access.

Capillary blood sampling is the collection of blood from a puncture on the finger, heel or an earlobe. Venous blood sampling is the blood from direct puncture to a vein, most often located in the antecubital area of the arm or the back of the hand. Most laboratory reference ranges for blood analyses are based on venous blood. It is more invasive than capillary beds. On the other hand, capillary blood testing has several advantages over venous blood sampling: it is less invasive, easily and faster to perform and it requires smaller amounts of blood volume. This technique has become more and more popular, especially with the widespread use of point-of-care testing (POCT), which has become the fastest growing area in laboratory medicine (Koumantakis , Watkinson .2010)

Parasite based confirmation of malaria ensures that a patient's condition is appropriately diagnosed to avoid the overuse of antimalarial medicines, provide best practices and rationalize antimalarial use to avoid parasite resistance to current antimalarial medicines.

1.2 Problem Statement

The World Health Organization reported in 2019, that there were an estimated 229 million cases of malaria worldwide and an estimated number of malaria death stood at 409 000. (WHO 2020).However, World Health Organization reported that there were an estimated 219 million cases of malaria in 2017 (uncertainty range: 135 – 287 million) and an estimated 345 000 deaths

(uncertainty range: 473 000 – 789 000), while 90% of all malaria deaths occur in sub-Saharan Africa.

According to World health organization (WHO), African Region continues to carry a disproportionately high share of the global malaria burden, the region recorded 92% of malaria cases and 93% of malaria deaths in 2017, while African Region carries a more disproportionately high share of the global malaria burden of 94% of malaria cases and of malaria deaths in 2019. (WHO 2017- 2020) In 2017, Children under 5 years of age are the most vulnerable group affected by malaria with the recent record of malaria death which accounted at an estimated 266 000 children i.e 1300 children every day or one child almost every minute (WHO 2017), and this increased in 2019, the malaria death record among children under 5 years of age was which accounted for 67% (274 000) worldwide. (WHO 2020) Malaria is a major public health problem in Nigeria, accounts for 60 percent of outpatient visits to health facilities, and 30 percent hospital admission. (Aina *et al*.,2013).

Global efforts to control malaria have recently led to reduction in overall disease burden, between 2000 and 2019 there was a marked reduction in global malaria cases incidence and mortality. (WHO 2020) The malaria case incidence rate fell from 80 in 2000 to 57 in 2019 with a total malaria cases declined from 238 million in 2000 to 229 million in 2019. In same period, the population in sub-Saharan Africa, which account for more than 90% of the global burden of malaria, increased from 665 million to over I billion (WHO 2020). In Africa an estimated 16% of all deaths among under five children was due to malaria. (WHO 2010)

Studies revealed that malaria over diagnosis has been a reoccurring problems globally especially in African countries. (Ghai, Thurber, *et al*., 2016). For example the presumptive approach based on clinical symptoms has resulted in over diagnosis of malaria and mismanagement of non-malaria fever, which results in unnecessary expenditure, incorrect use

of antimalarial drugs with increased risk of drug resistance spreading and a delay in establishing the correct diagnosis and treatment of patients. (Uneke CJ. 2008)

Malaria over diagnosis results in over inflation of actual malaria rates reported at the local and national level, it has contributed to over- prescription of antimalarial drugs and exaggerated perception of high malaria endemicity in regions which are no longer endemic for this infection.(Mwanziva, Charles, *et al.*, 2008). Health facilities tend to diagnose all fever as malaria in patients presenting with symptoms of fever and some laboratory testing give high false positivity rates of diagnosis by unqualified personnel. *(*Yegorov, Galiwango, *et al.*, 2016)

Some study underlines the importance of capillary sampling in the context of malaria elimination campaigns particularly in settings of where people with low-level parasitemia constitute an important reservoir of malaria parasites (W.H.O. 2015). Capillary blood sampling are prone to errors during pre-analytical phase, which are beyond the control of clinical laboratory personnel due to small volumes involves and variability in sample quality based on puncture site and technique. (Simundic, Nikolac et al.2010). If carried out incorrectly, capillary blood sampling can cause inaccurate test results, pain and tissue damage (Crabtree, Sharkey. 2014). Venous blood samples provide sufficient material for performing variety of diagnosis tests, including concentration procedures such as filariasis, trypanosomiasis. However, in some parasites diseases e,g malaria diagnoses, anticoagulants in the venous blood specimen can interfere with parasite morphology and staining characteristics; this problem can be further compounded by excessive delays priors to making the smears. In such cases, capillary blood samples are preferable.

Thus, additional studies are needed to proof that capillary blood is preferred than venous blood specimen in diagnosing malaria parasitemia in children.

1.3 Justification

World Health Organization (WHO) recommended that all cases of suspected malaria be confirmed using parasite –based diagnostic testing (either microscopy or rapid diagnostic test) before treatment. (WHO 2020). Malaria parasite is preventable, its preventions, among other ways, through malaria parasite screening via capillary or venous blood collection. The use of parasite-based diagnosis will permit better utilization of anti-malaria drugs and also afford an opportunity for other causes of fever to be identified and appropriately treatment. The availability of RDTs offers a good opportunity to extend parasitological confirmation of malaria infection to peripheral areas where quality microscopy cannot be guaranteed (WHO 2011).

Currently, no specific recommendation exists with regard to the source of blood sample that should be used for malaria diagnostics. Some studies have reported potentially superior performance of capillary blood samples for malaria diagnosis compared to venous blood samples. (Njunda, *et al*., 2013) Thus, the question whether certain blood sources may potentially influence the detection of parasitemia is also important for the clinical management of malaria as well as for research studies. (Macintyre, Adoke, *et al* 2017).

The desire for a total eradication of malaria in endemic areas in order to avoid its complications has led to the evaluation of the different diagnostic techniques to improve on the management of the disease. Diagnosis of malaria is usually based on samples of peripheral blood. However, it is unclear whether capillary or venous blood samples provide better diagnostic performance in detection of malaria among children in Nigeria. Thus, there is need for further investigation of this study aiming at comparing the preferred site either capillary or venous blood in detection of malaria parasitemia in children and the test validity of this two blood channels.

1.4 Research Questions

1. What is the prevalence of malaria parasitemia among venous and capillary blood using microscopy and RDT?
2. What is the test validity of microscopy and rapid diagnostic test for the detection of malaria in children?
3. What is the test validity of capillary and venous blood as the gold standard for detection malaria in children?
4. What are the factors affecting the malaria prarasitemia in capillary and venous blood

1.5 General Objective

The overall objective of this study is to compare capillary and venous blood using Rapid diagnostic test (RDT) and Microscopy (gold standard) in detection of malaria parasitemia among children ages 6 month to 15 years attending two selected health facilities in Ibadan.

1.6 Specific Objectives

1. To compare the prevalence of malaria parasitemia between capillary and venous blood using RDT and microscopy.
2. To test the validity of RDT in detection of malaria using capillary blood with microscopy as the gold standard.
3. To test the validity of RDT in detection of malaria using venous blood with microscopy as the gold standard.
4. To determine the factors associated with malaria parasitemia in capillary and venous blood using RDT and Microscopy

CHAPTER TWO

LITERATURE REVIEW

2.1 Epidemiology of Malaria

Malaria is a mosquito-borne infectious disease of human and other animals caused by protists (a type of microorganism) of the genus Plasmodium (pylum Apicoplexa). (Mueller I, Zimmerman PA, 2007). There are five species of plasmodium parasites namely *Plasmodium vivax, Plasmodium malariae, Plasmodium falciparum, Plasmodium ovale* and recently *Plasmodium knowlesi,* azoonotic specie prevalent in South Asia. (Mueller I, Zimmerman PA, 2007) and 2 of these species – *P.falciparum and P.vivax* - pose the greatest treat. (WHO 2020)

Plasmodium falciparum is the most malignant form of malaria that is able to infect red blood cells (RBCs) of all ages, resulting in high levels of parasitemia (>5% RBCs infected). In contrast, *P.vivax* and *P.ovale* infect only young RBC and thus cause a lower level of parasitemia (< 2%). This specie is the most dangerous; accounting for half of all clinical cases of malaria and 90 percent of deaths from the disease and it is transmitted primary during raining season. (Nadjm, Behrens. 2012) *Plasmodium vivax* is the most widely distributed parasite existing in temperate as well as subtropical area. It is found in South America, Africa, India and Pakistan. It's usually lasts 2-4 months with diminishing frequency and intensity of paroxysms and only infects only immature RBCs, resulting to limited parasitemia. *Plasmoddium ovale* are similar to *Plasmodium vivax* infections, although less severe. *Plasmodium ovale* often resolves without treatment. It infects only immature RBCs and parasitemia is usually less than that seen in *Plasmodium falciparum. Plasmodium malariae* accounts for up to 25% plasmodium infections in tropical Africa. It remains asymptomatic for a longer period of time than do those infected with *Plasmodium vivax* and *Plasmodium ovale*. *Plasmodium Knowlesi* is a parasite that causes malaria in humans and other primates found throughout Southeast Asia. It often associates with fatal outcome when infected.

In Nigeria, malaria contributes significantly to the burden of disease especially in communities where it is endemic and in quantifying the economic burden of malaria in the country. 97% of the population is at risk of having malaria in Nigeria. Jimoh *et al* reported that malaria is responsible for annual economic loss of 132 billion naira in treatment and loss in man-hour. Its accounts for nearly 110 million clinically diagnosed cases per year, 60 percent of outpatient visits, and 30 percent hospitalization. (FMOH, 2011) In addition, at least 50% of the population has at least one episode of malaria annually. The Federal Ministry of Health and the National Malaria Control Program reported that 25 percent infant mortality and 30 percent under five mortality is attributable to malaria infection in Nigeria. (FMOH, 2011) In spite of all efforts and resources directed towards the eradication of malaria worldwide, this ancient disease still constitute a huge public health problem especially in Sub-Saharan Africa. (W.H.O, 2013).

2.2 Transmission and Life Cycle of Malaria Parasite

The plasmodium parasites undergo many stages of development and their life cycle is completed in two hosts, viz; humans (intermediate host) and mosquitoes (definitive host). Malaria parasites are transmitted to humans by the bites of an infected female Anopheles mosquito. Sporozoites contained in the saliva of the mosquito are inoculated into the blood of human host when the mosquito takes a blood meal. Infection can also occur by transfusion of infected donor blood. Occasionally congenital transmission occurs when a mother is non-immune. (Owusu-Ofori , Parry, et al. 2010) These Sporozoites travel through the blood to the liver where they invade red blood cells (RBC). Inside the RBC the merozoites multiply rapidly until they force the red cell to burst, releasing into the blood stream new generation of merozoites that go to infect other RBCs. At this time the clinical symptoms of overt malaria in the infected individual become apparent, some merozoites divide to form gametocytes, i.e. immature male and female gametes. At this point the male and female gametocytes fuse and form a ookinete- afertilized, motile zygote. Ookinete develop into new Sporozoites that migrate

to the insect‘s salivary glands, ready to infect a new vertebrate host. The Sporozoites are injected into the skin, in the saliva, when the mosquito takes subsequent blood meals**.** (Zurovac , Midia , *et al*., 2006). Only female mosquito feed on blood; male mosquitoes feed on plant nectar, and thus do not transmit the disease. The female of the Anopheles genus of mosquito prefer to feed at night. They usually start searching for meal at dusk, and will continue throughout the night until taking a meal. Malaria parasite can also be transmitted by blood transfusion, although this is rare. (Owusu-Ofori , Parry C, 2010) .

2.3 Symptoms and Complications

The initial manifestation of malaria common to all species is similar to flu-like symptoms and can resemble other conditions such as septicemia and systemic viral illness. This includes headache, fever, fatigue, abdominal discomfort, muscle and joint aches, shivering, vomiting, anorexia, hemolytic anemia, jaundice and convulsions. (Andrej T, Matzjaz J, *et al,* 2003). This is a cyclical occurrence of sudden coldness followed by rigor, and then fever and sweating, occurring every two days (tertian fever) in *P. vivax* and *P. ovale* infections, and every three days (quartan fever) for *P. malariae*. *Plasmodium falciparum* infection can cause recurrent fever every 36-48 hours or less pronounced and almost continuous fever. (Fairhurst RM, *et al*., 2010). In study conducted in Turbo, Columbia among mothers of under five children on perception and response to febrile illness, majority (82%) of the mothers recognized fever, chills, vomiting and weakness as the most frequent symptoms of malaria in the region.(Lopez de Mesa, *et al*., 2012).

Plasmodium falciparum causes falciparum malaria, formerly known as sub tertian or malignant tertian malaria. (Halliday, Karanja *et.al*.,2012). It is the most wide spread accounting for up to 90% of malaria cases in Nigeria. *Plasmodium falciparum* is the most pathogenic of the human malaria species with untreated infections causing severe disease and death, particularly in

young children, pregnant women and non-immune adults. (Okrah JC, et al., 2002).The pathogenicity of *Plasmodium falciparum* is mainly due to cycloadherence of falciparum parasitized red cells, causing the cells to adhere to one another and to the walls of capillaries in the brain, muscles, kidneys and elsewhere and in pregnant women, in the placenta. Sequestration of parasitized cells in the microcirculation causes congestion, hypoxia, blockage and rupturing of small blood vessels. *Falciparum* malaria parasitaemia can exceed more than 250,000 parasites/µl of blood. Up to 30-40% of red cells may become parasitized. Severe falciparum malaria is associated cerebral malaria, hemoglobinuria, severe anaemia, hypoglycemia, and complications in pregnancy have been reported. (Murphy SC, Breman JG. 2001).

2.4 Prevalence of Malaria Parasitaemia

Malaria is the world's fourth leading cause of death in children younger than age 5 years. Internationally, malaria is responsible for approximately 1-3 million deaths per year, mostly children aged 5 years or younger, and 80-90% of the deaths each year are in rural Sub-Saharan African. (CDC, 2011). The prevalence and burden of malaria differ from one region to another depending on the endemicity of the disease. (Cuadros, Branscum , *et al* .,2011).

In a study conducted in Nyasa Health Center in Tabora region of Western Tanzania among 300 under five children with fever or history of fever in the past 2 weeks, Mazigo *et al* reported a prevalence of 12% with *Plasmodium falciparum* been the predominant species found. Although in a study from Gabon a decline in prevalence of *Plasmodium falciparum* among children below five years from 31.2% in 2005 to 18.3% in 2008 was observed. (Mawilli-Mboumba, Akotet, *et al*., 2013)

A prevalence of 54.6% was reported from a Health facility based study in Uganda which was higher than previous report. Olasehinde *et al*, (2010) reported a prevalence rate of 80.5%

among children under 12 years in a cross sectional study in Southwestern Nigeria. The result of this study differs from that of Uko *et al*.(1998), who recorded a low prevalence rate of(6.8%). this may be due to the fact that the study was carried out during dry season alone when infection rate was low. (Olasehinde G.I, Ajayi A.A, *et al*. 2010).

In a recent study conducted among under five children in health facilities in Jos, a malaria parasitemia prevalence of 48.06% was found. (Okoli C, Solomon M. 2014) Studies conducted in Eastern Nigeria on prevalence of malaria parasitemia gave a high prevalence of 76.4% and 80.3% respectively. These studies were conducted during the rainy season which is a high malaria transmission season and in rural community which lies within the humid tropical rain forest with Guinea Savanna Vegetation. (Nwaorgu B.N, Orajaka OC. 2011)The prevalence of malaria parasitaemia among individuals living with HIV including children from Osogbo, South Western Nigeria was 18.5%.(Ojurongbe O, *et al*., 2014) In another study conducted in Ota, Ogun State, South West Nigeria, 47.9% prevalence of *Plasmodium falciparum* was reported among under five children. (Olasehinde G.I., Ajayi A, *et al.*, 2010) This finding was similar to the report from the Nigeria malaria indicator survey that reported 42% prevalence of malaria parasitemia among under five children in 2010. He further reported that children 2-3 years old had the highest percentage (67.5%) of *Plasmodium falciparum* infections. (Olasehinde G.I, *et al*., 2010). A prevalence of 11.7% and 16.7% was identified by microscopy and PCR respectively. Jean-Bosco et al further reported that most of the infections were asymptomatic with anaemia observed in 82% of the children with parasitemia. (Jean-Bosco G, *et al*.,2011).

2.5 Diagnosis and Testing

As part of the effective management of malaria, WHO recommends prompt parasite- based diagnosis by microscopy or malaria rapid diagnostic test (RDT) in all patients suspected of

malaria before antimalarial treatment is administered.(WHO 2018). Treatment solely on the basis of symptoms should be considered only when a parasitological diagnosis is not possible. (WHO 2020)

Malaria microscopy allows identification of different malaria causing parasites, their various parasite stages, including gametocytes, and the qualification of parasite density to monitor treatment. Light microscopy is the diagnostic standard against which other diagnostic methods have traditionally been compared. The number of patients tested by microscopic examination increased to more than 208 million in 2017, the global total is dominated by India. (WHO 2019) Despite its widespread usage, the quality of microscopy diagnosis is frequently inadequate for ensuring good sensitivity and specificity of malaria diagnosis, adversely affecting health outcomes and optimal use of resources. (WHO, 2019) These disadvantages have favored the introduction and the use of RDTs based on immunochromatographic techniques (Lubell *et al*., 2008).

Malaria RDT is an alternate way of quickly establishing the diagnosis of malaria infection by detection specific malaria antigens in a person blood. Some RDTs detect a single species(either *P.falciparum* or *P.vivax),* some multiple species (*P.falciparum or P.vivax P.ovale and P.malariae*) and some further differentiate *P.falciparum* and non-falciparum infection or between specific species.

WHO reported a total of 276 million RDT sales in 2017 were most RDTs (66%) were supplied to Sub-Saharan Africa. In 2017, an estimated 75% of malaria tests in Sub-Saharan Africa were conducted using RDTs, up from 40% in 2010.The disadvantage for the RDT does not eliminate the need for malaria microscopy. The RDT may not be able to detect some infections with lower numbers of malaria parasites. Therefore all negatives malaria RDT must be followed by microscopy testing to confirm the result as well as all positive RDTs.(CDC-DPDx,2020). Since

RDTs generally cost less than a full course of ACT, their introduction should not only improve malaria management but should also limit malaria treatment costs. Molecular diagnosis is expensive and requires specialized laboratory, while serological diagnosis does not detect the on-going infection rather measures memory of past experience. (Noppadon , Chatnafa , *et al*. , 2009).

2.6 Capillary and Venous Blood

Many blood analyses can be performed either with venous blood or with capillary blood. Blood films for detection of malaria parasites are commonly prepared from capillary and venous blood. A recent nationwide survey of policies and practices related to capillary blood sampling shown that capillary procedures are no standardized. (Jasna Lenice Krleza et al.,205) .According to Johannes Mischlinger et al (2019), Capillary blood was shown to be of diagnostic superiority, manifesting in an 8% sensitivity gap between capillary and venous blood in the overall study. This capillary superiority in sensitivity can be explained by the comparatively higher parasite abundance in capillary blood as diagnosis of malaria in microscopy is based on the demonstration of asexual parasites. The issue of the sensitivity of capillary and venous blood when use to prepare blood films therefore arises and so too the need for further investigation. (Njundal *et al*., 2013) According to Njunda *et al* study, the difference in the rate of malaria parasite detection in capillary blood smear was significantly higher than that with the venous blood (P=0.0109).

Capillary is patient-centered ,more comfortable and minimizes pain and easier to collection Capillary blood is obtained by finger stick, a label pre-cleaned slides (preferably frosted-end) with the patient's name (or other identifier) and date and time of collection, site is well with alcohol and allow to dry then prick the side of the pulp of the 3rd or 4th finger (alternate sites include ear lobe, or in infants large toe or heel), the first drop of blood with clean gauze is wipe

away then prepare at least 2 thick smear and 2 thin smears. The venous blood is obtained by venipuncture following a well labeled collection tubes and pre-cleaned slides (preferably frosted-end) with the patient's name (or other identifier) and date and time of collection then the site is cleaned with alcohol and allow to dry. The venous blood in a vacuum tube containing anticoagulant (preferably EDTA); alternatively, collect the blood in a syringe and transfer it to a tube with anticoagulant; mix well. (CDC-DPDx 2020)

2.7 Factors Associated with Malaria

Variations in environmental or human related factors can have consequences for malaria transmission due to the low immune status of the human population especially children. (Divyan, Ramachandran, *et al.*2014)**.** Different factors can drive these changes by influencing the vector's transmission capacity and the malaria prevalence.

These factors can be grouped into three classes: (1) environmental factors such as altitude and climate (2) biological factors related to the Anopheles vector, the parasite and the human host and (3) human related factors such as socio-economic status, access to health facilities, migration, gender, control activities (IRS, Insecticide Treated Net, and Intermittent Preventive Treatment, use of prophylaxis).(O'Meara, Mangeni , Steketee *et al*. 2010) and land use (irrigation, deforestation, swamp drainage and living near breeding sites). Due to these factors several studies have been conducted aimed at assessing control activities. In a study among under-fives attending Primary Healthcare Clinics in Makurdi, Nigeria Jombo *et al.* 2010) reported a 25% rate of ownership and usage of insecticide treated bed net. In view of the vital role ITNs play in the actualization of the Roll Back Malaria initiative, Jombo opinioned that these rates of usage were very low. Another study reported 47.9% prevalence of malaria parasitaemia among children that used insecticide treated net as a method to prevent mosquito

bites and 90.9% prevalence among those not using insecticide treated net. (Olasehinde , Ajayi , *et al*. 2010).

Teklehaimanot opinioned that a strong correlation exists between malaria and poverty because it impedes economic growth and keeps households in poverty, hence the burden of the disease is higher among the poor living in rural setting. This is because they are more likely to be ignorant of preventive measures and their children poorly nourished. Stagnant pools and poor environmental conditions, encourages the breeding of mosquitoes, consequently mosquito vector are more abundant in the rural setting because of the usually unkempt environment, thereby increasing the intensity of transmission. (Teklehaimanot A, Mejia P.2008)

Olasehinde *et al* in their study observed malaria prevalence rates of 52.2% among children whose parents lived in a clean and hygienic environment compared with children whose parents live in a hygiene compromised environment a prevalence of 74.1%. Based on findings such as these, the promotion of ITN use has become a central element of national and international efforts against malaria. Important components according to the World Health Organization for reducing the burden of malaria morbidity and mortality include more sensitive diagnostic tools; effective use of antimalarial drugs, and improved personal protection and mosquito control.(World Health Organization. Geneva 2007). The approach to elimination or control of malaria includes these basics, along with improvements in tracking of human illness and parasite surveillance, and effective resource delivery. Fortunately, effective interventions for preventing malaria mortality in children are available and are being scaled-up across malaria endemic areas of Africa.

2.8 Parasite Determination

Since the erythrocytes (RBCs) have been lysed and the parasites are more concentrated, the thick smear is useful for screening for parasites and for detecting mixed infections. To examine the smear, use the 100x oil immersion objective lens. Select an area that is well-stained, free of stain precipitate, and well- populated with white blood cells (WBCs) (10-20 WBC/field).In determination of "No Parasites Found"(NPF): For malaria diagnosis, WHO recommends that at least 100 fields, each containing approximately 20 WBCs, be screened before calling a thick smear negative. Assuming an average WBC count of 8000 per microliltre of blood, this gives a threshold of sensitivity of 4 parasites per microliter of blood. In a non-immune patients, symptomatic malaria can occur at lower parasite densities and screening more fields (e.g, 200, 300, or even the whole smear) might be warranted, depending on the clinical context and the availability of laboratory personnel and time. (Cheesbrough, 2006).Malaria can be qualified against blood elements e.g. RBCs and WBCs, this quantification yields useful information. To quantify malaria parasites against RBCs, count the parasitized RBCs among 500-2000 RBCs on the thin smear and express the results as % parasitemia.

% parasitemia = (parasitized RBCs/ total RBCs) x 100

If the parasitemia is high (e.g.,>10%) examine 500 RBCs ;if is low (e.g.,< 1%) examine 2000 RBCs (or more); count asexual blood stage parasites and gametocytes separately.(Cheesbrough, 2006).Only the former are clinically important and gametocytes of *P.falciparum* can persist after elimination of asexual stages by drug treatment.To quantify malaria parasites against WBCs on the thick smear, tally the parasites against WBCs, until you have counted 500 parasites or 1000 WBCs, whichever comes first; express the results as parasites per microliter of blood , using the WBC count if known , or otherwise assuming 8,000 WBCs per microliter blood. .(Cheesbrough, 2006).

Parasites/ microliter blood = (parasites/WBCs) x WBC count per microliter < or 8,000>

Results in % parasitized RBCs and parasites per microliter blood can be interconverted if the WBC and RBC counts are known, or otherwise (less desirably) by assuming 8000 WBCs and 4000000 RBCs per microliter blood. (Cheesbrough, 2006).

CHAPTER THREE

METHODOLOGY

3.1.1. Study area

Ibadan is the capital and the most populous city of Oyo State, in Nigeria. it is the third largest city in Nigeria with a population of over 4 million as of 2021 and over 6 million people within metropolitan area. It's the country largest city by geographical area. Ibadan is located in south-western Nigeria in the south eastern part of Oyo State at about 119 kilometers northeast of Lagos and 120 kilometers east of Nigerian international border with the Republic of Benin. There 11 Local governments in Ibadan Metropolitan area consisting of five urban local government in the city and six semi- urban local government in the less city. The principal inhabitants of the city are Yoruba, as well as various communities from other parts of the country.

It has a tropical wet and dry climate (koopen climate classification) with a lengthy wet season and relatively constant temperatures throughout the course of the year. Ibadan's wet season runs from March through October, although August seems somewhat of a lull in precipitation. This lull nearly divides the wet season into two different wet seasons. November to February forms the city's dry season, during which Ibadan experiences the typical West African harmattan. The total rainfall for Ibadan is 14020.06mm, falling in approximately 109 days. There are two peaks of rainfall, June and September. The mean maximum temperature is 26.46 degree Celsius, minimum 21.42 Celsius and relative humidity is 74.55%.Ibadan is host to Nigeria's premier higher institution of learning, University of Ibadan. The university began in 1948 with 104 students and has grown to a full-fledged university with a drive for excellence in postgraduate and undergraduate studies The University College Hospital (UCH) Ibadan is federal teaching hospital attached to the University of Ibadan located in Ibadan North Local Government Area, Oyo State, Nigeria.

3.1.2. Study Site

The study was carried out from two selected health facilities in Ibadan; the University College Hospital, Ibadan located at Ibadan North Local Government Area and Oluyole Primary Health Centre, Ibadan. Primary health center is located at Oluyole Local Government area of Ibadan. The facilities were chosen because serve as the most utilized health care at the tertiary level and at the Primary level for treatment of malaria and are located in different Local Government Area of Ibadan.

The primary health center is managed by the Local government and has relatively medical officer who coordinates the activities of the health facilities. Government provides health care services through the primary health centers, secondary and tertiary hospitals. These health centers are equipped with microscopy and rapid diagnostic test kits are been supply to all PHCs in Ibadan.

3.1.3 Study Design

A comparative cross-sectional study was used to conduct the study. This study compared capillary and venous blood testing among children within ages 6 months and 15 years old with malaria parasitemia.

3.1.4. Study Population

The study was conducted at the hospital, selected tertiary hospital and selected Primary Health care in Ibadan, Oyo State. The 286 children made up the study population, the children from ages 6 months to 15 years, with signs and symptoms of malaria attending University College Hospital and Oluyole Primary Health Centre both in Ibadan. The participants were children who walked into the facilities with signs and symptoms of malaria within the period of study.

3.2.1. Inclusion criteria

i. Children with symptoms of Malaria; fever, chill& rigor, headache, abdominal pain, weakness, diarrhoea.

ii. Children of ages 6 months to 15 years attending the selected facility

iii. Those whose caregiver consented in the study.

iv. Only the two selected health facilities were included in the study

3.2.2. Exclusion criteria

i. Children on antimalarial therapy

ii. Children less than the age-bracket in this study

iii. Non consenting caregiver

iv. Those without symptoms or signs suggestive of malaria.

3.3. Sample Size Determination

The minimum sample size required for this study will be calculated based on the study on Performance of malaria rapid diagnostic test in febrile children under the age five years at Oni memorial children hospital Ibadan, Nigeria, 2016. (Ajayi *et al*., 2016)

The number of participants for this study was calculated using this formula:-

Where;

$$n = \frac{N = Z_{\alpha}^2 [p(1-p)]}{d^2}$$

p = the percentage prevalence of malaria among under five children at Oni memorial hospital Ibadan =21.6% (Ajayi *et al*., 2016)

q =1-P = (1-0.216)

Z_α= standard normal deviate at 95% confidence interval = 1.96

d^2= half width of the confidence interval = 0.05

$$n = \frac{\{(1.96\ (0.216)\}(1-0.216)}{(0.05)2}$$

n = 260.2

To adjust for non-response, 10% non- response or incomplete filled questionnaire, is allowed;

= 10/100*260 = 26

Desired sample size = 260.2+26= 286 approximately = 286

3.4. Sampling technique

Convenience sampling method was used for the study. From each selected facilities, children were selected based on the presenting history of fever, other symptoms such headache, malaise and willingness to take in the study.

3.5. Study Instrument

A pretested semi-structured questionnaire was prepared for this study and developed from earlier studies related to malaria. The questionnaire was reviewed for validity by the supervisor of this research work and a research expert who critically examined the items, checked for the relevance of the items to the research questions as well as the objectives of the study and effected corrections before a final copy was produced. The questionnaire consists of four sections: the socio-demographics information, Child health related information on temperature,

antimalarial drug use prior to presentation, factors affecting malaria parasitemia, and Laboratory investigations of the capillary and venous blood. The Socio-demographic information includes the Respondents relationship with the child, level of education, marital status, occupation and number of children and the child's age. The child health related information includes body temperature, weight of the child, height and history of fever and the antimalarial use prior to presentation.

3.6. Data Collection

A pretested survey questionnaire was used to conduct the study. The interviewers were trained on procedures for conducting the survey and also involved in the pretesting and revision of the questionnaires. Data collection was supervised by the lead investigator. Immediately after the questionnaire filling, then blood sample collection follows.

3.7. Laboratory Method

Blood sample collection: The first blood sample was collected from capillary bed through needle prick on the pulp of the finger. About 0.5mls of blood is collected from the capillary bed to test for malaria parasitemia both on the rapid diagnostic test kit (SD BIOLINE) and slide for thick and thin films to detect malaria parasitemia. The second blood sample was collected from the venous bed using the 2ml syringes, about 0.5mls of venous blood was collected aseptically and immediately dropped on the rapid diagnostic test kit (RDT) to detect malaria parasite and on slide to film for the thick and thin blood smear of malaria.

Microscopy diagnostic technique: A drop of blood each was place on two clean grease free glass slides for thin and thick blood film. The slides was made in duplicates and appropriately labeled. Thin and thick blood smears were prepared according to World Health Organization (WHO) guideline for malaria microscopy. (W.H.O. Learners Guide Part 1).The thin film was

fixed using methanol for about two seconds and both film was left to air dry for 24 hours and then stained with 3% quality controlled Giemsa stain at PH 7.2 for 45 minutes as recommended by WHO. Blood films were examined microscopically using 100 magnifications (Oil immersion) lens. The total parasite counts were recorded as number of parasites per microlitre of blood. The Parasite density per microlitre of blood was estimated from the thick film, taking the putative mean number of Leucocytes per microlitre of blood as 8,000 expressed as (Cheesbrough M. 2010).

Rapid diagnostic test kit: The SD BIOLINE Malaria Ag Pf/Pan test (Standard Diagnostic Inc. suwon City, South Korea) was used. The test kit contains a cassette format membrane strip and a differential test for detection of the HRP-2 antigen that is specific to *P.falciparum*. The membrane strip is pre-coated with monoclonal antibodies as two separate lines: a control line which indicates whether the test is valid or not (line 1) and a Pf line indicating infections due to the *P.falciparum*, single pan line indicating infection due to *plasmodium* species. The presence of two color bands (i.e. the test and the control) indicates a positive result, while the presence of only one band within the result window indicates a negative result. The test is considered invalid if the control line does not appear.

3.8. Data Analysis

Data were entered into computer using SPSS version 16.0 (Statistical Package for Social Sciences), cleaned through running of frequencies to check for completeness and outliers and analyzed. Descriptive statistics such as frequency, percentage, were used to summarize categorical variables while mean, standard deviation and range were used for continuous variables. Measures of performance such as Sensitivity, specificity, predictive value were used to determine validity; measure of accuracy, Chi-square was used to test significance in differences in performance of RDT and microscopy using capillary and venous blood. It was

also used to determine factors associated with parasitaemia using both blood samples for RDT and microscopy. Sensitivity is calculated by true positive divided by true positive plus false negative (TP/TP+FN). Specificity is true negative divided by true negative plus false positive (TN/TN+FP). Negative predictive value (NPV) is true negative divided by true negative plus false negative (TN/TN+FN), Positive predictive value (PPV) is true positive divided by true positive plus false positive (TP/TP+FP).

3.9. Ethical Consideration

The study protocol was granted approval by the Ethics and Research Committee of University College Hospital with the approval number of UI/UCH EC Registration Number NHREC/05/01/2008a. Participation was voluntary. The participants may withdraw at any time without consequences of any kind and also may refuse to answer any questions not wanted in the questionnaire. There is no penalty if withdrawn from the study and there is no loss of any benefits to which your child is otherwise entitled.

A written informed consent was obtained from parents/guardian after who were fully informed about the procedure involved in the research. Participant not exposed to harm during their participation. All the information collected is strictly confidential and remained anonymous throughout the study. Moreso, confidentiality was maintained by means of a code number. Your child may experience a little discomfort during the blood collection process for malaria diagnosis. The codes were used to identify participants and completed questionnaire was kept under lock and key. All data kept in a password protected computer by the investigator.

All caregivers will be educated on the current National guideline for the prevention of malaria infection especially among under- fives. The benefits include; diagnosis of malaria, treatment and management at no cost to the participants. The result of the test will also provide useful

information for Nigeria National Malaria control program on the burden of malaria parasite among children.

CHAPTER FOUR

RESULTS

4.1. Socio-demographic Characteristics

The socio-demographic information of the participants – caregivers and children, enrolled in the study is presented on Table 4.1 and Table 4.2. Out of 286 participants, 261 participants

were caregivers to the children, which include mother 227(79%), aunt 11(4%), sister 9(3%), father 8(3%), grandmother 5(2%), brother 3(1%) and self-23(8%).

The average age of the caregivers was 32 years; a few were below 20 years 17(6.5%) and 20 – 24 years 16(6%); about one-fifth were in the age category 25 – 29 years 53(20%); most were aged 30 – 34 years 73(28%); about 46(18%) were aged 35 – 39 years, others 58(22%) were 40+ years. Up to 24(93%) of the caregivers were females; others were males 19(7%). More than three-quarter of the caregivers were married 220(84%), a few were single 29(11%), widowed and separated 3(1%).

About a quarter of the caregivers attained a tertiary education 68(26%); most of the caregivers completed not more than secondary education 122(46%); a few had just the primary education 46(18%); one of ten of the caregivers 27(10%) had no formal education. More than one-third of the caregivers were self-employed 93(35%), about one-fifth reported they were employees 55(21%), 6% engaged in unskilled labor or petty trading; a quarter were housewives 66(25%), 23(9%) were unemployed, 10(4%) were students.

Table 4.1: Socio-demographic information of caregivers

	Frequency	**Percentage (%)**
Respondent relationship with child	**(n=286)**	
Mother	227	79.4
Self (Child)	23	8.0
Aunt	11	3.8
Sister	9	3.1
Father	8	2.8

Grandmother	5	1.7
Brother	3	1.0
Age of caregivers [mean = 32.7]	**(n = 263)**	
≤ 19 years	17	6.5
20 – 24 years	16	6.1
25 – 29 years	53	20.2
30 – 34 years	73	27.8
35 – 39 years	46	17.5
≥ 40years	58	22.1
Gender of caregivers	**(n = 261)**	
Male	19	7.2
Female	244	92.8
Marital status of caregivers		
Married	220	83.7
Single	29	11.0
Widowed	11	4.2
Separated	3	1.1
Level of education of caregivers	**(n = 263)**	
No formal education	27	10.3
Primary education	46	17.5
Secondary education	122	46.4
Tertiary education (ND, HND, B.Sc., M.A. M.Sc.)	68	25.9
Occupation of caregivers	**(n = 263)**	
Self-employed	93	35.4
Housewives	66	25.1
Employed for wages	55	20.9
Unemployed	23	8.7
Unskilled labour (Petty trading)	16	6.1
Student	10	3.8

4.2 Background information of the children

The background information of the children under study revealed that; more than half of the participants 147(51.4%) were aged less than 5 years, 82(28.7%) were aged 5-9 years, one-fifth were aged 10 – 15 years 57(20%). The study enrolled more male 178(62.2%) than females108 (37.8%). More than one-third of the children had high temperature 102(35.4%), others

184(64.3%) had normal temperature. The children who had antimalarial administered less than two weeks prior to presentation to the hospital was 21(7.3%) while about 265(92%) of the majority did not take any antimalarial before this study.

Table 4.2: Background information of children under study

	Frequency	Percentage
Age of child	**(n = 286)**	**(%)**

< 5 years	147	51.4
5 – 9 years	82	28.7
10 – 15 years	57	19.9
Gender of child		
Male	178	62.2
Female	108	37.8
Child body temperature		
Normal temperature(37^{o}c)	184	64.3
High temperature (≥37.5^{o}c)	102	35.4

Table 4.3: Information on the Use of medication for malaria

	Frequency	**Percentage**

		(100%)
Antimalaria administered ≤ two weeks	**(n = 286)**	
Yes	21	7.3
No	265	92.7
Type of malaria drugs taken	**(n = 21)**	
Coartem	4	30.8
Amaterm	2	15.4
Herbs	2	15.4
Lonart	1	7.7
Anti-malaria	1	7.7
Paracetamol	1	7.7
Flagyl	1	7.7
Can't recall	8	61.5

4.4 Laboratory result of the prevalence of parasitemia in capillary and venous blood using RDT and Microscopy

Results from the laboratory investigation showed that; the total of 286 samples of capillary blood was tested for malaria parasitemia using rapid diagnostic test (RDT) and examined under microscopy. Of these, 76(26.6%) samples were positive for RDT and 88(32%) positive for Microscopy while 210 and 198 were Negative for both test respectively. The proportion prevalence of capillary blood that is positive for Microscopy and RDT is 30.8% and 26.6% respectively. From the venous blood, a total of 286 samples were examined under microscopy and screened using RDT, 92 samples were positive for microscopy and 76 positive for RDT. However, the proportion prevalence of venous blood those were positive for both Microscopy and RDT were 32.2% and 26.6% respectively.

Table 4.4: Laboratory result of the prevalence of parasitemia in capillary and venous blood using RDT and Microscopy

(n = 286)s

	Frequency	Percentage (%)
Microscopy (Capillary)		
Positive	88	30.8
Negative	198	69.2
RDT (Capillary)		
Positive	76	26.6
Negative	210	73.4
Microscopy (Venous)		
Positive	92	32.2
Negative	194	67.8
RDT (Venous)		
Positive	76	26.6
Negative	210	73.4

4.5.1 Comparing the use of capillary against venous blood using microscopy

The result on Table 4.5.1 below compared the use of capillary blood against venous blood using microscopy (gold standard). From the microscopy results, the capillary and venous blood

were 88(30.8%) and 92(32%) positive respectively. The sensitivity of the test was 93.5%, specificity 98.9% and accuracy of 97%. The venous microscopy is significant higher than microscopy capillary, (x^2 =250.38, p=<0.001).

Table 4.5.1: Comparing the use of capillary blood against venous blood using microscopy

	Microscopy (Venous)

	Positive	Negative	Total	Chi-square	p-value
Microscopy (Capillary)					
Positive	86	2	88	250.38	< 0.001
Negative	6	192	198		
Total	92	194	286		

Sensitivity = TP/ (TP+FN)= 93.5%

Specificity = TN/ (TN + FP) = 98.9%

Negative Predictive Value (NPV)= TN/ (TN+FN) = 97.0%

Positive Predictive Value (PPV) = TP/ (TP+FP) = 97.7%

Accuracy = 97.2%

4.5.2. Comparing the use of capillary blood against venous blood using RDT

The result in Table 4.5.2 compared the use of capillary blood against venous blood using RDT, both capillary and venous blood had 76(26.6%) positive and 210(73.4%) negative, their

sensitivity and specificity is 96% and 99% respectively were obtained, with a test accuracy of 98%.

Table 4.5.2: Comparing the use of capillary against venous blood using RDT

	RDT (Venous)				
	Positive	**Negative**	**Total**	**Chi-square**	**p-value**
RDT (Capillary)					
Positive	73	3	76	256.08	< 0.001
Negative	3	207	210		
Total	76	210	286		

Sensitivity = TP/ (TP+FN) = 98.6%

Specificity = TN/ (TN + FP) = 96.1 %

Negative Predictive Value (NPV) = TN/ (TN+FN) = 98.6%

Positive Predictive Value (PPV) = TP/ (TP+FP) = 96.1%

Accuracy = 97.9%

4.6.1. Test of Validity of RDT using Capillary blood

In table 4.6.1.below, the result of capillary blood showed RDT Capillary had 76(26.6%) positive for malaria parasitemia while those tested with the gold standard Microscopy had 88 (30.8%) positive, the specificity of the test was 93.4%, and sensitivity was 72%, coupled with a test accuracy of 87%. Thus, Microcopy capillary is significant in detecting malaria parasitemia than RDT capillary. (x^2 =132.02, p=<0.001)

Table 4.6.1: Test of Validity of RDT using Capillary blood

	Capillary Microscopy(gold standard)				
	Positive	**Negative**	**Total**	**Chi-square**	**p-value**
Capillary (RDT)					
Positive	63	13	76		
				132.02	< 0.001
Negative	25	185	210		
Total	88	198	286		

Sensitivity = TP/ (TP+FN) = 71.5%

Specificity = TN/ (TN + FP) = 93.5 %

Negative Predictive Value (NPV) = TN/ (TN+FN) = 88.1%

Positive Predictive Value (PPV) = TP/ (TP+FP) = 82.9%%

Accuracy = 86.8%

4.6.2: Test of Validity of RDT using venous blood

Comparing the results in table 4.6.2, the venous blood tested using RDT against the gold standard Microscopy; Venous RDT had 76 (26.6%) positive for malaria parasitemia while those tested with the gold standard Microscopy had 92 (32.2%) positive, the specificity of the test was 94.8%, and sensitivity was approximately 71.7 %, coupled with a test accuracy of 87.5%.Venous microscopy showed more significant performance than venous capillary in detecting parasitemia,

Table 4.6.2: Test of Validity of RDT using venous blood

	Venous (Microscopy(gold standard)				
	Positive	**Negative**	**Total**	**Chi-square**	**p-value**
Venous (RDT)					
Positive	66	10	76	141.80	< 0.001
Negative	26	184	210		
Total	92	194	286		

Sensitivity = TP/ (TP+FN) = 71.7%

Specificity = TN/ (TN + FP) = 94.8 %

Negative Predictive Value (NPV) = TN/ (TN+FN) = 87.7%

Positive Predictive Value (PPV) = TP/ (TP+FP) = 86.8 %

Accuracy = 97.9%

4.7.1. Factors Associated with Malaria parasitemia in Capillary Blood

Table 4.7.1 below, shows the factors associated with malaria parasitemia using capillary blood; children age 10-15 years had higher parasitemia 25(43.9%) than 5-9 years and < 5 years that 29(35%) and 47(32%) respectively. More male tested positive at 64(36%) than the female at 37(34%) and children with high temperature 48(47.1%) tested positive for malaria, while 53(28.8%) of children with normal temperature tested positive to malaria. (x^2 = 9.57,p = 0.002).

Table 4.7.1: Factors associated with malaria parasitemia in Capillary blood

	Capillary			
	Negative	**Positive**	χ^2	**p-value**
Age				
< 5 years	100 (68.0)	47 (32.0)	2.54	0.281
5 – 9 years	53 (64.6)	29 (35.4)		
10 – 15 years	32 (56.1)	25 (43.9)		
Gender				
Male	114 (64.0)	64 (36.0)	0.09	0.771
Female	71 (65.7)	37 (34.3)		
Body temperature				
Normal temperature	131 (71.2)	53 (28.8)	9.57	0.002
High temperature	54 (52.9)	48 (47.1)		
Antimalaria administered ≤ two weeks				
Yes	13 (61.9)	8 (38.1)	0.08	0.782
No	172 (64.9)	93 (35.1)		

4.7.2: Factors associated with malaria parasitemia in venous blood

Similarly Table 4.7.2; shows the factors associated with malaria parasitemia using venous blood; children age 10-15 years had higher parasitemia 26(45.3%) than 5-9 years and < 5 years that 29(39%) and 44(29%) respectively. More male tested positive at 66(37.1%) than the female at 36(33.3%) and 50(49%) of the children with high temperature tested positive for malaria, while 52(28.3%) of children with normal temperature tested positive to malaria. The use of antimalarial drug >2 weeks prior to presentation recorded 8(38.1%) positive. A test of association between children's age, gender, body temperature and malaria test status showed that; only high body temperature of the children was associated with their malaria status (x^2 =12.32, p = <0.001).

Table 4.7.2: Factors associated with malaria parasitemia in venous blood

	Negative	Positive	χ^2	p-value
Age				
< 5 years	103 (70.1)	44 (29.9)	4.97	0.083
5 – 9 years	50 (60.9)	32 (39.0)		
10 – 15 years	31 (54.4)	26 (45.6)		
Gender				
Male	112 (62.9)	66 (37.1)	0.41	0.521
Female	72 (66.7)	36 (33.3)		
Body temperature				
Normal temperature	132 (71.7)	52 (28.3)	12.32	< 0.001
High temperature	52 (51.0)	50 (49.0)		
Antimalaria administered ≤ two weeks				
Yes	13 (61.9)	8 (38.1)	0.06	0.809
No	171 (64.5)	94 (35.5)		

4.7.3. Comparing the Factors associated with parasitemia in Capillary and Venous blood for both RDT and Microscopy.

The proportion of malaria parasitemia was higher in both capillary and venous among the age group of 10-15 years 25(44%) and 26(45.6%) respectively with the lowest seen in the venous blood among ≤ five years children 44(29%). Male has high positive venous blood 66(37%) with slightly difference from capillary blood at 64(36%) while female have almost similarly proportion tested positive for both capillary and venous blood(34%). However, the proportion positive for malaria parasitemia for high body temperature was seen in venous blood 50(49%) than capillary blood at 48(47%) and slightly similar proportion were positive at normal temperature with capillary 53(28.8%) and venous 52(28.3%). Therefore, the high temperature showed higher significant associate than the normal temperature.

Table 4.7.3: Comparing the Factors associated with parasitemia in Capillary and Venous blood.

	Capillary(Positive) (n = 101)	Venous (Positive) (n = 102)
Age		
< 5 years	47 (32.0)	44 (29.9)
5 – 9 years	29 (35.4)	32 (39.0)
10 – 15 years	25 (43.9)	26 (45.6)
Gender		
Male	64 (36.0)	66 (37.1)
Female	37 (34.3)	36 (33.3)
Body temperature		
Normal temperature	53 (28.8)	52 (28.3)
High temperature	48 (47.1)	50 (49.0)
Antimalaria administered ≤ two weeks		
Yes	8 (38.1)	8 (38.1)
No	93 (35.1)	94 (35.5)

Table 4.8.1: Factors associated with malaria parasitemia in Microscopy

	Negative	Positive	χ^2	p-value
Age				
< 5 years	108 (73.5)	39 (26.5)	5.79	0.055
5 – 9 years	51 (62.2)	31 (37.8)		
10 – 15 years	33 (57.9)	24 (42.1)		
Gender				
Male	117 (65.7)	61 (34.3)	0.42	0.517
Female	75 (69.4)	33 (30.6)		
Body temperature				
Normal temperature	137 (74.5)	47 (25.5)	12.54	< 0.001
High temperature	55 (53.9)	47 (46.1)		
Antimalaria administered ≤ two weeks				
Yes	14 (66.7)	7 (33.3)	0.002	0.962
No	178 (67.2)	87 (32.8)		

Table 4.8.2: Factors associated with malaria parasitemia in RDT

	Negative	Positive	χ^2	p-value
Age				
< 5 years	108 (73.5)	39 (26.5)	0.56	0.756
5 – 9 years	60 (73.2)	22 (26.8)		
10 – 15 years	39 (68.4)	18 (31.6)		
Gender				
Male	129 (72.5)	49 (27.5)	0.002	0.963
Female	78 (72.2)	30 (27.8)		
Body temperature				
Normal temperature	146 (79.3)	38 (20.7)	12.54	< 0.001
High temperature	61 (59.8)	41 (40.2)		
Antimalaria administered ≤ two weeks				
Yes	14 (66.7)	7 (33.3)	0.37	0.543
No	193 (72.8)	72 (27.2)		

4.8.3: Comparing the Factors associated with malaria parasitemia in RDT and Microscopy (gold standard)

In table 4.8.2 amd 4.8.3, the factors associated with malaria parasitemia using RDT and the microscopy as the gold standard among children from 6 months and 15 years were compared. 31(37.8%) and 24(42%) were positive in the children with the ages 5-9 and 10-15 years for microscopy and 22(26.8%) and 18(31.6%) positive for RDT for those age group. The male and female have more positive malaria parasitemia with proportion of 61(34.8%) and 33(30.6%) for microscopy than RDT with approximately 28% positive for both male and female. Moreso, the high temperature and normal Body temperature were positive for microscopy at 46% and 25.5% respectively, while the high temperature and normal body temperature were positive for RDT at 40.2% and 20.7% respectively. Thus, high temperature has higher significance of associates in detection malaria parasitemia using microscopy. (x^2=12.54, p=<0.001).

Table 4.8.3: Comparing the Factors associated with malaria parasitemia RDT and Microscopy.

Variables	Microscopy Positive (Capillary& venous) (n = 94)	RDT Positive (Capillary & venous) (n = 79)	X^2	P -value
Age				
< 5 years	39 (26.5)	39 (26.5)		
5 – 9 years	31 (37.8)	22 (26.8)		
10 –15 years	24 (42.1)	18 (31.6)		
Gender				
Male	61 (34.3)	49 (27.5)		
Female	33 (30.6)	30 (27.8)		
Body temperature			12.54	< 0.001
Normal temperature	47 (25.5)	38 (20.7)		
High temperature	47 (46.1)	41 (40.2)		
Antimalaria administered ≤ two weeks				
Yes	7 (33.3)	7 (33.3)		
No	87 (32.8)	72 (27.2)		

CHAPTER FIVE

5.1. DISCUSSION

This study compared capillary against the venous blood (gold standard) using RDT and microscopy (gold standard) in detection of malaria parasitemia in children, ages 6 months to 15year from two selected health care facilities in Ibadan, Oyo state.

In comparing the present of parasitemia, testing capillary blood using RDT and microscopy, microscopy showed significantly detected parasitemia more than RDT. (x=250.38, p=<0.001). Comparing the present of parasitemia testing, venous blood using RDT and microscopy, microscopy showed significantly detected parasitemia higher than RDT. (X=256.08, P=<0.001). Comparing capillary and venous blood when used for RDT, both had gave same proportion of 76(26.6%) parasitemia (x=308, p=<0.001).Comparing capillary and venous blood when used for microscopy, the venous showed higher proportion 92(32.2%) of parasitemia than capillary blood 88(30.8%) (x=132, p=<0.001).

In the Cameroonian study, those presenting with symptoms of malaria had positive capillary smears in 29% cases but only 17% of venous smears(p=0.011).(Njunda et al., 2013), while the gabon study found that capillary blood had 8% higher sensitivity than the venous blood.(J. Mischlinger *et al*., 2019).However, the microscopy positivity report 35.1% by Uzochukwu *et al*., 2009, 59% by Azikiwe *et al*.2012 and 78% by Harchut *et al*., 2013, were higher than the microscopy result in this study. However, RDT positivity of this result was quite lower than what was obtained in these studies but higher than 2.3% obtained by Elechi *et al.* 2015) and 14% by Harchut *et al*.,2013. Reasons for these variations may be attributable to different sample size, methodology, and types of RDT kits used.

The sensitivity, specificity, Negative Predictive Value and Positive Predictive Value of RDT using capillary blood with microscopy as gold standard were 93.4%, 71.5%, 88.1%, and 82.9% respectively. The sensitivity, specificity, NPV and PPV of RDT using venous blood with

microscopy as gold standard were 94.8%, 71.7%, 87.7%, and 86.8 % respectively. Accuracy for RDT using capillary blood or venous blood was 86.8% and 87.5% respectively.

Johannes Mischlinger et al, reported 81.5% capillary sensitivity of microscopy relative to the gold standard versus 73.4% venous sensitivity which is lower than the result from this study, while their specificities of 91% is higher than this study. (Johannes Mischlinger et al., 2019).

Most studies that have been carried out to compare microscopy and RDT showed both to be sensitive in the diagnosis of malaria which is similar to this study. (Ojurongbe O, *et al*.,2013, Azikiwe CC *et.al*.,2012, Nwachukwu C,2014, Reyburn H,*et. al.,* 2007). (Batwala *et al.*2011) in Uganda found RDT to be not only sensitive but also more feasible than microscopy. This is not in consonance with the findings in (Angola *et.al.,*2013) and(Hopkins H *et.al*.,2008), where RDT was found to have higher sensitivity and specificity. However, some study, found RDT not to be a reliable test in under five children with acute uncomplicated malaria as their sensitivity of 8.3% was also low which is not comparable to our finding. (Elechi *et al.*, 2015) The sensitivity to RDT for both capillary and venous blood were higher than the 69.6%, and 82.0% reported from Lagos and Enugu, respectively. (Ben-Edet AE.*et. al*., 2004 and Adesanmi TA, *et.al*., 2011) The sensitivity of RDT reported in this study is lower than previous reports in Nigeria (Ajumobi *et al*., 2015). Sensitivities of 96%, 97% and 97.6% had been reported in Zambia, Zanzibar and Thailand, respectively (*Hopkins et al*., 2008; Msellem *et al*., 2009; Nicastri *et al*., 2009). However, the specificity 87% is similar to 88% reported by Msellem *et al*.,2009 but lower than 93 and 100% recorded in Thailand (Buchachart *et al*., 2004) and among Nigerian travellers (Dougnon *et al*., 2015). The sensitivity reported in this study is yet to attain the 95% recommended World Health Organization value (WHO. 2000). This low sensitivity is disadvantageous as it will impair control intervention since a fraction of the infected population will be left untreated especially if RDT is the only available diagnostic tool.

However, the high specificity will improve the cost effectiveness of malaria diagnosis since the RDT is unlikely to miss out the non-infected individuals.

Some study reported Microscopy has an average sensitivity of about 50-100 parasites per microliter of blood while Rapid diagnostic tests are not sensitive to detect parasitemia intensity of less than 100 parasites per microliter of blood. Low parasitemia level in these patients could be as a result of self-medication in which the patients might have taken some antimalarial drugs or herbs without doctor's prescription before coming to the Health centre for malaria test which could have wiped out significant amount of the parasite from the blood.

The age of the children was observed to increase in positivity rate of parasitemia in capillary and venous blood for both RDT and microscopy. This contrary to Garbal *et al*., that no observed increase in positivity rates with age of the children for both RDT and microscopy.(Acheampong D.O,*et al*.,2011) and (Abeku TA *et al*.2008) similarly did not observe an increase in RDT positivity with age. This is consistent with findings by Elechi HA *et al*., where they observed an increase in sensitivity with advancing age. Reasons for the variations may be due to differences in sample size and age group studied. There was no significant association between gender and RDT similar to what was obtained by Elechi *et al,*.

The body temperature showed an association with both capillary and venous when used on RDT and microscopy and high temperature was significantly higher than the normal temperature. Therefore, a test of association between children's age, gender, body temperature and use of antimalarial drug prior to presentation showed that only high body temperature at presentation was associated with having malaria parasitemia for both RDT and microscopy using capillary and venous blood ($p<0.001$).Thus present of high body temperature does not necessary means the child has malaria rather other disease entity may present with fever and

may need to be investigated. The study reported by Azikwe *et al.,* 2012, also support that a good number of febrile cases is not due to malaria.

Quite high number of both negative RDT and microscopy were obtained from either capillary or venous blood, which may suggest children were not infected with malaria parasite. This may also mean that a high proportion of children are still over-diagnosed with malaria; which is in consonance with what was obtained by Uzochukwu *et al*.,2009, Ojurongbe et al.,2013 and Azikiwa *et al*.,2012 and Batwala *et al*,2011.

However, the accuracy of a clinical diagnosis is dependent on the disease endemicity level, malaria season and the age group under consideration (Dicko *et al*., 2005; Mwangi *et al*., 2005), thus the discrepancies observed in RDT sensitivities in several observational studies (Grobusch *et al*., 2003; Iqbal *et al*., 2003; Fernando *et al*., 2004).The reasons for the low positivity rates in RDT may be due to external factors that may have affected the stability of the RDT such as exposure to extreme temperatures which has been found to be a major contributor to poor performance of RDTs, especially during transport as well as storage. (UNICEF.2014) High humidity has also been found to rapidly degrade RDTs. (Abanyie FA.*et.al*., 2011). RDT technical problems can be from quality performance or assurance, test quality and accuracy, and the packaging of the kits. (Mouatcho JC.*et al*.,2013) RDTs are more expensive relative to microscopy and also the intensity of test band varies with amount of antigen present at low parasite densities which may lead to reader variation in test results.(UNICEF.2014, Moody A.*et al*., 2002)s

Maintaining a cold chain from the point of arrival of the RDTs into the country, storage and during transportation to point of care cannot be ascertained to be optimal; however this was not looked at in our study.

5.2. CONCLUSION

This study has compared capillary against venous (gold standard) blood using RDT and microscopy as the gold standard in detection of malaria parasitemia among children attending selected health facilities in Ibadan, Oyo state. It is vital to properly diagnose malaria

especially in malaria-endemic regions, because it will help improve the diagnosis and treatment of other febrile infections and limit antimalarial usage to only malaria parasite-based test true positives.

Microscopy analyses revealed the highest prevalence of the infection; however, it is expensive and requires a very standard laboratory with well trained personnel. The rapid diagnostic test revealed the lowest prevalence of the infection which could probably be as a result of its inability to detect parasites when counts are very low but it is very quick and convenient to use. Majority of the health facility rare use RDT in diagnosing malaria for the reason of perceived reliability, cost and supply issues.

In summary, there are slight significant differences in parasitemia detection between capillary and venous blood for both RDT and microscopy. The microscopy was more sensitive than RDT in both venous than capillary blood. No difference was found in malaria detection between venous and capillary using RDT. Therefore, use of capillary blood is preferred on microscopy for malaria diagnosis due to easy access, less invasive, minimal blood loss which is far different with invasive approach of venous blood. However, RDT should be used to complement microscopy or alone when expert on microscopy is unavailable especially in rural malaria, endemic areas of developing countries which lack well-equipped laboratories or expert microscopy for malaria diagnosis.

5.3 RECOMMENDATIONS

Based on the results from this study, the following problems should be addressed in improving the adherence to malaria diagnosis and treatment guidelines among children in both tertiary and primary health care facilities in Ibadan;

1. Based on the finding in this study, the capillary and venous blood were similarly effective, although venous was slightly significant than capillary blood. Therefore, due to venous drawbacks, we recommend capillary blood.
2. Microscopy still remains the choice for detection malaria parasitemia. However, in the absence of microscopy, RDT is a good alternative as it was find to be effective in detection of malaria.

REFERENCES

Ajumobi O, Kabir S, Patrick N, Jacob K, Godwin N, Sheba G, Rutebemberwa E, Wellington O, Peter N, Mark M and Gabriele P. 2015. "Performance of an HRP- 2 rapid diagnostic

test in Nigeria children less than 5 years of age" American Journal Tropical Medicine Hygiene; 92(4): 828-833. PubMed | Google Scholar.

Acheampong D.O, Appiah M.G, Boamponsem L.K, ABoampong J.N, Afoakwah R.2011. "The efficacy of rapid diagnostic test (rdt) in diagnosing *Plasmodium falciparum* malaria in some selected health facilities in the capecoast metropolis of Ghana." Advance Applied Science Research 2:348-56.

Abeku T.A, Kristan M, Jones C, Beard J, Mueller D.H and Okia M. 2008. "Determinants of the accuracy of rapid diagnostic tests in malaria case management: Evidence from low and moderate transmission settings in the East African highlands." Malaria Journal; 7: 202.

Adesanmi T.A, Okafor H.U, Okoro A.B, and Mafe A.G. 2011. "Diagnosis of malaria parasitemia in children using a rapid diagnostic test". Niger Journal Clinical Practice; 14: 195-200.

Azikiwe C.C, Ifezulike C.C, Siminialayi I.M, Amazu L.U, Enye J.C and Nwakwunite O.E. 2012 "Comparative laboratory diagnosis of malaria: Microscopy versus rapid diagnostic test kits". Asian Pacific Journal Tropical Medicine; 2:307-10.

Bastiaens G.J.H, Schaftenaar E, and Ndaro A. 2011. "Malaria diagnostic testing and treatment practices in three different *Plasmodium falciparum* transmission settings in Tanzania: before and after a government policy change" Malaria Journal; 10:76.

Batwala V, Magnussen P and Nuwaha F. 2011. "Comparative feasibility of implementing rapid diagnostic test and microscopy for parasitological diagnosis of malaria in Uganda". Malaria Journal; 10:373.

Bear N.A, Taylor TE, Harding S.P. 2006 Malaria retinopathy: A newly established diagnostic sign in severe malaria. America Journal Medical Hygiene; 75 (5): 790-797.

Ben-Edet A.E, Lesi F.E, Mafe A.G, and Grange A.O. 2004. "Diagnosis of *falciparum* malaria in children using the immunochromatographic technique". Nigeria Journal Paediatric; 3(13): 7178.

Bjorkman A. 2002."Malaria associated anaemia, drug resistance and antimalarial combination therapy". International Journal Parasitology; 32: 1637–1643.

Bradley D.J, Newbold C.I and Warrel D.A. 2000. "Malaria. In Concise Oxford Textbook of Medicine". Weatherall D.J, Ledingham J.G and Warrel D.A. 3rd edition. Oxford Medical Publication, Oxford; 1735-1750.

Center for Disease Control and Prevention. National Center for Infectious Diseases, Division of Parasitic Diseases 2004. "Center for Disease control and Prevention. The History of Malaria Ancient Disease".

Center for Disease Control and Prevention. 2011."Malaria". Available at http;//www.cc.gov/malaria. Accessed Sept 15,.

Chaterjee K.D. 2006. "Parasitology and Helminthology.20th edition". Chaterjee Medical Publishers, 4 Amrita Banerjee Road, Calcutta; 216.

Clinical and Laboratory Standards Institute (CLSI) document GP42-A6 (former H04-A6): 2008. "Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens.Approved Standard – Sixth Edition". Clinical Laboratory Standards Institute; Wayne, Pennsylvania, USA.

Cuadros D.F, Branscum A.J, Crowley P.H. 2011. "HIV-malaria co-infection: effects of malaria on the prevalence of HIV in East sub-Saharan Africa". International Journal Epidemiology; 40 (4): 931–939.

D'Acremont V, Lengeler C, and Genton B. 2010. "Reduction in the proportion of fevers associated with *Plasmodium falciparum* parasitaemia in Africa: a systematic review". Malaria Journal; 9: 240.

Ekeh E.L and Teclaire N.N. 2008. "Prevalence of malaria parasitaemia and associated factors in febrile under five children seen in PHC centres in Jos, north central Nigeria. Niger". Postgrad Med J.; 15 (2) : 65-68.

Elechi H.A, Rabasa A.I, Muhammad F.B, Garba M.A, Abubakar G.F and Umoru M.A. 2015. "Prevalence and pattern of malaria parasitaemia among under-five febrile children attending peadiatric outpatient clinic at University of Maiduguri teaching hospital, Maiduguri. Niger J Paediatric." 42(4): 319-324. Google Scholar

English M, Reyburn H and Goodman C. 2009. "Abandoning presumptive antimalarial treatment for febrile children aged less than five years–A case of running before we can walk?" PLoS Med; 6(1): e1000015

Fançony C, Sebastião Y.V, Pires J.E, Gamboa D and Nery S.V. 2013. "Performance of microscopy and RDTs in the context of a malaria prevalence survey in Angola: A comparison using PCR as the gold standard." Malaria Journal;12:284.

Falade C.O, Ajayi I.O, Nsungwa-Sabiiti J, Siribié M, Diarra A, Sermé L. 2016. "Malaria rapid diagnostic tests and malaria microscopy for guiding malaria treatment of uncomplicated

fevers in Nigeria and pre-referral cases in 3 African Countries." Clinical Infectious Disease. 63(suppl 5):S290–7.

Federal Ministry of Health. Malaria control in Nigeria. 2004. "A strategy for behavioural change communication". Abuja FMOH.

Federal Ministry of Health (FMOH). 2009. "Federal Republic of Nigeria training manual for management of malaria in Nigeria Participants' Manual Federal Ministry of Health National Malaria and Vector Control Division, Abuja- Nigeria".

Graz B, Willcox M, and Szeless T. 2011. "Test and treat or presumptive treatment for malaria in high transmission situations? A reflection on the latest WHO guidelines". Malaria Journal; 10:136

Harani M.S, Beg M.A, Khaleeq L, Adil S.N, Kakepoto G.N and Kurshid M. 2006. "Role of ICT Malaria Immunochromatographic Test for Rapid diagnosis of Malaria." Journal of Pakistan Medical Association; 56: (4).

Hartman T.K, Rogerson S.J, and Fischer P.R. 2010. "The impact of maternal malaria on newborns." Annual Tropical Paediatric; 30 (4): 271–82.

Hendriksen Ilse C.E, Mtove George Pedro and Arjen M.Dondorp. 2011. "Evaluation of a PfHRP (2) and apLDH based rapid diagnostic test for the diagnosis of severe malaria in 2 populations of African children." Clinical Infectious Disease; 52:1100–7.

Hopkins H, Bebell L, Kambale W, Dokomajilar C, Rosenthal P.J and Dorsey G. 2008. "Rapid diagnostic tests for malaria at sites of varying transmission intensity in Uganda" Journal Infectious Disease; 197:510-8.

Harchut K, Standley C, Dobson A, Klaassen B, Rambaud-Althaus C, and Althaus F. 2013. "Over-diagnosis of malaria by microscopy in the Kilombero Valley, Southern Tanzania: An evaluation of the utility and cost-effectiveness of rapid diagnostic tests." Malaria Journal; 12:159.

Idro R, Bitarakwate E, Tumwesigre S and John CC. 2005. "Clinical Manifestations of Severe Malaria in The Highlands of Southwestern Uganda." American Journal of Tropical Medicine and Hygiene; 72 (5): 561-567.

Iglesias N, Subirats M, Trevisi P, Ramirez-Olvencia G, Castan P and Puente S,Toro C. 2014. "Performance of a new gelled nested PCR test for the diagnosis of imported malaria: comparison with microscopy, rapid diagnostic test, and real-time PCR". Parasitology Research.; 113(7):2587-91.doi:10.1007/s00436-014-3911-z.Epub 2014 Apr 27.PMID: 24770719.

Ikeh E.I and Teclaire N.N. 2008. "Prevalence of malaria parasitaemia and associated factors in febrile under-5 children seen in primary health care centers in Jos, North Central Nigeria" Nigeria Postgraduate Medical Journal; 15(2): 65-69. PubMed | Google Scholar

Iqbal J, Khalid N and Hira P.R. 2002. "Comparison of Two Commercial Assays with Expert Microscopy for confirmation of symptomatically Diagnosed Malaria" Journal of Clinical Microbiology; 40 (12): 4675-4678.

Jimoh A, Sofola O, Petu A,Okorosobo T.2007. "Quantifying the Economic Burden of Malaria in Nigeria Using the Willingness to Pay Approach, Cost Effectiveness and Resource Allocation" 5:6.doi:10.1186/1478-7547-5-6 .PMID:175171446; PMICID: PMC1890276.

Kiggundu V.L, O'Meara W.P, Musoke R,Nalugoda K, Kigozi G, Baghendaghe E,Lutalo T, Achienge M, Reynolds J, Makumbi F, Serwadda D and Gray R.H. 2013. "High prevalence of malaria parasitaemia and anaemia among hospitalized children in Rakai, Uganda" PLoS ONE 8 (2); e82455.

Klein E.Y, 2013. "Antimalaria drug resistance: a review of the biology and strategies to delay emergies and spread". Internaional Journal. Antimicrobial Agents

Krause P.J. Malaria (Plasmodium). 2000. In: Behrman R.E, Kliegroan R.M, Jeson H.B editors. "Nelson Textbook of Pediatrics 17th edition. Philadelphia". Saunders; 10491043. .

Krief S, Ananias A.Escalante, M.Andreina Pacheco, Lawrence Mugisha, Claudine Andre, Michel Halbwax, Anne Fisher, Jean-Michel Krief, John M. asenene, Mike Crandfield, Omar E.Cornejo, Jean-Marc Chavatte, Clara Lin, Frank Letourneur, Ann Chaelotte Gruner, Thomas F. McCutchan, Laurent Renia and Georges Snounou. 2010. "On the Diversity of Malaria Parasites in African Apes and the Origin of *P. falciparum* from Bonobos". PLoSPathog; 6(2):1000765.

Lippi G, Becan-McBride K, Behúlová D, Bowen RAR, Church S, Delanghe JR,Granvist K, Kitchen S, Nybo M, Nauck M, Nikolac N, Palick V, Plebani M, Sandberg S and Simundic AM. 2013. "Preanalytical quality improvement: in quality we trust". Clinical Chemistry and Laboratory Medicine ; 51: 229-41.

Lwanga S.K and Lemeshow S. 1991. "Sample size determination in health studies, a practical manual." World Health Organization" 1-22. Google Scholar

McAdam A.J and Sharpe A.H. 2004. "Infectious Diseases." In: Kumar V, Abbas AK and Fausto N editors. Robins and Cortan "Pathologic Basis of Disease 7th edition". Saunders an Imprint of Elsevier. Philadelphia, Pennsylvenia; 401-403.

McMorrow M.L, Aidoo M, and Kachur S.P. 2011. "Malaria rapid diagnostic tests in elimination settings-can they find the last parasite?" Clinical Microbiology Infection; 17 (11):1624-31.

Menendez C, Fleming A,F and Alonso P.L. 2000. "Malaria-related anaemia". Parasitology Today; 16: 469–476.

Mordi RM, Borke ME. 2013. "The prevalence of malaria in Edo State, Nigeria". Nigerian Journal Parasitology; 34(2):41-6.

Mohan, D.R. and M. Ramaswamy. 2007. "Evaluation of larvicidal activity of the leaf extract of a weed plant, Ageratinaadenophora, against two important species of mosquitoes, Aedesaegypti and Culexquinqefasciatus" Africa Journal Biotechnology, 6: 631-638.

National Malaria Elimination Programme (NMEP), National Population Commission (NPopC), National Bureau of Statistics (NBS) and ICF International. 2016. "Nigeria Malaria Indicator Survey 2015". Abuja, Nigeria and Rockville, Maryland, USA: NMEP, NPopC and ICF International.

National Population Commission (NPC) (Nigeria), National Malaria Control Programme (NMCP) (Nigeria) and ICF International. 2012. "Nigeria Malaria Indicator Survey 2010" Abuja, Nigeria: NPC, NMCP and ICF International.

Njama-Meya D, Clark TD, Nzarubara B,Staede S, Kamya MR and Dorsey G. 2007. "Treatment of malaria restricted to laboratory-confirmed cases: A prospective cohort study in Ugandan children" Malaria Journal; 6:7.

Nwachukwu C. 2006. "Evaluation of BID® Plasmodium Lactate Dehydrogenase (pLDH) Rapid Test for Detections of Malaria Parasite in Calabar, Nigeria." Institute of Tropical Disease Research and Prevention, University of Calabar Teaching Hospital; Calabar:

Available from: www2.sciencewithamission.org/ pdf_instructions /malaria_clinical-evaluation-report.pdf.

Ojurongbe O, Adegbosin O.O, Taiwo S.S, Alli O.A, Olowe O.A, Ojurongbe T.A, Bolaji O.S, and Adeyeba OA. 2013. "Assessing of clinical diagnosis, microscopy, rapid diagnostic tests and polymerase chain reaction in the diagnosis of *Plasmodium falciparum* in Nigeria" Malaria Research and Treatment. doi:10.1155/2013/308069. Epub Nov 24.PMID:24371538;PMCID:PMC385910

Oguonu T and Okafor H.U. 2007. "Comparison of clinical, microscopic and rapid diagnostic test methods in the diagnosis of *Plasmodium falciparum* malaria in Enugu, Nigeria" Nigeria Postgraduate Medical Journal; 14(4): 285-289. PubMed | Google Scholar

Okell LC, Ghani AC, Lyons E and Drakeley CJ 2009 "Submicroscopic infection in P. falciparum endemic populations: A systematic review and meta-analysis" Journal Infectious Disease 200:1509-1517

Okoli C, and Solomon M. 2014. "Prevalence of Hospital-Based Malaria among Children in Jos, North Central Nigeria". Br J Med Med Res.; 4(17): 3231-3237. Google Scholar

Olasehinde G.I, Ajayi A.A, Taiwo S.O, Adekeye B.T and Adeyeba O.A. 2010. "Prevalence and management of falciparum malaria among infants and children in Ota, Ogun State, Southwestern Nigeria" Africa Journal Clinical Experiment Microbiology; 11(3): 159-163.

Olasehinde G.I, Ojurongbe D.O, Akinjogunla O.J, Egwari L.O and Adeyeba A.O. 2015. "Prevalence of Malaria and Predisposing Factors to Antimalarial Drug Resistance in Southwestern Nigeria" Research Journal Parasitology; 10(3): 92-101.

Olorunfemi E.A and Adekoya G.I. 2013. “Impact of health education on malaria prevention practices among nursing mothers in rural communities in Nigeria” Nigeria Medical Journal; 54 (2): 115-122

Onwujekwe O, Hansan K. and Uzochukwu B. 2010. “Are malaria treatment expenditures catastrophic to different socio- economic and geographic groups and how do they cope with payment? A study in Southwest, Nigeria” Tropical Medicine International Health; 15 (1): 18-25. doi:10.1111/j.1365-3156.2009.02418.x.Epub 2009 Nov 3.PMID:19891758.

Oresanya O.B, Hoshen M. and Sofola O.T. 2008. “Utilization of insecticide-treated nets by under-five children in Nigeria: Assessing progress towards the Abuja targets”. Malaria Journal; 7:145

Osterbauer B, Kapisi J, Bigira V, Mwangwa F, Kinara S, Kamya M. and Dorsey G. 2012. “Factors associated with malaria parasitaemia, malnutrition, and anaemia among HIV-exposed and unexposed Ugandan infants; a cross-sectional survey” Malaria Journal; 11:432.

Palmer C.J, Bonilla A, Bruckner D.A, Barett E.D, Miller N.S, Haseeb M.A, MascI, J.R.and Stauffer WM. 2003.”Multicenter study to evaluate the optimal test for Rapid Diagnosis of Malaria in U.S. Hospitals” Journal of clinical Microbiology; 41 (11): 5178-5182. doi:10.1128/jcm.41.11.5178-5182.2003. PMID:14605156;PMCID: PMC 2622482.

Pembele G.N, Lázara R.R. and Jorge F. 2015. “Detection and species identification of malaria parasites by Nested-PCR : comparison with light microscopy and with SD BIOLINE malaria Ag Test in Luanda, Angola.” International Journal Tropical Disease Health; 10(1):1-13.

Phillips RS. 2001. “Current Status of Malaria and Potential for Control”. Clinical Microbiology Reviews; 14 (1): 208-226.

Plebani M . 2006. “Errors in clinical laboratories or errors in laboratory medicine?” Clinical Chemistry Lababoratory. Med;44:750-9 . http:// dx .doi .org/10 .1515/CCLM.123.

Ramnik Sood: 2006. “Medical Parasitology: In Text book of Medical Laboratory Technology, First edition”. Published by Jitendar P Vij. New Deihi India. ISBN 818071-591-X.Pg 183-185,

Reyburn H., Ruanda J. and Mwerinde O. 2006. “The contribution of microscopy to targeting antimalarial treatment in a low transmission area of Tanzania” Malaria Journal; 5:4. https://doi.org/10.1186/1475-2875-5-4

Sani U, Jiya N, and Ahmed H. 2013. “Evaluation of a malaria rapid diagnostic test among febrile children in Sokoto, Nigeria” International Journal Medicine Science; 3: 433-440.

Sherman, I.W., Eda, S.and Winograd, E. 2003. “Cytoadherence and sequestration in Plasmodium falciparum: defining the ties that bind.” Microbiology Infection; 5(10), 897-909. Snow

Sheyin Z, and Bigwan I. 2013. “Comparison of CARE START HRP2 rapid malaria test with light microscopy for guiding patient's treatment of fever in Nigeria endemic areas” Journal Medicine Science; 4(9): 353-356. Google Scholar

Shillcutt S, Morel C, Goodman C,Coleman, P,Bell D, Whitty C.J, and Mills A. 2008 Feb. “Cost- effectiveness of malaria diagnostic methods in sub-Saharan Africa in an era of combination therapy. Bull World Health Organisation.” 86:101-10. doi:10.2471/blt.0.042259. PMID:18297164; PMCID:PMC264734.

Singh N, Mishra A.K, Shukla M.M, Chand S.K, and Bharti P.K. 2005. "Diagnostic and prognostic utility of an inexpensive rapid on site malaria diagnostic test (ParaHIT) among ethnic tribal population in areas of high, low and no transmission in central India" BMC Infect Dis; 5:50.

The World Health Organization: 2006. "Malaria vector control and personal protection: report of a WHO study group". Geneva [http:// www.who.int/malaria/docs/ WHO-TRS-936s.pdf

Tierney L.M, McPhee S.J and Papadakis M.A. 2005. "Malaria. In: Current Medical diagnosis and Treatment 49th edition." 1417-1426.

Tine R.C, Ndiaye M.H and Hansson H.H. 2012. "The association between malaria parasitaemia, erythrocyte polymorphisms, malnutrition and anaemia in children less than 10 years in Senegal: a case control study." BMC Research Notes; 5, 565.https://doi.org/10.1186/1756-0500-5-565

Todd W.T.A, Lockwood D.N.J, Nye F.J, Wilkins E.G.L and Carey P.B. 2004. "Infection and immune failure." In: Haslett C, Chilvers ER, Boon NA and College NR editors. "Davidsons Principles and Practice of Medicine 19th edition." Churchill Livingstone, Edinburgh, London; 51-57.

Uzochukwu B.S, Obikeze E.N, Onwujekwe O.E, Onoka C.A, and Griffiths U.K. 2009. "Cost-effectiveness analysis of rapid diagnostic test, microscopy and syndromic approach in the diagnosis of malaria in Nigeria: Implications for scaling-up deployment of ACT". Malaria journal: 8:265.

Warrell D.A, Turner G.D and Francis N. 2002. “Pathology and Pathophysiology of human malaria” In: Warrell DA and Gilles HM editors. “Essential Malariology. 4th edition” Arnold A member of the Hodder Headline Group, London, 236-251.

Webb Jr 2009. “Humanity‘s Burden: A Global History of Malaria”. Cambridge University Press. ISBN 978-0-521-67012,

White N.J, Breman J.G, Kasper D.L, Fauci AS, Longo D, Braunwald E, Hauser S and Jameson J.L 2005. Editors. “Harrisons Principles of Internal Medicine 16th edition” McGrow Hill, New York; 1203-1210.

White N.J., Gordon C, Cook and Zumla A, 2003. . “Malaria. In: Editors. Manson s Tropical Diseases, 21st edition”. Saunders Elsevier Science, Health Science Division, London; 1205-1295.

Wongsrichanalai C, Barcus M.J, Muth S, Awalludin M.S. and Walther H.W. 2007. “A review of malaria diagnostic tools: microscopy and rapid diagnostic test (RDT).” American Journal Tropical Medicine Hygiene;77:119-27.

World Health Organization WHO 2016: “World Malaria Report “

World Health Organization WHO 2020: “World Malaria Report”

World Health Organization.2010. “Basic Malaria Microscopy. Learners Guide Part 1”. Second Edition.

World Health Organizations 2010. “Guidelines for the treatment of malaria”. Geneva: World Health Organization;.

World Health Organization.2005. “Malaria: Disease Burden in SEA region”. Regional Office For South-East Asia.

World Health Organization. 2004. “Malaria. Division of control of Tropical Diseases 2004”. World Health Organization. Regional office for South-East Asia. Malaria situation in SEAR countries. Bangladesh .

World Health Organization: 2010 “Parasitological confirmation of malaria diagnosis”. WHO technical consultation, Geneva, 6-8 October 2009. Geneva:

World Health Organization (WHO). 2011: “World malaria report 2011. Geneva”. Accessed August 23, 2019

Zarocostas J. Hundi B, Xaerstases E. 2010. ”Malaria treatment should begin with parasitological diagnosis where possible, says WHO”. BMJ; 340: c1402.

Appendix 1

QUESTIONNAIRE

COMPARISON OF CAPILLARY AND VENUOUS BLOOD IN DETECTION OF MALARIA PARASITEMIA AMONG CHILDREN ATTENDING SELECTED HEALTH FACILITIES IN IBADAN, OYO STATE.

UI/UCH EC Registration Number NHREC/05/01/2008a

Date..... H/FACILITY:

QUESTIONNAIRE NO [ ]

INTRODUCTION

I am a postgraduate student of University College Hospital, Ibadan, Department of Epidemiology and Medical Statistics, is conducting a study to Comparison of capillary and venous blood in detection of malaria among children between ages 6 months and 15 years attending a selected health facilities. You are invited to present your child to participate in this study and your participation is completely voluntary. Your decision to either take part or not in the study will NOT affect the type of service that you receive at this clinic.

You are invited to respond to the questions below with respect to your child. This interview will take about 12 minutes. Please note that participation is voluntary and you are at liberty not to answer any question you do not feel like answering. Information you provide will be kept confidential. Thank you.

A: SOCIO-DEMOGRAPHIC DATA:

1. Respondents relationship with child……

2. Age of respondent at last birthday (in years)……

3. Gender [ ] Male [ ] Female

4. Marital status [ ] Single [ ] Married [ ] Widowed [ ] Separated [ ] others

(please specify)……

5. Level of education [ ] No formal education [ ] Primary school [ ] Secondary School [ ] Tertiary (please specify ND, HND, B.Sc, M.A etc.)……

6. Occupation [ ] Employed for wages [ ] Self-employed [ ] Unskilled labor (petty trading) [ ] unemployed [ ] housewives [ ] others (please specify)……

8. Number of children in the family.....

9. Position of child in family.....

10. Age of child at last birthday (in years)……

B: CHILD HEALTH-RELATED INFORMATION

11. Body Temperature ……

12. Sex of the child [ ] Male [ ] Female

13. Weight (Kg) [ ] Height (M) [ ] MUAC Taken [ ] other [ ]

C.KNOWLEDGE ON MALARIA AND FEVER MANAGEMENT

14. What do you think causes fever in Children? Circle as appropriate (a) drinking dirty water (b) change in weather (c) teething (d) It is natural for children to have fever (e) Bacterial infections. Others specify…….

15. How do children get malaria infection? Circle as appropriate (a) when bitten by infected mosquito (b) when exposed to cold weather (c) exposure to stagnant water (d) playing with other children (e) others specify……

16. What are some things that can happen to a child when he/she has malaria?

Circle as appropriate: (a) Fever (b) Rigor and chills (c) Rashes (d) Muscle aches (e) (f) Flu-like illness (g) Poor appetite ……

17. When your child present with fever (increase in body temperature above 37.5^{o}C) typically what is your first response? Circle as appropriate:

(a) Home management with local herbs (b) Visit patent medicine store (c) Go to the nearest Clinic/hospital (d) Give any available drug (specify)…… (e) Tepid sponge, administer antipyretics and go to clinic/hospital (f) Others specify

……

18. Typically how long does it take from when your child present with fever and when you seek help from an approved health facility? Circle as appropriate

(a)Immediately (b) 2- 3 days (c) 3-4 days (d) I do not take the child to hospital

19. When you want to buy drug for a child with malaria fever, which of these is most important? (Only one response)

[ ] Paracetamol [ ] Antimalarial (CQ, SP, ACT, etc) [ ] Haematinics /multivitamins

[ ] Antibiotic [ ] others

20. Have your child taken any anti malaria drug in the past two weeks? Yes [ ] No [ ]

If yes which drug? ……..

D.LABORATORY INVESTIGATIONS

Blood sample collected Yes [ ] No [ ]

Capillary blood: Microscopy [ ]

RDT [ ]

Venous blood : Microscopy [ ]

RDT [ ]

Microscopic examination of Peripheral blood Film:

Thick film: MP negative / MP positive

Parasite count: (Capillary blood) (Venous blood)

Thin Film: Falciparum / Vivax/ Ovale / Malaria

INFORMED CONSENT FORM

UI/UCH EC Registration Number NHREC/05/01/2008a

My name is ……a postgraduate student of University College Hospital, Ibadan, Department of Epidemiology and Medical Statistics, is conducting a study to Comparison of capillary and venous blood in detection of malaria parasitemia among children

in a selected health facilities in Ibadan, Oyo state between ages 6 months and 15 years. You are invited to present your child to participate in this study and your participation is completely voluntary. Your decision to either take part or not in the study will NOT affect the type of service that you receive at this clinic.

What is the Purpose of this Study?

Malaria infection is a serious and sometimes fatal disease that is caused by a parasite called Plasmodium. These parasites are carried by mosquitoes that became infected from biting someone who already has the disease. Malaria is transmitted to other people when the infected mosquitoes bite them. Children who are infected with malaria become very sick with fever, shaking chills, tiredness, and sometimes vomiting and diarrhea may occur. Malaria is curable. The purpose of this study is therefore to detect the presence of malaria parasite in the blood of your child, so as to treat immediately before any form of complication set in.

Who will take part in the study and for how long?

Children between the ages of 6 months old and 15 years with symptoms; Headache Fever, vomiting, abdominal pain ,weakness of the body, Excessive crying, Irritable.

What will be done?

Should you accept to participate in this study, as part of the routine check up on your child‘s health, 0.5mls of blood will be collected from your child to test for the presence or absence of this parasite using a standard testing instrument known as Microscope.

To identify which type of the parasite is found in your child‘s blood in order to know which drug will be most appropriate, a blood smear will be made on a clean slide and examined using the microscope. The body temperature of your child will be taken to establish the presence or absence of fever. Other tests and treatment your child receives from this clinic will continue

whether you decide to allow your child participates or Not. Also you will be asked some further questions about your child and general social life at home as it relates to malaria prevention and control.

Confidentiality

Any information that is obtained in connection with this study and that can be identified with your child will be kept secret and no disclosed only with your permission. Confidentiality will be maintained by means of a code number. We will not use your child's name in any of the information we get from this study or in any of the research reports.

What are the Benefits and Risks?

All parents/caregivers was educated on the current National guideline for the prevention of malaria infection especially among under- fives. The benefit includes; diagnosis of malaria, treatment and management at no cost to the participants. The result of the test will also provide useful information for Nigeria National Malaria control program on the burden of malaria parasite among children. Your child may experience a little discomfort during the blood collection process.

Participation and Withdrawal

You can choose whether or not to be in this study. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. You may also refuse to answer any questions you do not want to answer. There is no penalty if you withdraw from the study and you will not lose any benefits to which your child is otherwise entitled.

Identification of Investigator

You can ask any questions that you have about the study. If you have a question later that you didn‘t think of now Email:- steleziafa@gmail.com.

I understand the concept of the research described above. My questions have been answered to my satisfaction, and I agree to allow my child participate in this study. I have been given a copy of this form.

_____ Date _____

Name and signature of caregiver

_____ Date _____

Name and Signature of Investigator

_____ Date _____

Witness