MALARIA TREATMENT OUTCOME AMONG UNDER-FIVE CHILDREN ATTENDING PRIMARY HEALTH CARE CENTRES IN UMUAHIA NORTH LOCAL GOVERNMENT AREA OF ABIA STATE NIGERIA.

BY

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ABSTRACT

Malaria remains a major health problem in Africa where one child in 10 dies before the age of five years. Despite the availability of affordable preventive/curative interventions in the Primary Health Centres (PHC) in Nigeria, morbidity and mortality from malaria remains high. This study was carried out to determine factors associated with malaria treatment outcome of under-five children that were treated for malaria at the PHC facilities in Umuahia North Local Government Area (LGA) of Abia State.

An analytical cross sectional study involving caregivers of children less than five years attending PHCs in Umuahia North LGA was carried out. A three stage sampling technique was used to select four of 31 PHCs, at Amaogwugwu, Umuawa-Alaocha, Ojike and World Bank Housing Estate, based on site and population of under-five attendees. Key Informant Interview (KII) was carried out with the PHC coordinator of the LGA and heads of the four selected PHC facilities to assess their knowledge and practices of malaria treatment. A semi-structured questionnaire was administered on caregivers of 562 consecutive children presenting with fever to determine factors associated with malaria treatment outcome. Outcome was considered good when a sick child recovers within 48hrs of commencing treatment. Data were analyzed using descriptive statistics, Chi square test and logistic regression at 5% level of significance.

From KII, the facility health workers based malaria treatment on presumptive diagnosis. Median age for children was 24 months (Range = 2 – 59 months) and mean age of caregivers was 32.5 ± 6.6 years. Two hundred and fifty-five (45.4%) of the children were brought to the health centre early. Among the mothers, 355 (63.2%) had been taught homecare of malaria. At presentation, 48 (8.5%) of the children had anaemia; 248 (44.1%) of them were sleeping under Insecticide Treated Nets (ITN). About 416 (74%) of the children had good treatment outcome. More

children (77.9%) treated on outpatient basis had a good treatment outcome compared with those who were admitted for observation (22.1%) $p < 0.05$. Also, a higher proportion of children presenting without anaemia (76.7%) had a significantly good treatment outcome compared with those that presented with anaemia (23.3%). Presence of anaemia [O.R 0.25 (C.I 0.13-0.500)] and being admitted [O.R 3.40 (C.I 2.22-6.49)], were both associated with poor treatment outcome. Providing health education on homecare of malaria to caregiver [O.R 3.85 (C.I 2.31-5.55)], making a child to sleep under ITN [O.R 2.37 (C.I 1.52-3.71)] and taking a sick child early to the health centre [O.R 2.07 (C.I 1.34-3.18)], were all significant predictors of good treatment outcome.

Educating caregivers on home management of malaria for their children, children sleeping under insecticide treated nets and taking sick children to the health centre promptly would improve malaria treatment outcome in the health centres.

Key words: Malaria, Treatment outcome, Caregiver, Under-five, Primary health care centre

Word count: 452

DEDICATION

This work is dedicated to the Almighty God, to my aged mother, my darling wife, son and my course mates for their support and understanding.

CERTIFICATION

This is to certify that this work titled "**Malaria treatment outcome among under-five children attending primary health care centres in Umuahia North Local Government Area of Abia State Nigeria",** is the original work of Akhimien Obeimen Moses and is submitted in partial fulfillment for the requirements for the award of Masters in Public Health Field Epidemiology Practice in the department of Epidemiology Medical statistics and Environmental Health of the Faculty of Public Health, University of Ibadan, Nigeria.

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Operational definitions

A child with malaria: Was any child below 5 years who presented in any of the selected PHCs in Umuahia North LGA with a fever of at least 2-3 days duration with or without vomiting, chills and rigors or any other signs of severe malaria in the absence of runny nose, measles, abscess, ear ache or signs and symptoms of any other well known causes of fever (WHO malaria manual for community health workers 1996, Sirima *et al.*, 2003).

Baseline status: The baseline status of the presenting children with fever were assessed both from clinical history taken from the care givers and physical examination by the researchers. The essence of this is to help us determine the children's status before treatment was commenced so as to eliminate those factors that may confound our results from the study.

Treatment outcome: This could either be good or poor.

Good outcome: A good outcome was when a child less than 5 years is treated in any of the selected PHCs for malaria and respond well to the administered anti malaria drugs (fever stops, and the child does not require any further treatment/visit to the health centre for the same ailment) at 48 hrs after treatment was started.

Poor outcome: A poor outcome was when an <5 years child is treated in any of the selected PHC for malaria and responds poorly to the administered anti malaria drugs (fever persist, convulsion sets in, severe anaemia, readmission in the health facility, requires immediate referral or death) 48 hrs after anti-malaria drugs were given.

Key informant interview

The PHC coordinator of Umuahia North LGA as well as the head of the four selected PHC facilities participated in the structured Key informant interview that was administered by the researchers.

Abbreviations

ABSEED	**Abia State economic empowerment development**
ACT	**Artemisinin – based combination therapy**
AIDS	**Acquired immunodeficiency syndrome**
ARDS	**Acute respiratory distress syndrome**
CD36	**Cluster of differentiation 36**
DDT	**Dichlorodiphenyltrichloroethane**
DEET	***N*,*N*-Diethyl-*meta*-toluamide**
GPI	**Glycosylphosphatidylinositol**
HLA	**Human leukocyte antigen**
HIV	**Human immunodeficiency virus**
ICAM – 1	**Intercellular adhesion molecule** 1
IL	**Interleukin**
IMCI	**Integrated management of childhood illnesses**
iNOS	**Induction of nitric oxide synthase**
ITN	**Insecticide treated net**
MDG	**Millennium developmental goal**
NDHS	**National demographic and health survey**
PfEM – 1	***Plasmodium falciparum* erythrocyte membrane protein – 1**
TNF	**Tumor necrotic factor**
UNICEF	**United nation children's fund**
VAT – genes	**Visceral adipose tissue – gene**
V – CAM – 1	**Vascular cell adhesion molecule – 1**
WHO	**World health organization**

CHAPTER ONE

1.0 INTRODUCTION

Malaria is a major infectious disease in tropical and subtropical countries. It has continued to be a major global health problem, with over 40% of the world's population – more than 2,400 million people – exposed to varying degrees of malaria risk in some 100 countries (Hay *et al.*, 2004, WHO, 2005). Most countries in Sub Sahara Africa have struggled in recent years to define affordable alternatives to the rapidly declining effectiveness of chloroquine and other social cultural factors that are affecting the treatment outcome of malaria in the Health care facilities (Etuk *et al.*, 2008). The treatment and control of malaria pose a serious challenge in sub-Saharan Africa where each year about 300 – 500 million attacks occur, from which 1.5–2.7 million people die (WHO Bulletin, 2000). These deaths occur mainly among children under five years old and pregnant women (Shane, 2001, Steketee *et al.*, 2001, Heggenhougen *et al.*, 2003). The epidemiological, medicinal and entomological aspects of malaria are well documented, as are its consequences for the social and economic outlook of countries in which it is endemic (NDHS, 2003, WHO, 2003, Bryce *et al.*, 2005, Breman *et al.*, 2004). Strategies for combating malaria in sub Sahara Africa and Asia now focus on reducing morbidity and mortality through prompt diagnosis and treatment (Bruce-Chwatt, 1984, Hetzel *et al.*, 2007). Eradication attempts in earlier days were largely successful in Europe and North America with Mass Drug Administration (MDA) strategy. Although, it failed in Africa, Central America, South America and Asia due to lack of resources and poor political will (Von Seidlein *et al.*, 2003, Kaneko *et al.*, 2000). However some local successes were achieved in South East Asia and this was mainly due to a combination of MDA and Artemisinin Combination Therapy (ACT) treatment campaign (Greenwood *et al.*, 1987, Song *et al.*, 2010). The number of malaria cases worldwide appears to be growing until the advent of the Artemesinin combination therapy (ACT), due to the increasing risk of transmission in areas where malaria control has declined and as a result of increasing prevalence of drug-resistant parasite strains (e.g. chloroquine resistance). In a relatively few

cases, because of increasing international travels, with modern rapid means of travel, large numbers of people from non-malarious areas are being exposed to the infection, which may seriously affect them only after they return home (Pasvol, 2005). The reported cases of increasing resistance of chloroquine and even more recently that of the ACTs in some south East Asian countries to malaria has led to a growing concern that in future no effective remedies will be available. The strategy adopted in the 1990s emphasized early diagnosis and prompt and efficient treatment. It was to be supplemented by initiatives aimed at prevention, the control of epidemics and continued observation of each country's malaria situation (Global malaria control strategy, 1992). There is currently a renewed interest in MDA (White, 2008, Song *et al.*, 2010) because of the previous successes in malaria control (Okiro *et al.*, 2007); highly efficacious anti-malarial drugs with a transmission reducing potential (Shekalaghe *et al.*, 2007, Nosten et al., 2000) and new insights in the nature of malaria transmission using sensitive parasite detection methods (Babiker *et al.*, 2008). Mathematical modeling has shown that malaria transmission is, in theory, susceptible to mass treatment programmes if all subjects within an endemic community could be given anti-malarias that clear parasitaemia during a period of absent or very low vector densities in areas where the intensity of transmission is already low (Maude *et al.*, 2010). Only time would tell if these strategies would work. However, it is worth noting that global targets for malaria prevention, treatment, and disease reduction are unlikely to be achieved without considerable investment in health delivery systems (O'meara *et al.*, 2009). In some areas, the malaria mortality rate remains high for a number of reasons including limited access to healthcare and/or increased drug resistance (Dzeing-Ella *et al.*, 2005). A better understanding of predictive factors that can make an uncomplicated malaria among under–five progress to severe malaria could aid health workers at the primary level of care to avoid delays in the referral of such cases so identified to the next level of care thereby reducing the probability of these children dying from malaria.

1.1 Background

According to the Carter Center, each year, malaria kills more than 1 million people, mostly children, with 350–500 million cases reported worldwide. Approximately 90% of all cases of malaria (a preventable disease) are in Africa, where one child in 10 dies before the age of five (WHO, 2005, FMOH, 2000). Malaria is a major threat to public health in Africa (Nafo-Traore, 2005) and remains the leading cause of death as well as debilitating fevers, low birth weights, anaemia, epilepsy and death in children under 5 years in this region (Black *et al.*, 2003). Bryce *et al.*, 2005 reported that 94% of deaths due to malaria worldwide occur in Africa where the economic impact is to the tune of $12 billion in lost productivity and health costs a year. However, national and international malaria control programs have been implemented, including: Integrated Management of Childhood Illness (IMCI), Roll Back Malaria initiative, the United States President Malaria Initiatives and the Global Fund. Major progress in the prevention and treatment of malaria has been reported from several countries through the adoption of Artemisinin-based combination therapy (ACT) (WHO, 2006), the use of insecticide treated bed nets (ITN), and Intermittent Preventive Treatment (IPT) for pregnant women and children. However, despite the existence of these effective treatment and protective measures, malaria continues to be of concern (Yamey, 2004). One strategy of the Roll Back Malaria Initiative to halve malaria mortality by 2010 is through prompt access to effective anti-malaria treatment, especially among under-five years children (Nabarro *et al.*, 1998, WHO, 2003). Primary Health Centres (PHCs) are the main channel through which key treatment and preventive interventions for malaria are delivered and for effective treatment of clinical malaria (Noor et al., 2007). However recent findings suggest that despite these affordable preventive and curative interventions in the Primary Health Centres (PHC), morbidity and mortality from malaria still remains high in most African countries and this may be as a result of not having quality paediatric care in both outpatient and inpatient services of health facilities; though this is essential for a credible and efficient primary health care system (Duke *et al.*, 2002). It has been

shown from most studies that the poor child, health care delivery in many developing countries are mainly as a result of incorrect diagnosis and assessments, misuse and inappropriate prescription of drugs and long waiting hours (Abubakar, 2006, Rowe *et al.*, 2000 and 2001). This could be a likely reason for the malaria treatment failure normally seen in the PHC facilities leading to severe consequences where referrals are delayed. The need to focus on improving primary health care delivery is essential in all developing countries (Zurovac *et al.*, 2006). The World Health Organization health Statistics (2009) showed that in 2007, there were an estimated 9 million child deaths. This was, significantly fewer than the 12.5 million estimated in 1990, and amounts to a 27% decline in the under-5 mortality rate over that period to 67 per 1000 live births in 2007. Also a UNICEF data shows a 28 percent decline in the under–five mortality rate, from 90 deaths per 1000 live births in 1990, to 65 deaths per 1000 live births in 2008. According to these estimates, the absolute number of child deaths in 2008 declined to an estimated 8.8 million from 12.5 million in 1990; the base line year for the Millennium Development Goals (MDGs). Reducing child mortality increasingly depends on tackling neonatal mortality on one hand and reducing morbidity and mortality from vaccine preventable diseases as well as malaria, HIV/AIDS and diarrhea diseases on the other and this would help countries to attain the Millennium Development Goals 4, 5 and 6 especially in Africa.

The Integrated Management of Childhood Illnesses (IMCI) strategy was introduced by the WHO and UNICEF to improve skills of health workers, the health system itself; and also the knowledge and practices of families in relation to the care of their young children (Oluwole *et al.*, 2000, Zurovac *et al.*, 2006). Yet, each year approximately 10 million children less than 5 years of age mainly in developing countries still die mostly from one of the following five conditions: pneumonia, diarrhea, malaria, measles and malnutrition. Surveys performed prior to the IMCI intervention revealed that many sick children were not properly assessed and treated by health care providers and that their parents were poorly advised on importance of home care and

how it can be done and as a result effective homecare was lacking in most cases (Duke *et al.*, 2002, Tangpukdee *et al.*, 2007).

The major causes of death in under-five children in Nigeria are malaria, vaccine preventable diseases, Acute Respiratory Infection (ARI) particularly pneumonia, diarrhea and malnutrition (FMOH, 2005). Despite initiating an integrated approach by the Federal Government of Nigeria to tackle these diseases by using the IMCI strategy, not much has been achieved largely due to the low coverage of this intervention. Evidence suggests that universal coverage of those interventions with evidence of impact on the major causes of death can significantly reduce childhood mortality.

In Nigeria, malaria is endemic throughout the country with more than 90 % of the population living in areas with constant risk of infection. Malaria is responsible for 25 % of infant mortality and 30 % of childhood mortality (FMOH, 2005). Nigeria accounted for one fourth of all estimated malaria cases in the WHO African Region in 2006. Nigeria like most other African countries is home to the most deadly form of the parasite (*Plasmodium falciparum*) and has the conducive climate for the vector (*Anopheles* mosquito species), to proliferate. Due to lack of funds, political will and/or infrastructure the federal government can not single-handedly mount effective anti-malaria campaigns, so there are a number of International Organizations rendering their full support to the malaria control effort in Nigeria.

Abia state, is located in the southeastern region of Nigeria and lies within approximately latitudes 4^0 40' and 6^0 14' north, and longitudes 7^0 10' and 8^0 east. It covers an area of about 5,243.7 sq. km which is approximately 5.8 per cent of the total land area of Nigeria and shares common boundaries to the north with Ebonyi State; the south and southwest with Rivers State; and, to the east and southeast with Cross River and Akwa lbom States, respectively. To the west is Imo State, and to the northwest is Anambra State. It has a total population of 2.8 million people and is divided roughly equally between females and males (1.39million and 1.43million

respectively). The population is projected to grow at three per cent per annum meaning that the state will have a population of about 3,379,168 in 2015. Due to the climatic condition of the State which is favourable for the breeding of the *Anopheles* mosquitoes, malaria remains a scourge affecting the populace especially the vulnerable group (women of child bearing age and under – five children who constitute 25 per cent and 21 percent of the state population respectively). Malaria is the leading cause of ill health and death in Abia; accounting for over 35 per cent of mortality and more than 60 per cent of morbidity (Abia State Health Data Bulletin, 2007 and Abia SSHDP, 2010). The Abia State Economic Empowerment Development Strategy (ABSEEDS) document, 2005 stated that chloroquine resistant strain of *Plasmodium falciparum* is responsible for most of the malaria deaths in the State. In Umuahia North LGA of Abia state, of the estimated 49,418 under-five year population, 1,011 cases of malaria were recorded in the health facilities in 2009 and nearly half of them needed immediate referral to secondary or/and tertiary health facilities (Umuahia North LGA Annual health report, 2010). Meanwhile, there is gross under reporting of these cases from the health facilities due to poor patronage by the populace, suggesting that this figure may be an underestimation of the real burden of malaria in Umuahia North LGA.

1.2 Statement of the problem

Despite affordable and effective anti-malaria therapy, the disease remains a leading cause of under-five mortality worldwide. A lot of factors are believed to be responsible for this trend. Such factors include late presentation at the health centres; cultural practices of caregivers of under – five children, availability of antimalarial drugs have been documented in most documents. So, it is pertinent to identify which of the above factors are responsible for the poor malaria treatment outcome that was found in Umuahia North LGA PHC facilities among under – five children from a pilot study done in two PHC facilities in Umuahia (21%). Identifying probable causes of poor malaria treatment outcome among under – five children is very

important considering the fact that it could lead to progression of uncomplicated malaria to the severe form with its accompanying high morbidity and mortality.

1.3 Purpose of the study

This study was carried out to identify reasons while despite the huge amount of money government and cooperate bodies are sinking into the prevention and control of malaria at the primary health care level, a lot of under – five children still die every year even after presenting at the health facility.

1.4 Significance of the study

This study is to assist the health workers in the local government health facilities, to timely identify factors contributing to poor treatment outcome of under-five children and so, reduce the number of late referrals to the secondary health facilities. With the anticipated drop in <5 years mortality, the society would be geared toward achieving the millennium development goal 4; so in the long run individual households, health care worker and the society shall benefit immensely from this study.

1.5 Research questions

What are those factors that if well addressed can improve the treatment outcome of under – five children receiving treatment for malaria fever in Umuahia North LGA PHC facilities while drastically reducing the incidence of referral to higher health facilities (secondary/tertiary)?

1.6 Assumptions

The assumption is that there are certain factors that may be associated with malaria treatment outcome in under – five children. These include

(a) Stage of the disease when the patient first presented to the clinic

(b) Level of home treatment activities carried out before coming to the clinic

(c) Duration of fever before the commencement of treatment

(d) Type of treatment given

(e) Maternal education

(f) Socio-economic status of mother and/or father

The variables that appear to be associated with malaria treatment outcome would then be subjected to appropriate statistical test to determine association.

1.7 Limitations

The results of the study may not be generalisable to the whole State given the fact that the study was undertaken in a town in one of the 17 LGAs making up Abia State. So it is possible socio-cultural practices may differ in the various senatorial districts or LGAs. It may be necessary therefore to conduct a bigger study to have a comprehensive picture of the problem but it can however be generalised for Umuahia North LGA. Also it is worth noting that malaria diagnosis was made presumptively and this could affect the specificity and sensitivity of the diagnosis so made.

1.8 Justification of the study

The major causes of mortality in Nigerian children include malaria (30%), vaccine preventable diseases particularly measles (22%), diarrhea (19%), acute respiratory infections (16%) with malnutrition underlying about 60% of these childhood deaths (National Health Management Information System, 1999). This child health situation poses a serious threat to future national productivity and development. From the National Demography and Health survey 2008, the under – five mortality rate was 157 deaths per 1,000 live births in the country an improvement from the figure of 201 in the 2003 NDHS, which is quite high compared to other African countries. However it is still a far cry from the target of the MDG. From the NDHS 2008, 42.4%

of under – five who developed fever in the 2 weeks before the survey in the urban areas took anti-malaria drugs as against 30.2% in the rural areas. In the urban areas 19.9% of the children took the treatment within 48 hours while 13.7% did so in the rural area. In 2003 Abia state had a life expectancy of 55 years for women and 54 years for men at birth higher than the national life expectancy at birth of 47.7 years. The high under – five mortality rate of 142 deaths per 1,000 live births contributing a great deal to this life expectancy. According to the Abia State Hospitals Management Board Statistical Data/ Information, 2008, over 75% of the Abia population resides in the rural areas where PHC serves as the main source of health care to the populace and only the privilege few patronizes the private clinics. Also about 14% of the children and 5% of pregnant women in the State would treat malaria fever with any available anti malaria drugs.

1.9 Aims and objectives

1.9.1 Aims:

This study aimed at determining factors that contribute to malaria treatment outcome among under – five children seen at Primary Health Centres in Umuahia North LGA of Abia State.

1.9.2 Specific objectives

1. To determine the outcomes of malaria treatment in under five children seen at the PHC facilities in Umuahia North LGA
2. To determine the human and material resources available for the provision of malaria treatment services for under – five children attending Primary Health Care facilities in Umuahia North LGA, of Abia State.
3. To identify factors that could affect under – five malaria treatment outcome in PHC facilities in Umuahia (health facility or household/caregiver) related.

CHAPTER TWO

2.0 LITERATURE REVIEW

Much work has been done on malaria largely because of the interest it has generated in recent past and the huge funding from the Bill Gates foundation, the "Global fund" as well as other international funding agencies. In a study carried out by Biritwum *et al.*, 2000 in Accra Ghana, they reported that malaria was the most common ailment reported by the caregivers in the two communities where their study was carried out (an average of two episodes in the nine months periods of their study). They also discovered that the level of education of the caregivers determine their use of left over drugs and un-prescribed drugs to treat their under – five children when they come down with malaria. Children of the poor and uneducated mothers among the study population were less likely to be taken to a clinic for treatment early when they are sick. This fact alone can cause high mortality rate among those children because they will end up been taken to the clinics when the sickness becomes severe (such that severe anaemia, convulsion and dehydration) may have set in. Efforts have been made to reduce the incidence of malaria among the vulnerable groups (pregnant women and under – five children) in most community through a lot of multi-agency collaborations using various means and techniques such as early diagnosis, prompt treatment of cases, withdrawal of resistant drugs from the malaria treatment protocol and vector control (elimination or reduction of contact with man) by using bed nettings. However a lot of factors would influence the way these insecticide treated bed nettings are used by the public. For instance, in a study conducted by Nuwaha in Mbarara, Uganda in 2001, he recommended that in order to increase the use of bed nets among the rural dwellers, it has to be affordable and there should be increase dissemination of health educational messages that stress

the benefits and ways of using bed nets in homes. He arrived at this conclusion because he found that owning a television, having mosquito nets in ventilators of houses, being a skilled worker or a professional, or living in a permanent house, believing that bed nets prevent malaria and believing that bed nets are not expensive affected the use of bed nets by the study group (ownership of a television were higher predictors). Salako *et al.*, 2001, *carried* out a study in Nigeria and found that the commonest form of first-line treatment given to under five children when they are sick was drugs gotten from patent medicine vendors or drug hawkers. They also found a configuration of signs and symptoms associated with chloroquine use, to include perception of the child having malaria, high temperature and loss of appetite. This is in order just that chloroquine has been abandoned for newer combination therapy drugs for malaria. The ability of the child's caregivers, both parental and professional, to make these distinctions in medication use will provide the foundation for health education in the promotion of appropriate early treatment of childhood fevers.

2.1 Malaria

Malaria, which is a life-threatening disease, has been around since ancient times. The early Egyptians wrote about it on papyrus, and the famous Greek physician Hippocrates described it in detail. It devastated the invaders of the Roman Empire (NIAID, 2002). In ancient Rome, as in other temperate climates, malaria lurked in marshes and swamps. People blamed the unhealthiness in these areas on rot and decay that wafted out on the foul air, or, as the Italians were to say, “Mal aria” or bad air. In 1880, Laveran a French physician working in Algeria, first identified the causative agent for human malaria while viewing blood slides under a microscope, to be the one-celled *Plasmodium* parasite (The Nobel foundation, 2007, Cox, 2010). Eighteen years later, they attributed the transmission of malaria to the bites of infected *Anopheles* mosquito (NIAID, 2002). Though in rare cases, a person may contract malaria through contaminated blood during transfusions (Kitchen *et al.*, 2005). There are equally documented

cases where a fetus may become infected transplacentally by its mother during pregnancy (Uneke, 2007).

The *plasmodia* responsible for malaria are protozoan parasites distinguished by their largely intracellular location in the human host and their dependence upon a vector both for completion of their life cycle and the transmission necessary for their survival. Unlike many of the larger metazoan parasites, plasmodia can multiply within the human host, so that a single infection can lead to an overwhelming parasitic burden. Malaria is the most important human parasitic disease in terms of the morbidity and mortality for which it is responsible. Of the four major species of plasmodia that routinely infects humans (*P. falciparum, P. vivax, P. malariae and P. ovale*), one (*P. falciparum*) is responsible for nearly all the severe diseases and mortalities due to malaria (1million to 2.5 million deaths every year) (Obionu, 2007). The other species cause febrile illness, sometimes leading to anaemia but rarely to death. A fifth species, *Plasmodium knowlesi*, is a zoonoses that causes malaria in macaques but can also infect humans (Fong YL *et al.*, 1971, Singh B *et al.*, 2004). *Plasmodium vivax*, the most geographically widespread of the *plasmodium* species and the cause of most malaria cases diagnosed in the United States, produces less severe symptoms. Relapses, however, can occur for up to 3 years in *P. vivax* infection, and the resulting chronic disease can be debilitating (Adak *et al*., 1998). Once common in temperate climate, *P. vivax* is now found mostly in the tropics, especially throughout Asia (Mendis *et al*., 2001). *Plasmodium malariae* infections not only produce typical malaria symptoms but they can also persist in the blood for very long periods, possibly decades, without ever producing symptoms (Gilles, 2002). A person with asymptomatic (no symptoms) *P. malariae*, however, can infect others, either through blood donation or mosquito bites. *P. malariae* has been wiped out from temperate climates, but it persists in Africa.

Various stages of the parasite include *sporozoites*, *hepatic-stage parasites*, circulating *intra-erythrocytic* asexual parasites, *gametocytes* and *hypnozoites* (the latter develop in *P. vivax* and *P.*

ovale only) and they do not cause symptoms. Three processes fundamental to the parasite's life cycle are believed to result in disease manifestation:

(1) The release of *merozoites* and other red cell contents when mature blood-stage *schizont* rupture;

(2) The accompanying destruction of infected erythrocytes and

(3) The adherence of parasitized erythrocytes to vascular endothelia, leading to the sequestration of parasitized erythrocytes in micro vascular beds (this process of cytoadherence and sequestration is peculiar to *P. falciparum)* (Miller *et al*., 2002, Molyneux *et al*., 2008)

2.2 Signs and symptoms

Symptoms of malaria include fever, shivering, arthralgia (joint pain), vomiting, anemia (caused by haemolysis), hemoglobinuria, retinal damage (Beare *et a.,l* 2006) and convulsions. The classic symptom of malaria is cyclical occurrence of sudden coldness followed by rigor and then fever and sweating lasting four to six hours, occurring every two days in *P. vivax* and *P. ovale* infections, while every three days in *P. malariae* infection (Malaria life cycle & pathogenesis, 2006). *P. falciparum* can have recurrent fever every 36–48 hours or a less pronounced and almost continuous fever. This fever with its accompanying malaise, anorexia, headache, chills, sweating and rigors (a cytokine mediated host response) is common to infections by almost all pathogens (Molyneux *et al*., 2008). Malaria fever is not usually distinguishable clinically from fever due to other agents. A periodicity of fever may develop that becomes highly suggestive of malaria, but this is usually in prolonged untreated infections. Periodicity results from synchronization of the parasite population, which may be due to the fact that elevated body temperature differentially slows the growth of late-stage parasites, allowing younger parasites to 'catch up'.

Monoclonal antibody to tumour necrosis factor (TNF) has been shown to reduce fever in West African children suffering from severe malaria. What triggers the host cytokine response in

malaria is unknown but is likely to be a toxin, or possibly several toxins, released from the rupturing *schizont.* Glycosylphosphatidylinositol (GPI) of parasite origin is one candidate for the role of a 'malaria toxin' (Molyneux *et al*., 2008). When administered as a vaccine to mice, a *P. falciparum* GPI conjugated to a suitable carrier prevents complications and death in animals challenged with a subsequent *P. falciparum* infection. A comparable effect is yet to be demonstrated in human malaria. It is probable that the 'antitoxic immunity' that is characteristic of older children and adults in endemic areas (less fever and illness, for a given density of parasitaemia, than in non immune people) may result from immune mechanisms directed against some of such parasite 'toxin' (Molyneux *et al*., 2008).

2.3 Epidemiology

2.3.1 Burden

Directly, malaria causes about 250 million cases of fever and approximately one million deaths annually (WHO Malaria report, 2008). The vast majority of cases occur in children under 5 years old (Greenwood *et al.*, 2005); pregnant women are also especially vulnerable. Despite efforts to reduce transmission and increase treatment, there has been little change in those areas at risk of this disease since 1992 (Hay *et al.*, 2004). Indeed, if the prevalence of malaria stays on its present upwards course, the death rate could double in the next twenty years (Brema, 2001). Precise statistics are unknown because many cases occur in rural areas where people do not have access to hospitals or the means to afford health care. As a consequence, the majority of cases are undocumented (Brema, 2001). Malaria is presently endemic in a broad band around the equator, in areas of the Americas, many parts of Asia, and much of Africa; however, it is in sub-Saharan Africa where 85 – 90% of malaria fatalities occur (Layne, 2007). The geographic distribution of malaria within large regions is complex, and malaria endemic and malaria-free areas are often found close to each other (Greenwood and Mulabingwa, 2002). In drier areas

within the malaria endemic belt, outbreaks of malaria can be predicted with reasonable accuracy by mapping rainfall (Crover *et al.*, 2005). Malaria is more common in rural areas than in cities; this is in contrast to dengue fever where urban areas present the greater risk (Van Benthem *et al.*, 2005). For example, the cities of Vietnam, Laos and Cambodia are essentially malaria-free, but the disease is present in many rural regions (Trug *et al.*, 2004). By contrast, in Africa malaria is present in both rural and urban areas, though the risk is lower in the larger cities (Keiser *et al.*, 2004). The global endemic levels of malaria have not been mapped since the 1960s. However, the Wellcome Trust, UK, has funded the Malaria Atlas Project (Hay, 2006) to rectify this, providing a more contemporary and robust means with which to assess current and future malaria disease burden.

Indirectly, malaria affects human development by impairing intellectual development and cause developmental abnormalities (especially following cerebral malaria). In endemic areas the disease is responsible for most lost school attendance and decrease productivity at work. Malaria also impacts negatively the economies of countries where the disease is endemic, by retarding the economy (the cost of a single bout of malaria is equivalent to over ten working days in Africa). Also the cost of treating an episode of malaria is in the range of $0.08 to $5.30 depending on the type of drugs prescribed as required by the local pattern of drug resistance. Meanwhile, it has been estimated in 2001 that 1.1 billion people had consumption levels below one dollar a day (Arrow *et al*., 2004).

2.3.2 Correlates/risk factors

Epidemics are caused by migration (i.e. Introduction of susceptible hosts), the introduction of new vectors, or changes in the habits of the mosquito vector in the human host (Pates and Curtis, 2005). Epidemics have occurred in North India, Sri Lanka, South East Asia, Madagascar and Brazil. What determines whether a particular individual infected with *P. falciparum* would

develop negligible, mild, moderate, severe or fatal disease is the result of an inter-play of several parasite, host, vector and circumstantial factors (Brema, 2001, Brema *et al*., 2007).

Parasite factors

We know that the different species of plasmodia cause different degrees of illness, with only *P. falciparum* commonly causing severe and fatal disease. Even within the species *P. falciparum*, different parasite 'strains' have different capacities to cause disease, a fact well known to physicians who administered malaria parasites to generate fever for the treatment of syphilis early in the last century (Raju, 2006). Virulence in *P. falciparum* may depend on the parasite's growth (multiplication) rate, its PfEMP-1 expression (affecting its cytoadherence characteristics or tissue specificity), its capacity for agglutination or rosette formation, and its toxin-releasing and cytokine-inducing potential (Molyneux *et al*., 2008). Parasite mutations are known to affect susceptibility to drugs for example, point mutations in the genes for parasite enzymes dihydrofolate reductase and *dihydropteroate synthetase* confer degrees of resistance to drugs, such as pyrimethamine and sulfadoxine respectively, that target these enzymes. While not affecting parasite virulence, these mutations may impair responses to initial treatment and thus influence disease severity (Kyabayinze et al., 2003).

Host factors

The most obvious host determinant of the severity of malaria is the level of acquired specific anti-malarial immunity (Kwiatkowski, 1999). Thus adults in an area of intense *P. falciparum* transmission tend to suffer few or mild symptoms while children in the same areas are at risk of severe and fatal disease. Immunity is directed against all stages of the parasite's life cycle in the human host (sporozoites, liver stages, blood stage asexual parasites and gametocytes) and probably also against 'toxins'. Both antibody and T cell–mediated mechanisms contributes to acquired specific immunity (Miller *et al*., 2002). Humans are diverse both in their capacity to mount an effective specific immune response and also in components of most or all of the non-

specific disease mechanisms (Molyneux *et al*., 2008). Since *P. falciparum* can kill large numbers of people before they reach reproductive age, it is likely that the parasite has exerted a selective pressure on many genes in populations in malarious areas. The most readily demonstrable example of such an effect is the gene mutation causing substitution of valine for glutamic acid at position 6 in the beta chain of hemoglobin (Chitins, 2001). An individual inheriting this mutation from both parents suffers from sickle cell disease, with frequent hematological crises and a strong likelihood of dying in childhood. An individual inheriting the mutation from only one parent has almost no clinical disease from the mutation but is dramatically protected against severe and fatal malaria. A balanced polymorphism results in the population, accounting for much higher prevalence of the sickle mutation in malarious than other areas of the world, and the prevalence of the heterozygous sickle state among children with severe malaria is about one tenth or less of its prevalence in the population as a whole (Kwiatkowski, 1999). Similar, but usually less powerful and less consistent, host genetic contributions to malaria susceptibility are now being identified through large case-control and parent–child studies with carefully defined severe disease in the index patients. Mutations affecting HLA class I and II antigens, the promoter region of TNF genes, ICAM-1 expression on vascular endothelium and many other mutations have been reported to be under or over represented among children with severe or fatal malaria (Molyneux *et al*., 2008). Some of these effects are seen in some populations but not in others, and some are associated with certain malaria complications (e.g. coma or severe anaemia) and not others. With the completion of sequencing of both human and *P. falciparum* genomes and with the increasing use of multicentre epidemiological studies, it is likely that more will be learned in the near future about parasite and host characteristics that determine disease severity and about particular combinations of host and parasite that may be critical for morbidity or mortality (Warrell and Gilles 2002).

Influence of transmission pattern

Even within malarious areas, there are great geographical differences in the frequency and seasonality of infections. There is some evidence to suggest that although children bear the brunt of disease in all such areas, the patterns of disease in children differ. Where transmission of *P. falciparum* is intense year 'round, the commonest complication is severe anemia in infants and toddlers, while in areas with restricted seasonal transmission, encephalopathy in toddlers and slightly older children is more common (Anumudu *et al*., 2007, Angyo *et al*., 1996). Whether and how disease patterns will be affected by the introduction of measures that alter infection rates such as impregnated bed nets remains to be seen as these methods are increasingly widely introduced.

Human host

The behavior of man plays an important role in the epidemiology of malaria. There must be a human reservoir of gametocytes to transmit the infection. In areas of high transmission, infants and young children are more susceptible to malaria.

Circumstance affecting the impact of malaria on a population

The impact of malaria in a population is partly determined by how quickly the disease is recognized and how well it is treated (Meremikwu *et al*., 2008, Noor *et al*., 2003). These are dependent upon the availability of health services, the quality of diagnostic and therapeutic facilities and the accessibility of these to all sectors of the population (Raso *et al*., 2005). The efficacy of drugs used in the first-line treatment of uncomplicated disease is also an important factor: there is epidemiological evidence of increasing malaria mortality associated with decreasing efficacy of chloroquine in parts of Africa over recent decades (Warsame *et al*., 2002, Sudre *et al*., 1992). Adequate drugs are an important though they are not a sufficient defence against severe malaria. However, as many fatal illnesses develop over a matter of hours and even

the most immediate therapy could not be expected to rescue the patient. Malaria control must therefore advance along all fronts, and the development of a vaccine continues to be a priority.

2.4 Signs and symptoms

Initially the symptoms resemble those of a minor viral illness. These include: lack of sense of well being, headache, fatigue, abdominal discomfort, muscle aches followed by fever and nausea/vomiting. These may ultimately be followed by typical malaria picture such as fever spikes (sudden rise and fall in temperature), chills and rigors (Warrell and Gilles, 2002).

Cold stage: As the temperature begins to rise, there is intense headache and muscular discomfort. The patient feels cold, clutches blankets, and curls up shivering and uncommunicative. Within minutes the limbs begin to shake and teeth chatter, and the temperature climbs rapidly to a peak (chills and rigor). The rigor usually lasts 10-30 minutes but can last up to 90 minutes.

Hot stage: By the end of rigor there is peripheral vasodilatation and the skin feels hot and dry and the temperature becomes high.

Sweating: Profuse sweat then breaks out lasting for 2-4 hours. The patient is soaked in sweat and the temp falls. The blood pressure is relatively low. The patient feels exhausted and may sleep off. Defervescence usually takes 4-8 hours. Fever is irregular at first with temperature exceeding 39°C and may rise up to 40°C.

Incubation time: The time interval between mosquito bite and development of malaria is 13-14 days except for *P. malariae* (35 days). If the infection is left untreated, the fever would recurs every third day in *P. vivax* and in *ovale* infection establishing a 2-day cycle (tertian). If the spike occurs every three days (Quartan) as in *P. malariae* infection i.e. fever recurs every fourth day (Obionu, 2007).

The pattern of fever in *P. falciparum* infection is erratic. Paroxysms with rigors are more common in *P. vivax* & *P. ovale* than in *P. falciparum* and *P. malariae* related malaria. True

rigors are unusual in naturally acquired *falciparum* malaria. As the infection continues the spleen and liver enlarge and anemia develops (Warrell and Gilles, 2002). The patient loses weight. If no treatment is given the natural infection stabilizes for several weeks or months and then gradually resolves.

Associated Symptoms: Mild abdominal discomfort, constipation and diarrhea are associated with malaria. Children would be irritable and have less appetite.

Malaria in Pregnancy: There is increased risk of severe *Falciparum malaria* in the second and third trimester of pregnancy. In areas of less transmission, it is an important cause of fetal death and results in high maternal mortality. In areas of intense transmission, it may be associated with low birth weight (Duffy and Fried, 2003). The infected mothers may even be asymptomatic.

Malaria in children: The majority of childhood malarial infections present with fever and malaise. In addition to the clinical features mentioned for adults, malaria in children may lead to; convulsions, coma, hypoglycaemia, metabolic acidosis and severe anaemia (Warrell and Gilles, 2002).

Diagnosis: Malaria is diagnosed by microscopic examination of the blood where thick and thin blood films are made on clean, grease free glass slides. This diagnosis rests on the demonstration of asexual forms of the parasite in peripheral blood smears stained with Giemsa's stain. Clinically, any patient suffering from fever with rigors in an endemic area should arouse a suspicion of malaria. Thus in endemic areas a doctor or any health worker can make a diagnosis of malaria based on the signs and symptom (presumptive diagnosis) (FMOH, 2005).

2.5 Clinical types

According to severity of illness, malaria can be broadly classified into two types viz Uncomplicated (Benign) and Complicated (Malignant) malaria.

Uncomplicated (benign) malaria

This form of malaria is a relatively milder disease which is generally caused by P. vivax and is seldom fatal. The chance of involvement of other organs (complications) is much less.

Complicated (malignant) malaria

This is malaria where the disease has become severe taking a rapid downhill course. It is caused mainly by *P. falciparum* and rarely by *P. vivax.* It has a poor prognosis (outcome).

Severe malaria

Severe malaria is almost exclusively caused by *Plasmodium falciparum* infection, and usually arises 6–14 days after infection (Trampuz *et al.,* 2003), especially in the non-immune and untreated, to cause possibly life-threatening organ or tissue dysfunction. In children in endemic areas, the common complications are severe anaemia, acidosis, prostration, hypoglycemia and encephalopathy (convulsions and altered consciousness); these may occur singly or in any combination. For reasons that are poorly understood, but that may be related to high intracranial pressure, children with malaria frequently exhibit abnormal posturing, a sign indicating severe brain damage (Molyneux et al., 2008). Malaria has been found to cause cognitive impairments, especially in children. It causes widespread anemia. This neurologic damage results from cerebral malaria to which children are more vulnerable (Boivin *et al* 2002 and Holding *et al* 2001). Cerebral malaria is associated with retinal whitening (Maude et al 2009), which may be a useful clinical sign in distinguishing malaria from other causes of severe fever (Beare *et al* 2006). Non-immune adults may suffer the same complications but are also liable to develop spleenomegaly (enlarged spleen), severe headache, cerebral ischemia, hepatomegaly (enlarged liver), hypoglycemia, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation and intravascular haemolysis giving rise to hemoglobinuria which can cause renal failure, (renal failure may cause black water fever, where hemoglobin from lysed red blood cells leaks into the urine) (WHO, 2000). Severe malaria can progress extremely rapidly and cause death within hours or days (Trampuz *et al.,* 2003). In the most severe cases of the disease, fatality rates can exceed 20%, even with intensive care and treatment (Kain *et al.,* 1998). In endemic areas, children suffer most of the severe disease, adults being protected by a combination of innate and acquired immunity (Kwiatkowski, 1999). Even in children in endemic

areas, it is only a minority of infections that progress to severe disease. In endemic areas, treatment is often less satisfactory and the overall fatality rate for all cases of malaria can be as high as one in ten (Mockenhaupt *et al.,* 2004). Over the longer term, developmental impairments have been documented in children who have suffered episodes of severe malaria (Taylor *et al*., 2004, Carter *et al.,* 2005).

Relapsing malaria is seen in both *P. vivax* and *P. ovale*, but not in *P. falciparum*. Here, the disease can relapse months or years after exposure, due to the presence of latent parasites in the liver. Describing a case of malaria as cured by observing the disappearance of parasites from the bloodstream can, therefore, be deceptive. The longest relapse period reported for a *P. vivax* infection is 30 years (Trampuz *et al.,* 2003). Approximately one in five of *P. vivax* malaria cases in temperate areas involve over wintering by hypnozoites (i.e., relapses begin a year after the mosquito bite) (Hulden *et al*., 2005, Adak *et al.,* 1998).

2.6 Pathogenesis of complicated disease

Cytoadherence and sequestration

Erythrocytes containing mature stages of *P. falciparum* adhere to micro-vascular endothelium and thereby accumulate in capillaries and venules of deep tissues (*sequestration*). Several lines of evidence suggest that the process of sequestration may be important in the pathogenesis of severe disease: (1) sequestration is peculiar to *P. falciparum*, which is the only plasmodia species causing severe disease; (2) histological samples from various tissues in fatal malaria commonly reveal intense sequestration of parasitized erythrocytes; (3) sequestration is maximal in those tissues or organs that are most susceptible to functional impairment in severe *falciparum* malaria i.e. brain, bone marrow, intestinal mucosa and the lungs (Molyneux *et al*., 2008). Cytoadherence involves a specific linkage between proteins expressed on the surface of the infected red cell and receptors on host tissues. As the parasite matures in the infected erythrocyte, a family of highly variable parasite genes (‘var’ genes) begin to encode proteins that pass to the surface of the cell,

where they are collectively known as *P. falciparum erythrocyte membrane protein 1 (PfEMP-1)* (Beeson and Brown, 2004). Other parasite-derived proteins are similarly expressed on the red cell surface but remain to be characterized. Variability in the PfEMP-1 expressed by a particular population of parasites has been estimated at around 2% per parasite life cycle, a property that may enable the parasite to evade some of the host's specific acquired immune responses directed at these proteins. When studied in an *in vitro* culture, PfEMP-1 expression and specific cytoadherence are accelerated and enhanced with elevation of the surrounding temperature from 37◦ to 40◦C, suggesting that fever may have a similar effect *in vivo* (Molyneux *et al*., 2008). Host receptors capable of mediating cytoadherence include CD36, ICAM-1, chondroitin sulphate A, hyaluronic acid, e-selectin, V-CAM-1 and thrombospondin. ICAM-1 may be the principal receptor mediating cytoadherence in the brain, CD36 in most other tissues and chondroitin sulphate A in the placenta. Cytoadherence of parasitized erythrocytes resembles that of host leucocytes in that there are rolling and static components and it is likely that different receptors mediate each of these processes. Cytokines such as TNF-α up-regulate the expression of host endothelial receptors, providing another mechanism by which malaria infection enhances its own sequestration. Parasitised erythrocytes cytoadhere not only to endothelial cells but also to other parasitized *erythrocytes*, a process leading to 'auto-agglutination' of infected red cells. In some (not all) instances, platelets appear to be a necessary intermediary between adjacent cells. Auto-agglutination may account for the appearance of heavily sequestered venules and capillaries, in which parasitized cells towards the centre of the vessel lumen are some distance from the vascular endothelium and unlikely to be adherent to it (Wahlgreen *et al*., 1999). Parasitized erythrocytes may also adhere to *uninfected erythrocytes*, resulting in the formation *in vitro* of 'rosettes', each consisting of a parasitized red cell surrounded by several uninfected erythrocytes (Chitnis, 2001). Although some studies have shown that parasites with a capacity to form rosettes are more likely than others to be associated with severe disease, this has not been found in all surveys, and rosettes have not been identified in human tissues from patients dying of

falciparum malaria, so that the contribution of rosetting to sequestration is uncertain. There is still no incontrovertible evidence that sequestration mediates tissue or organ dysfunction, but the circumstantial evidence is strong. Several mechanisms are plausible and require continued research: (1) actively metabolizing parasites may 'rob' local tissues of ingredients essential to their viability, such as glucose and micronutrients; (2) the perfusion of tissues may be impaired by the mass of stationary parasitized red cells; (3) damage can be demonstrated to junctions between adjacent endothelial cells, with loss of integrity of the vessel wall (which in the brain constitutes the 'blood-brain barrier') (Taylor *et al*.,); (4) the eventual rupture of *P. falciparum* schizont, with the local discharge of merozoites, 'toxins' and haemozoin (pigment resulting from the parasite's digestion of hemoglobin) must provide a large additional local stimulus. Consequences of this include demonstrable recruitment of leucocytes, deposition of fibrin and platelets, and the induction of nitric oxide synthase (iNOS), which suggests that nitric oxide, may be generated locally (Molyneux *et al*., 2008). It is clear that sequestration commonly has no detectable adverse effect on tissue or organ function, because sequestration is also a feature of uncomplicated *falciparum* malaria (no late-stage parasites are visible in the peripheral blood). It remains to be determined whether impaired tissue function results when there is an over whelming mass of sequestered parasites or from a crucial distribution or quality of the sequestered cells.

Cytokine responses

Cytokines mediate the characteristic fever of malaria, as of other infections (discussed above). Whether cytokines are essential to the pathogenesis of severe and fatal disease remains a subject of important inquiry (Molyneux *et al*., 2008). Several studies have demonstrated an association between circulating cytokine concentrations (TNF, IL-1, IL-6, IL-8) and disease severity, but whether this association is causal and if so in which direction remains to be elucidated. A large randomized controlled trial of recombinant anti-TNF in West African children with malarial coma demonstrated an anti-fever effect but no benefit to survival. This however does not

disprove a role for TNF in pathogenesis of fatal disease, as the intervention may have been too late or in other ways ineffectual (Grau *et al*., 2003). A lot of studies using drugs that ameliorate cytokine responses such as pentoxyfilline, have so far failed to provide evidence that such drugs prevent or reverse severe disease. Several problems make it difficult to study the role of cytokines in the pathogenesis of fatal malaria. There is no readily available animal model of severe falciparum malaria. Malaria in common animal models have different pathology; trials of anti-cytokine treatments in patients with severe malaria may enroll subjects after crucial damage has already been done and important cytokine effects may occur locally in tissues not accessible to study during life (Molyneux *et al*., 2008). Similar problems surround the study of other mediators and downstream effects of cytokine activity.

Severe anaemia

A degree of anaemia develops in most malaria infections, and severe anaemia (packed cell volume 15% or less, hemoglobin concentration 5 g/dl or less) is a common and important single complication, especially in infants and toddlers in endemic areas (Orimadegun *et al*., 2007, Anumudu *et al*., 2007). Mechanisms that may contribute to the development of anaemia include (1) the destruction of red cells by parasites at schizont rupture; (2) reduced life span of un-parasitized erythrocytes, possibly resulting from cross-reacting antibodies developed against the surface of parasitized cells – increased splenic clearance of un-parasitized red cells can be demonstrated during malaria; and (3) impaired bone marrow function, as dyserythropoiesis is visible on light microscopy of bone marrow smears and reticulocytes are absent from the peripheral blood even when anaemia is severe (Molyneux *et al*., 2008). Sequestration of parasitized erythrocytes in bone marrow sinusoids is a common finding and it seems likely that dyserythropoiesis is mediated by altered local cytokine secretions. Some studies suggest that in severe anaemia there is a relative deficiency of the IL-10 response that normally modulates TNF activity (Miller *et al*., 2002). It is possible that haemozoin, released with rupture of schizont-

infected red cells, is toxic to the macrophages that consume it, with consequent deficient secretion of IL-12, leading to impaired generation of a TH1 host response. This impairment of macrophage function may partially explain the increased occurrence of non-typhoid salmonella infections observed in children with severe malarial anaemia (Graham *et al*., 2000).

Coma and convulsion

In an individual with altered consciousness and *P. falciparum* parasitaemia, several possibilities must be considered: (1) the illness may have another cause, with incidental parasitaemia, this is a strong possibility in populations having a high prevalence of asymptomatic parasitaemia; (2) the patient may be having a seizure, sometimes extraneous movements are not obvious, and the true nature of the event is revealed by electro-encephalography: malaria fever is particularly likely to precipitate a febrile convulsion in infants and young children, and more complex seizures are also common in malaria in this circumstance, consciousness may be regained within a few minutes or hours after the seizure stops or is treated; (3) the patient may be in the post-ictal phase after a recent convulsion again, recovery of consciousness may then be imminent; (4) there may be a metabolic complication of malaria, such as hypoglycemia; or (5) the disease may have none of the foregoing explanations and be directly due to *P. falciparum* infection (Molyneux *et al*., 2008). Mechanisms by which intra cerebral sequestration may contribute to encephalopathy have been discussed above. In considering the likely pathophysiology of malaria coma, two observations must be recognized: (1) about 90% of children and 95% of adults who recover from a malaria coma do so without detectable neurological sequelae: whatever the principal mechanisms of coma, they do not generally produce irreversible damage to brain tissue; (2) conversely, 10% of children and 5% of adults who recover consciousness have detectable neurological sequelae, and these are often accompanied by areas of infarction demonstrable by computed tomography of the brain (Grau *et al*., 2003). It is likely that coma is usually the result of a diffuse impairment of cerebral function related to sequestration and that sequelae result in a minority of cases when a vessel or group of vessels become secondarily obstructed by parasites,

pigment and fibrin deposition, leading to localized infarction (Grau *et al.,* 2003). In the majority of children with 'cerebral malaria', the opening pressure of the cerebrospinal fluid is high. Papilloedema is occasionally found and is associated with a poor prognosis. At autopsy, brain weights tend to be higher than appropriate for the child's age and weight, and flattened gyri and filled sulci suggest that the brain has been swollen within the skull. All these features suggest that cerebral oedema is a common component of the pathology of fatal cerebral malaria (Taylor *et al*., 2004). Frank herniation of brain between compartments is, however, rarely found at autopsy in a patient dying of malaria coma.

Hypoglycemia

Children with malaria of vary grade commonly have hypoglycemia, but correction of the plasma glucose concentration with a dextrose infusion rarely restores consciousness, suggesting additional causes of coma (Molyneux *et al*., 2008). Hypoglycemia in these circumstances may be due to a combination of reduced hepatic glycogen reserves, inhibition of hepatic glucuronyl transferase (and therefore of gluconeogenesis) by cytokines and anaerobic glycolysis in hypoxic or under perfused tissues (Maitland *et al.,* 2003). Plasma insulin concentrations are appropriately low. Hypoglycemia may also develop through a different mechanism in individuals especially pregnant women who are receiving treatment with quinine. This drug is a potent stimulus to the secretion of insulin from the pancreatic beta cells, which have increased activity and sensitivity in pregnancy, and plasma insulin concentrations in this circumstance are higher than appropriate for the plasma glucose concentration.

Acidosis

Often indicated clinically by the patient's characteristically deep breathing, acidosis may be largely the result of impaired tissue oxygenation through a combination of anaemia, hypovolaemia and impaired tissue perfusion and metabolism in the presence of sequestered parasites (Maitland *et al.,* 2003).

Acute renal failure

Rarely seen in children in malarious areas, acute renal failure is a grave and quite common complication of falciparum malaria in non-immune adults. It develops in the context of hypovolaemia and hypotension that may follow fluid losses through anorexia, vomiting, sweating and hyperventilation (Maitland *et al.,* 2003). Clinically and histopathologically, the underlying event is acute tubular necrosis, and recovery is usual within a few days or weeks if the patient survives the illness and is appropriately dialyzed (Molyneux *et al*., 2008).

Disseminated intravascular coagulation

An overt bleeding tendency in severe malaria is uncommon (rare in children), but some degree of activation of the coagulation cascade is usual and some degree of thrombocytopenia is almost invariable. In most patients with symptomatic malaria, plasma antithrombin III concentrations are low, in association with increased plasma levels of thrombin–antithrombin III. Platelet survival is reduced and bone marrow appearances suggest dyspoietic thrombogenesis (Miller *et al*., 2002). Intravascular deposition of platelets can be demonstrated in sites of intense sequestration, sometimes in association with micro-thrombi (Warrell and Gilles, 2002).

Pulmonary oedema and acute respiratory distress syndrome (ARDS)

These two complications may resemble each other clinically and radiologically but have a different pathogenesis. Pulmonary oedema may follow excessive infusion of fluids, especially in

the presence of impaired renal function (Maitland *et al*., 2003). In ARDS, there has not been over-hydration, and pulmonary wedge pressures are low or normal. Histology indicates the presence of both parasitized red cells and leucocytes in pulmonary micro-vessels. This condition is uncommon in children and is often fatal when it occurs in adults (WHO,2000, Molyneux *et al*., 2008).

2.7 HIV and malaria

Although co-infection with HIV and malaria does cause increased mortality, this is less of a problem than with HIV/tuberculosis co-infection, due to the two diseases usually attacking different age-ranges, with malaria being most common in the young and active tuberculosis most common in the old (Korenromp *et al.*, 2005). Although HIV/malaria co-infection produces less severe symptoms than the interaction between HIV and TB, HIV and malaria do contribute to each other's spread. This effect comes from malaria increasing viral load and HIV infection increasing a person's susceptibility to malaria infection (Abu-Raddad *et al.*, 2006).

2.8 General treatment guidelines

When a patient in or from a malarious area presents with fever, a blood smear should be prepared and examined to confirm the diagnosis and identify the species of infecting parasite. The management of malaria depends very much on the health facilities available and the endemicity of the disease, i.e. the likely immune status of the patient. For example, in areas of intense transmission asymptomatic parasitaemia is common in older children and adults, and fever is more likely to be the result of some other infection. On the other hand fever may precede detectable parasitaemia in non immune adults or young children. Patients with severe malaria or those unable to take oral drugs should receive parenteral anti malarial therapy. If there is any doubt about the resistance status of the infecting organism, then quinine, quinidine or artemisinin combination therapy (ACT) should be given. If the temperature is high on admission (greater

than 38.5oC) then symptomatic treatment with antipyretics and tepid sponging brings symptomatic relief, and also reduces the likelihood that the patient will vomit the oral anti-malarials. This is particularly important for young children. Several drugs are available for oral treatment, and the choice of drug depends on the likely sensitivity of the infecting parasites. Chloroquine and amodiaquine used to be the treatment of choice for the benign human malarias. This has been abandoned for the newer ACTs like artemether + lumefantrine (co-artem), Artesunate + Amodiaquine, Artesunate + mefloquine and Artesunate + sulfadoxine/pyrimethamine due to the development of resistance by the parasite (FMOH, 2005, Obionu, 2007).

In uncomplicated malaria: Infections due to *P. vivax, P. malariae, P. ovale* and known sensitive strains of *P. falciparum* should be treated with oral sulfadoxine/pyrimethamine (Ross *et al*., 2008).

Patients should be monitored for vomiting for 1 hour after the administration of any oral antimalarial drug.

Symptom based treatment with tepid sponging and acetaminophen administration lowers fever and thereby reduces the patient's propensity to vomit these drugs (WHO, 2001). Minor central nervous system reactions (nausea, dizziness, and sleep disturbances) are common. Pregnant women, young children, patients unable to tolerate oral therapy and non immune subjects (e.g. travelers) with suspected malaria should be hospitalised.

If there is any doubt as to the identity of the infecting malarial species, treatment for falciparum malaria should be given. A negative blood smear does not rule out malaria; thick blood films should be checked 1 and 2 days later to exclude the diagnosis.

Non immune subjects with malaria should have daily parasite counts performed until negative thick films indicate clearance of the parasite. If the level of parasitaemia does not fall below 25 percent of the admission value at 48 hours or if the parasitaemia has not cleared by 7 days (and

compliance is assumed), drug resistance is likely and the regimen should be changed (WHO, 2001).

In severe malaria: Severe falciparum malaria constitutes a medical emergency requiring intensive nursing care and careful management. The patient should be weighed and if comatose, placed on his or her side and given a single parenteral dose of phenobarbital (5 to 20 mg/ kg) to prevent convulsions especially in children. Frequent evaluation of the patient's condition is essential. The choice of antimalarial drug depends on knowledge of the prevailing sensitivity of *P. falciparum* to anti-malaria (Ross *et al*., 2008) and if there is any doubt, quinine should be given. The optimal therapeutic range for quinine in severe malaria is not known with certainty, but total plasma concentrations between 8 and 20 mg/ml are effective and do not cause serious toxicity. An initial loading dose should be given so that therapeutic concentrations are reached as soon as possible. If the patient remains seriously ill or in acute renal failure for more than two days, the maintenance dose should be reduced by 30 to 50 percent to prevent toxic accumulation of the drugs. The initial doses should never be reduced if chloroquine is given, dose reduction is unnecessary even in renal failure (White, 2005). Provided that it can be performed safely, exchange transfusion is indicated for patients with high level parasitaemia (greater than 15 percent) and vital organ dysfunction. Exchange transfusion should be considered for severely ill patients with a level of parasitaemia between 5 and 15 percent (Brema *et al*., 2006).

When patient is unconscious: The blood glucose level should be measured every 4 to 6 hours, and values below 40mg/dl indicate prompt treatment with intravenous dextrose. All patients treated with intravenous quinine should receive a continuous infusion of 5 to 10 percent dextrose. The parasite count and hematocrit level should be measured every 6 to 12 hours. Anaemia develops rapidly; if the hematocrit falls below 20%, then whole blood (preferably fresh) or packed cells should be transfused slowly, with careful attention to circulatory status and judicious use of a small dose of a diuretic to prevent fluid overload. Exchange transfusion should be strongly considered for patients with a high level of parasitaemia (greater than 10 %) and

altered mental status. Renal function should be checked daily. Management of fluid balance is difficult in severe malaria because of the thin dividing line between over hydration (leading to pulmonary oedema) and under hydration (contributing to renal impairment). If necessary, pulmonary artery occlusion pressures should be measured and maintained in the low normal range. As soon as the patient can take fluids, oral therapy should be substituted for parenteral treatment (Gilles, 2002).

In acute renal failure: If the level of blood urea nitrogen or creatinine rises despite adequate rehydration, fluid administration should be restricted to prevent volume overload. Even with adequate peritoneal dialysis, secondary bacterial infections are common in the tropics, and hemo-dialysis and hemo-filtration are preferable. Some patients will pass small volumes of urine sufficient to allow control of fluid balance; these cases can be managed conservatively if other indications for dialysis do not arise (Warrell and Gilles, 2002).

Renal function usually improves within days, but full recovery may take weeks.

In other complications: Patients who develop spontaneous bleeding should be given fresh blood and intravenous vitamin K. Convulsions should be treated with intravenous or rectal benzodiazepines. Aspiration pneumonia should be suspected in any unconscious patient with convulsions, particularly with persistent hyperventilation. Intravenous antimicrobial agents and oxygen should be administered, and pulmonary toilet should be undertaken. Hypoglycaemia or gram negative septicaemia should be suspected and treated when any patient suddenly deteriorates for no obvious reason while receiving anti-malaria treatment.

2.9 Malaria parasite life cycle

The life cycle of the parasite in the mosquito take about 12 days to complete, depending on the atmospheric temperature (optimum temperature is 17°C to 80°C). The incubation period in mosquito which is the interval elapsing from the ingesting of infected blood by the mosquito to the appearance of sporozoites in the saliva of the mosquito is known as the extrinsic incubation

period. The pre-latent period (intrinsic incubation period) is the time which elapses between the infection of man by the sporozoites and the first appearance of erythrocytic parasites in the blood and this is usually 6 – 9 days except in *P. malariae* in which it can range from 13 – 16 days. Thereafter symptoms of malaria appear as the parasitaemia builds up (Molyneux *et al*., 2008).

The life cycle of malaria parasite (*plasmodium*) takes place partly in the mosquito – sexual phase and partly in man – the asexual phase. Infection is initiated when the female *Anopheles* mosquito inoculates sporozoites into the body during a blood meal. In all the four species of *Plasmodium,* the sporozoites after a few hours (usually 30 minutes to one hour) invade the liver parenchyma cells to form the primary tissue schizont or pre-erythrocytic or (the primary exo-erythrocytic) liver schizont. When mature, the liver cells rupture liberating thousands of merozoites which invade the red blood cells.

In *P. ovale* and *vivax*, the pre-erythrocytic schizonts produce, in addition to the blood merozoites, other merozoites which invade more liver cells (secondary exo-erythrocytic phase) to liberate more merozoites into the blood stream. These merozoites resulting from the secondary (persistence) liver phase (the hypnozoites) are responsible for relapse at a later stage (Cogswell, 1992). Some of these asexual forms of the parasite in the red blood cells differentiate to trophozoites, appearing first as ring trophozoites and later develop to form mature schizont containing daughter merozoites (erythrocytic schizont). The red cells rupture releasing merozoites and initiating clinical attack (Obionu, 2007). Clinical symptoms are thus produced by the rupture of large numbers of erythrocytic schizont. The asexual cycle last approximately 48 hours in *P. falciparum, ovale and vivax* and 72 hours in *P. malariae.* Some of the asexual cells in the red blood cells differentiate into sexual forms called gametocytes. The gametocytes in the infected red blood cells serve as source of infection when they are picked up by mosquitoes during blood meals. In the mosquito, the gametocyte escapes from the containing red blood cells and mature into male and female gametes (micro and macro-gametes). Fertilization takes place giving rise to ookinate, then oocyst. The oocyst undergoes some mitotic division producing large

numbers of sporozoites, the infective parasitic forms. These are however found in all parts of the insect body, some eventually reaching the salivary glands from where they are injected with the saliva into the human host (Obionu, 2007).

2.10 Vector

The epidemiology of malaria results from the demands of its life cycle, which requires reservoirs of infected and uninfected humans, competent anopheline vectors, and multiple opportunities for contact between the vector and its human host. Vectors are insects, which transmit infection by biting or by depositing infected material on the skin, food or other objects Vectors for malaria are female *Anopheles* mosquitoes. Vectors differ considerably in their natural abundance, feeding, and resting behaviours, breeding sites, flight ranges, choice of blood source and vulnerability to environmental conditions and insecticides Malaria is often seasonal, coinciding with the rainy season which provides water for mosquito breeding and increased humidity favoring mosquito survival For transmission of malaria, the mosquito must live at least 10 days after an infective blood meal during which it must bite a susceptible human host.

Mosquito from the Spanish meaning little fly is a common insect in the family *Culicidae* (from the Latin *culex* meaning midge or gnat) (Brown, 1993). Mosquitoes resemble crane flies (family *Tipulidae*) and chironomid flies (family *Chironomidae*), with which they are sometimes confused by the casual observer. Mosquitoes go through four stages in their life cycle: egg, larva, pupa, and adult or imago. Adult females lay their eggs in water, which can be a salt-marsh, a lake, a puddle, a natural reservoir on a plant, or an artificial water container such as a plastic bucket. The first three stages are aquatic and last 5–14 days, depending on the species and the ambient temperature; eggs hatch to become larvae, then pupae. The adult mosquito emerges from the pupa as it floats at the water surface. Adults live for 4–8 weeks (Western County Department of health, 2010). Mosquitoes have mouthparts which are adapted for piercing the skin of plants and animals. While males typically feed on nectar and plant juices, the female

needs to obtain nutrients from a "blood meal" before she can produce eggs. There are about 3,500 species of mosquitoes found throughout the world (Leisnham, 2010). In some species of mosquito, the females feed on humans, and are therefore vectors for a number of infectious diseases affecting millions of people per year (Molavin, 2003; American Mosquitoes Control Association, 2008).

All forms of human malaria are transmitted in nature by the bites of *Anopheles* mosquito though other forms of infections seldom occur i.e. transfusion of blood containing erythrocytic phase of the parasite (transfusion malaria) or even from mother to child through the placenta (congenital malaria). The major vectors of human malaria are *Anopheles gambiae*, *Anopheles arabiensis, Anopheles funestus* and *Anopheles melas. Anopheles arabiensis* are most dominant in the savannah and cities while *Anopheles gambiensis* are found mainly in the forested regions of the tropics. *Anopheles funestus* are unevenly distributed while *Anopheles melas* are found in coastal areas as it has a high affinity for salty waters. The female mosquito get infected when it ingest human blood containing male and female gametocytes (Warrell and Gille, 2002).

Mosquitoes of different species lay their eggs in a variety of water sources that range from small containers to vast expanses of marshland. The larval stage is always aquatic and shuttles from the subsurface where it filters feeds on micro-organisms to the surface to obtain oxygen through a snorkel-like breathing apparatus. The pupa stage does not feed but unlike most Insect pupae is extremely active. The adult emerges from the pupa case using air pressure and assume a terrestrial existence.

Mosquito larvae have a well-developed head with mouth brushes used for feeding, a large thorax with no legs and a segmented abdomen. Larvae breathe through spiracles located on the eighth abdominal segment, or through a siphon, and therefore must come to the surface frequently. The larvae spend most of their time feeding on algae, bacteria, and other micro-organisms in the

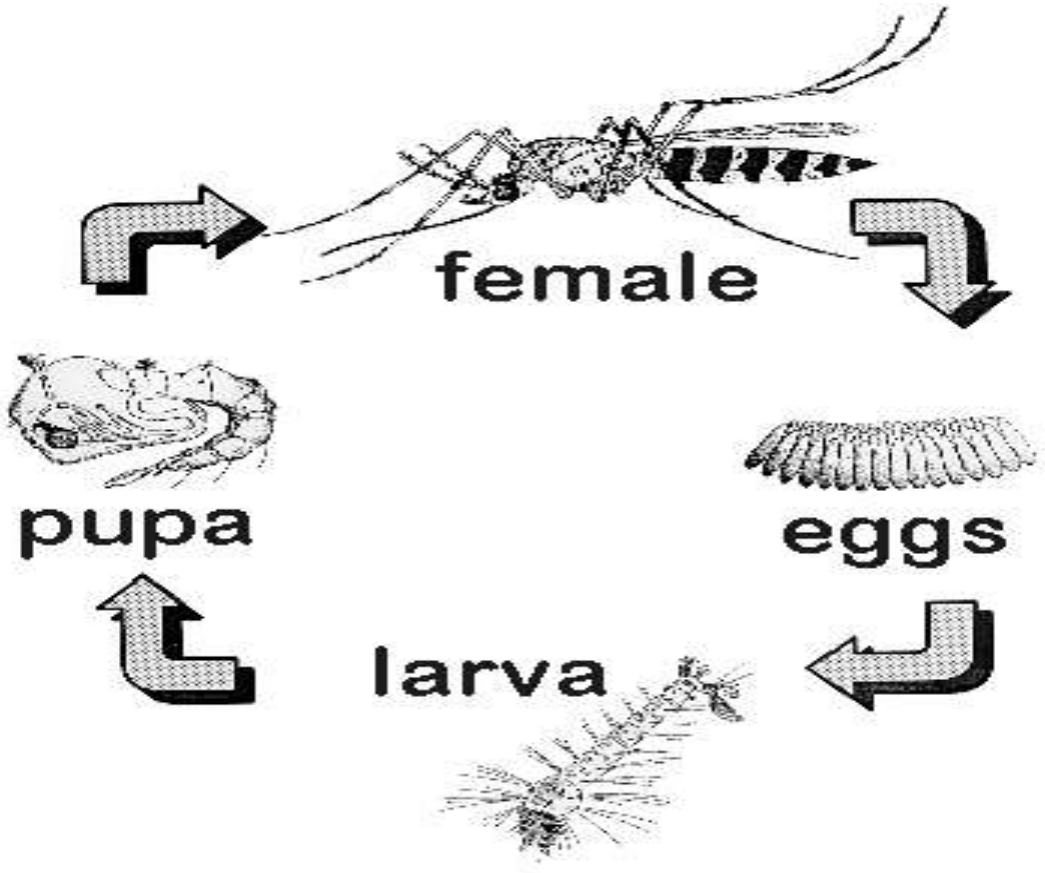

Fig 1: Life cycle of the female *Anopheles* mosquito

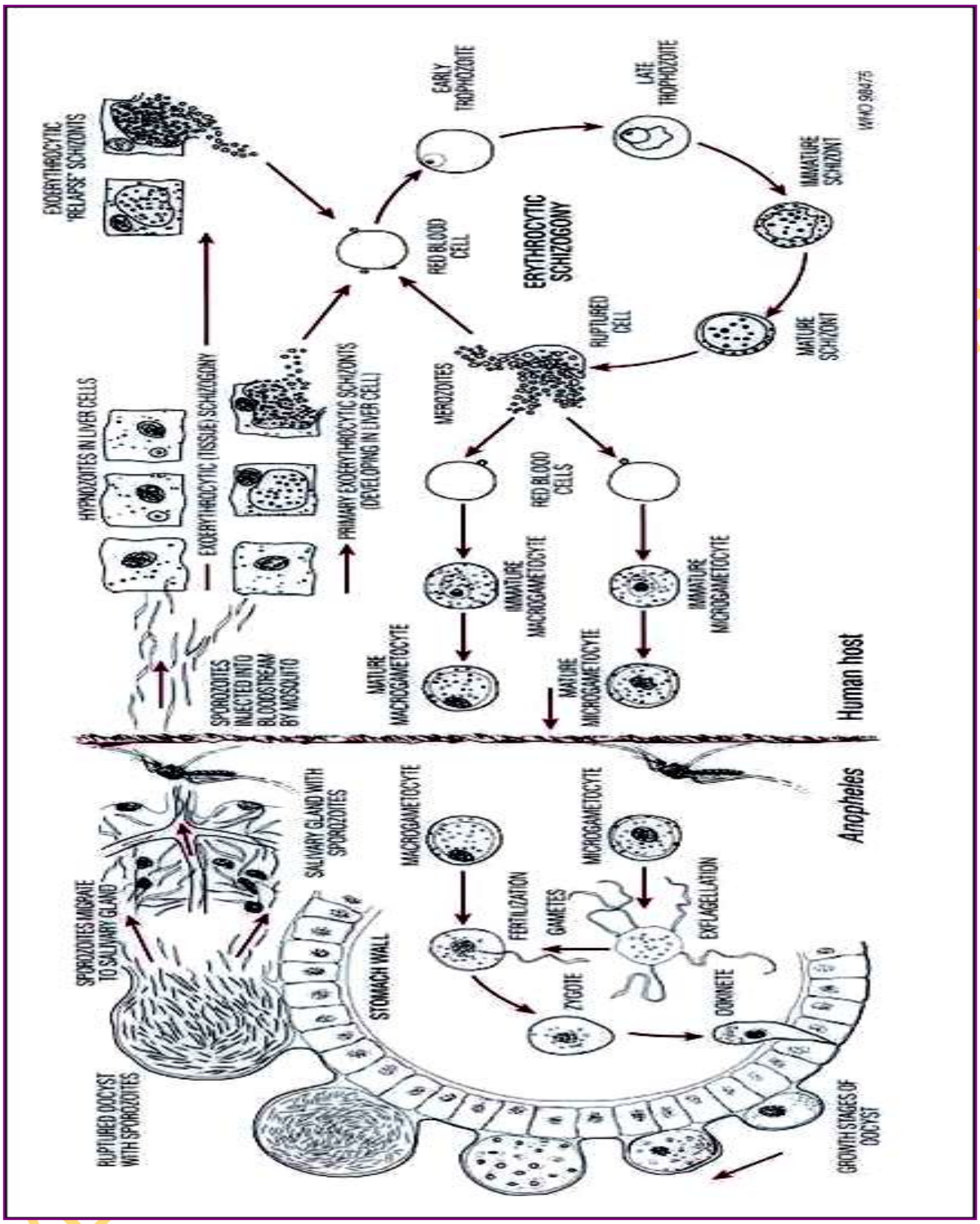

Fig 2: The sexual and asexual life cycle of *Plasmodium* specie in man and mosquito

surface micro-layer. They dive below the surface only when disturbed. Larvae swim either through propulsion with the mouth brushes, or by jerky movements of the entire body, giving

them the common name of "wigglers" or "wrigglers". Larvae develop through four stages, or instars, after which they metamorphose into pupae. At the end of each instar, the larvae molt, shedding their exoskeleton, or skin, to allow for further growth.

The pupa is comma-shaped, as in *Anopheles* when viewed from the side, and is commonly called a "tumbler". The head and thorax are merged into a cephalothorax with the abdomen curving around underneath. As with the larvae, pupae must come to the surface frequently to breathe, which they do through a pair of respiratory trumpets on the cephalothorax. However, pupae do not feed during this stage. After a few days, the pupa rises to the water surface, the dorsal surface of the cephalothorax splits and the adult mosquito emerges. The pupa is less active than larvae..

Mosquitoes can develop from egg to adult in as little as five days but usually takes 10–14 days in tropical conditions. The duration from egg to adult varies considerably among species and is strongly influenced by ambient temperature. The variation of the body size in adult mosquitoes depends on the density of the larval population and food supply within the breeding water. Adult flying mosquitoes frequently rest in a tunnel that they build right below the roots of the grass. Adult mosquitoes usually mate within a few days after emerging from the pupa stage. In most species, the males form large swarms, usually around dusk, and the females fly into the swarms to mate. Males live for about a week, feeding on nectar and other sources of sugar. Females will also feed on sugar sources for energy but usually require a blood meal for the development of eggs. After obtaining a full blood meal, the female will rest for a few days while the blood is digested and eggs are developed. This process depends on the temperature but usually takes 2–3 days in tropical conditions. Once the eggs are fully developed, the female lays them and resumes host seeking. The cycle repeats itself until the female dies. While females can live longer than a month in captivity, most do not live longer than 1–2 weeks in nature. Their lifespan depends on temperature, humidity, and also their ability to successfully obtain a blood meal while avoiding host defenses. Length of the adult varies but is rarely greater than 16 mm (0.6 in) (Virginia Tech,

2007) and weight up to 2.5 mg (0.04 grain). All mosquitoes have slender bodies with three sections: head, thorax and abdomen. The head is specialized for acquiring sensory information and for feeding. The head contains the eyes and a pair of long, many-segmented antennae. The antennae are important for detecting host odors as well as odors of breeding sites where females lay eggs. In all mosquito species, the antennae of the males in comparison to the females are noticeably bushier and contain auditory receptors to detect the characteristic whine of the female. The compound eyes are distinctly separated from one another. Their larvae only possess a pit-eye ocellus. The compound eyes of adults develop in a separate region of the head (Harzsch *et al.*, 2006). New ommatidia are added in semicircular rows at the rear of the eye; during the first phase of growth, this leads to individual ommatidia being square, but later in development they become hexagonal. The hexagonal pattern will only become visible when the carapace of the stage with square eyes is molted (Harzsch *et al.*, 2006). The head also has an elongated, forward-projecting "stinger-like" proboscis used for feeding, and two sensory palps. The maxillary palps of the males are longer than their proboscis whereas the females' maxillary palps are much shorter. (This is typical for representatives of subfamilies.) As with many members of the mosquito family, the female is equipped with an elongated proboscis that she uses to collect blood to feed her eggs. The thorax is specialized for locomotion. Three pairs of legs and a pair of wings are attached to the thorax. The insect wing is an outgrowth of the exoskeleton. The *Anopheles* mosquito can fly for up to four hours continuously at up to 1–2 km/h (Kaufmann *et al.*, 2004), travelling up to 12 km (7.5 miles) in a night. The abdomen is specialized for food digestion and egg development. This segmented body part expands considerably when a female takes a blood meal. The blood is digested over time serving as a source of protein for the production of eggs, which gradually fill the abdomen.

2.10.1 Distribution

While many species are native to tropical and subtropical regions, some such as *Aedes* have successfully adapted to cooler regions. In the warm and humid tropical regions, they are active the entire year long; however, in temperate regions they hibernate (over winter). Eggs from strains in the temperate zones are more tolerant to the cold than ones from warmer regions (Hawley *et al.*, 1986; Hanson *et al.*, 1995). They can even tolerate snow and temperatures under freezing conditions. In addition, adults can survive throughout winter in suitable microhabitats (Romi *et al.*, 2006).

2.10.2 Means of dispersal

Over large distances the worldwide distribution is carried out primarily through sea routes, in which the eggs, larvae, and pupae in combination with water-filled used tires and cut flowers are transported around. As with sea transport, the transport of mosquitoes in personal vehicles, delivery trucks, and trains plays an important role.

2.11 Malaria control

Malaria is entrenched in the tropical part of the world because of three main factors viz, (environmental factors, biological factors and human related factors). We will be able to effectively control and possibly eliminate malaria from our world only when we have a good understanding of how these factors interact. The current thinking in tackling malaria is the curative, preventive and vector control approach.

Curative approach: This is focused on making early diagnosis treating all infected persons with the right drugs preferably the ACTs and at the right dosage so as to prevent the development of resistance to the drugs by the parasites.

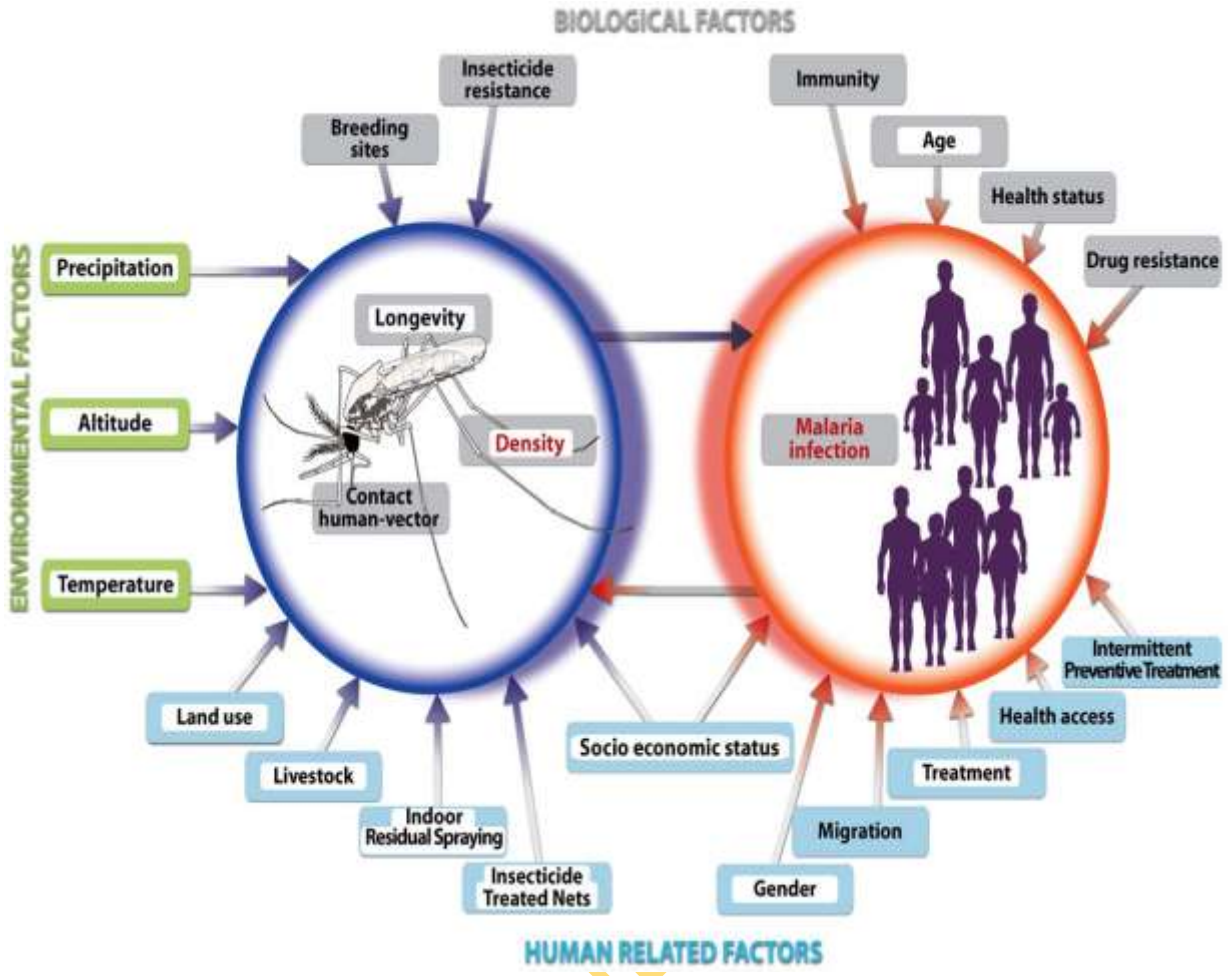

Fig 3: Conceptual model of important risk factors affecting malaria prevalence in the tropics and points of control efforts

Preventive approach: This implies the use of anti malaria drugs to prevent malaria before infection occurs or before it becomes obvious. The aim is to prevent the occurrence of the disease by acting on the parasites while still confined to the liver (causal or true prophylaxis) or to prevent any of the disease symptoms by suppressing the number of malaria parasites in the blood to such a low level that they will not cause any clinical symptoms (clinical prophylaxis or suppression).

In highly endemic areas, the use of chemoprophylaxis is limited to people who are at high risk from severe and complicated malaria (pregnant women, persons with sickle cell disease and non immune visitors or residents).

Integrated vector control: Vector control aims at eliminating or reducing the mosquito population through chemical control using insecticides, environmental control, personal protection (barrier) and biological control.

Vector control

Fig 4: Larvae in stagnant water

There are many methods used for mosquito control. Depending on the situation, source reduction, bio-control, larvicides to kill larvae, or specifically the adults may be used to manage mosquito populations. These techniques are accomplished using habitat modification, such as removing stagnant water and other breeding areas, pesticide like Dichloro-diphenyl-trichloroethane (DDT), natural predators, (e.g. Dragonflies, larvae-eating fish), and trapping.

Organic repellents

With increasing reports of the harmful effects *N*,*N*-Diethyl-*meta*-toluamide, abbreviated **(**DEET) has on humans, there has been a gradual move to rely on repellents that are devoid of it, specifically to repellents that are organic and otherwise are of the kind that have had traditional

household purposes prior to their becoming used now more often as mosquito repellents (Agency for Toxic Substance and Disease Registry, 2004).

Natural predators

Fig 5: Dragonflies are natural predators of mosquitoes

The dragonfly nymph eats mosquitoes at all stages of development and is quite effective in controlling populations (Singh *et al.*, 2003). Although bats and Purple Martins can be prodigious consumers of insects, many of which are pests, less than 1% of their diet typically consists of mosquitoes. Neither bats nor Purple Martins are known to control or even significantly reduce mosquito populations (Fradin, 1998). Some cyclopoid copepods are predators on first instars larvae, killing up to 40 *Aedes* or *Anopheles* larvae per day (Marten *et al.*, 2007). Larval of *Toxorhynchites* mosquitoes are known as natural predators of other *Culicidae*. Each larva can eat an average of 10 to 20 mosquito larvae per day. During its entire development, a *Toxorhynchites* larva can consume an equivalent of 5,000 larvae of the first instar (L1) or 300 fourth instar larvae (L4). However, *Toxorhynchites* can consume all types of prey, organic debris, or even exhibit cannibalistic behavior. A number of fish are also known to consume mosquito larvae, including bass, bluegill, piranha, catfish, fathead minnows, the western mosquito-fish (*Gambusia affinis*),

goldfish, guppies, and killifish *Bacillus thuringiensis israelensis* has also been used to control them as a biological agent.

2.12 Malaria elimination

Recent data shows that large-scale use of WHO recommended strategies could rapidly reduce malaria, especially in areas of high transmission such as Africa. WHO and Member States have made significant gains in malaria elimination efforts. For example, the Maldives, Tunisia and the United Arab Emirates have eliminated malaria. Country successes are due to intense national commitments and coordinated efforts with partners.

Community mobilization and education have been part of efforts aimed at achieving the efforts to eliminate malaria. There have equally been global efforts to eliminate malaria such as the Roll Back Malaria Initiatives.

Roll Back Malaria Initiative

The World Health Organization in 1998 declared malaria control one of its priority assignments and announced the introduction of a new initiative- the Roll Back Malaria (RBM) initiative. The RBM was a global health sector wide partnership approach to combat malaria worldwide, using available knowledge, skills and tools to launch a new concerted effort against the disease. The general objective of the initiative is to reduce malaria burden by 50% by 2010 and to halve it again in the following five years through interventions adapted to local needs and by reinforcement of the health sector.

The specific objectives are:

- To increase to 60% the use of insecticide treated bed nets (ITN) by pregnant women and children under-five years of age.
- To ensure that 60% of children under five receive appropriate treatment within 24 hours of onset of illness.

- To ensure that at least 60% of all pregnant women at risk of malaria will have full intermittent preventive treatment.
- To develop an effective environmental management strategy for RBM (integrated vector management)

Also the six elements of the RBM strategy are; prompt diagnosis and treatment, multiple prevention strategies, well coordinated effort, dynamic global partnership, effective management and evidence based responses and to have focused research on malaria..

CHAPTER THREE

3.0 SUBJECT AND METHODS / METHODOLOGY

3.1 Background of study area

Abia state is located in the southeastern region of Nigeria. Umuahia North is one of the 17 Local Government Area (LGA) of the state and it has situated in it Umuahia town which is the administrative capital of Abia State. The inhabitants are basically Ibos whose main occupation includes civil service, petty trading and subsistence farming. It has a total population of 240,537 and under - five populations of 48,108. The vegetation of this town and the heavy rain fall encourage the breading of mosquitoes. Though malaria is endemic in the area, its transmission is highest at the peak of the rainy seasons (March – July).

There are 31 PHC facilities, 1 secondary health facility, 1 tertiary health facility and about 50 private health facilities in the Local Government Area. Only 17 of the 31 PHC facilities in the LGA render at least the essential three child health services (growth monitoring, immunization and sick child consultations) out of the full range of child health services (growth monitoring, immunization, nutrition and breast feeding support services, oral rehydration and treatment of common childhood illnesses). Six of these 17 PHC facilities are in the urban area (metropolis) while the remaining 11 are in the suburb. The PHCs are manned by health workers ranging from community health nurses, registered nurses/midwives and health extension workers. Just like in other parts of Africa, the people would prefer to patronize the medicine vendors and would only present at the health centres when the illness becomes very severe.

3.2 Study Design

This is an analytical cross sectional study.

3.3 Study Period

This study was carried out between April 2010 and June 2010.

3.4 Selection of the facilities

Umuahia North LGA was chosen out of the 17 LGAs that make up Abia State because of its' accessibility and patients turn over rate at the health care facilities been the administrative capital of Abia State. Four PHC facilities were selected from the 17 PHC facilities rendering the three essential child health services in the LGA using a three stage (multistage) random sampling method. Stratification was by rural and urban location. Two health facilities were selected from the six urban PHCs using a table of random numbers and two PHCs from the 11 PHC facilities in the rural PHCs using the same table of random numbers. All the facilities render essentially the same services.

3.5 Study Population

(i) Umuahia North LGA PHC coordinator (1 person).

(ii) Caregivers of under-five children presenting at the selected PHCs

(iii) Under- five children presenting with febrile illness at the selected PHCs

(iv) Heads of the selected PHC facilities (4 persons).

Inclusion criteria: Any under five child who presented in the selected four health facilities in Umuahia North LGA, with fever (Children who were found to be febrile, with a temperature ≥ 38.0°C) of at least 2-3 days duration with or without vomiting, chills and rigors in the absence of runny nose, measles, abscess, ear ache or signs and symptoms of any other well known causes of fever and who received medication for malaria in the health facilities or purchase from the chemist shop within 24 hrs of consultation either as an in-patient or out-patient and it is possible to asses the child's response 48 hrs after treatment through direct observation either in the hospital (in-patients) or at home (out-patients).

Exclusion criteria: Any under five child presenting at the selected health facilities in Umuahia North LGA, with fever (Children who were found to be febrile, with a temperature ≥ 38.0°C) of at least 2-3 days duration with or without vomiting, chills and rigors that is associated with runny nose, or other known causes of fever or children meeting our case definition of malaria who could not get their drugs within 24hrs of consultation or where it is not possible to assess the child's response to treatment after 48 hrs either in the clinic or at home or where there was risk to the child (i.e. a life-threatening illness that required immediate treatment and evacuation to a specialized hospital).

3.6 Sample size determination

The sample size was calculated using the formula (reference)

$$n = \frac{z^2pq}{d^2} \times 2$$

Where P = Proportion of < 5 yrs children with good treatment outcome after 48 hrs of commencing treatment. (This was 79% from a pilot study we done in 2 PHC facilities in Umuahia).

q = 100 – p

d = 0.5

z = Standard normal deviate at 95% confidence interval (1.96)

(Where 2 is a multiplication factor for the design effect, in order to increase our precision to get minimal variance since the study is not a prevalence study and we would be doing a lot of comparisms and sub group analysis.

$$n = \frac{1.96^2 \times 79 \times 21}{5^2} \times 2 = 510$$

The anticipated non response is 10% (Abubakar, 2006) = 10/100 x 510 = 51.0 (510 + 51 = 561) (rounded up to an even number of 562).

562 questionnaires would be administered on care givers and similar number of children would be examined clinically for signs and symptoms of un-complicated as well as complicated malaria (anaemia, jaundice, convulsion, severe vomiting, and dehydration among other).

3.7 Sampling technique

Stratified sampling technique (using proportionate allocation) based on the average number of children who made use of the child health services in the last two months (February – March 2010) at the four selected PHCs was used to select the number of children to be examined as well as the number of care givers to be interviewed in each facility.

The number of children who attended the four selected PHCs between February and March 2010 were;

Ojike street PHC (Urban) - 780

World Bank Housing Estate PHC (Urban) - - - - - - - - - - - - - - - - - 330

Amaogwugwu PHC (Rural)- -270

Umuawa-Alaocha PHC (Rural) - 600

Total - 1980

$$= \frac{\text{Average patients seen in Ojike street PHC from February – March 2010}}{\text{Total patients seen in all four selected PHC from February – March 2010 (i.e. Ojike Street, Amaogwugwu, Umuawa-Alaocha and World Bank Housing estate PHCs)}} \times 562$$

Doing same for each PHC gave the number of caregivers of under-five children with presumed malaria cases interviewed at each facility as well as the number of children to be examined.

(a) For Ojike street PHC; the average monthly attendance was 780 and the total average monthly attendance for the 4 PHC facilities was 1980. So, the number of caregivers interviewed as well as the number of children to be examined were;

$$\frac{780}{1980} \quad X \quad 562 \quad = \quad 221$$

(b) For World Bank Housing Estate PHC;

$$\frac{330}{1980} \quad X \quad 562 \quad = \quad 94$$

(c) For Umuawa-Alaocha PHC;

$$\frac{600}{1980} \quad X \quad 562 \quad = \quad 170$$

(d) For Amaogwugwu PHC;

$$\frac{270}{1980} \quad X \quad 562 \quad = \quad 77$$

On the whole 562 children/caregivers were enrolled at the minimum.

Since patient attendance at the PHC facilities are a floating population, all caregivers who brings an under-five child with fever that meet our inclusion criteria at the four selected PHC facilities during the study periods were recruited consecutively after informed verbal consent was obtained, till the allocated sample to each facility was obtained.

3.8 Data collection tools/instrument

The following tools, (a) interviewer administered structured questionnaires for exit interviews of caregivers. (b) Guided (structured) key informant interviews for health care facility head and the PHC coordinator of Umuahia North LGA. (c) Assessment of the sick child before treatment and 48hrs after treatment were developed and used to collect data after having pretested them at two

health facilities in the LGA (Nkata PHC and Nkwuegwu PHC) that were not chosen for the main study.

The key informant interviews as well as questionnaires were structured in a way to capture the following variables:

Characteristics and knowledge of the mothers

- Level of education
- Occupation
- Level of income, monthly expenditure and cost of managing incidence of malaria in the < 5 child
- The number of antenatal visits made during pregnancy
- If exclusive breastfeeding was done
- Awareness of the causes of malaria and the possible preventive strategies
- If child was fully immunized
- Knowledge about child's health promotion activities and home management of some common childhood conditions like ORT preparation for diarrhea, febrile conditions
- Who makes the decision to take a sick child to the clinic in the house
- Was she accompanied to the clinic by the husband?
- If she was educated on how to continue with home care for the child each time she brings him/her to the health facility
- Attitude of staff at the health centers
- Acceptability of the services available at the facility
- Distance from the facility

The health care facility head

- Level of training acquired and if any have had some trainings on Integrated Management of Childhood Illness (IMCI)

- Number of trained staff in the facility
- How they diagnose and care for malaria (type of anti-malaria drugs used).
- Do these health facilities have a national malaria case management algorithm
- Number of hours of services rendered
- Availability of basic materials like thermometer, weighing scale, growth monitoring charts
- Average number of patients per day
- Routine immunization records and how many children got completely immunized at the facilities
- Good record keeping i.e. year the facility became operational and what year record is available and if they are up to date
- Availability of drugs for malaria
- The level of community patronage would be assessed
- If there are supervisory visits

The LGA PHC coordinator

- Organizational/managerial structure of the entire PHC in the LGA
- Staffing of the facilities
- Availability of in-service training especially; on IMCI
- Total immunization coverage of the LGA
- Supply of drugs and materials to the facilities
- Monitoring of activities (how often these are done)
- If the IMCI strategies is been operated by the LGA
- If the LGA have a protocol of systematic supervision of health workers
- Cost of treating malaria in the health facilities.

Determination of treatment outcome: This was done by looking at the treatment given in the facility retrospectively (clinic record) were consultation had taken place before the team gets there and monitoring the response to treatment of the children prospectively after 48 hrs of commencing treatment (by interviews of the care givers and physical examination of children either in the clinic for those on admission or at home for out-patients.

Assessment of the sick child: All the children meeting our inclusion criteria seen at the selected health centers were assed for their clinical state when they were brought to the health centers by examining them for signs of fever (with a thermometer), anaemia, drowsiness, spleenomegaly and sunken eyes.

The age of the sick: The caregivers were asked how old the sick child was.

Data collection method

Four research assistants were recruited from the Department of Nursing Services of the Abia State Ministry of Health and they were given a 4 - day intensive training on how to collect both qualitative and quantitative data with the above tools trying as much as possible to reduce the inter and intra observer concordance/differences.

3.9 Data Management and Analysis

Data obtained from the questionnaire were checked for accuracy, completeness and consistency of information. Data cleaning was done before entering them into statistical soft ware (Epi-info version 3.8). Descriptive statistics was used to summarize the data obtained. Univariate and bivariate analysis were done to ascertain the degree of association between various factors that may be responsible for the outcome of malaria treatment in children brought to the health facilities; by comparing both quantitative variables and proportions among more than two groups using Chi-square test at 5% level of significance. Multivariate analysis using logistic regression was done to model those variable that when altered affects the malaria treatment outcome of

under-five children that are attended to in Umuahia North Local Government Area of Abia State PHC facilities.

3.10 Ethical considerations

Permission and approval was obtained from the Ethical and scientific committee of the Abia State Ministry of Health, Umuahia.

Informed verbal consent was obtained from all those that participated in the study (facility heads, PHC coordinator and caregivers).In conformity with the ethical requirement, all vital information obtained from the respondents were accessed only by the investigators

CHAPTER FOUR

4.0 RESULTS

The result of the study is presented in line with the objective of the study to ascertain the malaria treatment outcome among under five years children managed at the primary health care centres (PHCs) in Umuahia North LGA. The second part present the health resources (human, material and financial) available at these health facilities for the provision of malaria treatment for under five years children. The next part presents those factors that affected under five malaria treatment outcome at the health facilities in Umuahia.

Grouping the four facilities into urban and rural, World bank housing estate health centre and Ojike road health centre were classified as urban each hosting 94 (16.7%) and 221(39.3%) of the caregivers interviewed/recruited under five years children respectively. While Umuawa - Alaocha health centre and Amaogwugwu health centre were grouped as rural each also hosting 170 (30.3%) and 77 (13.7%) of the caregivers/recruited under five years children respectively.

4.1 Treatment outcome among the under five children studied

The prevalence of good treatment outcome among the 562 under five year children that participated in this study was 73.5% as shown in Table 1. Meanwhile 305 (54.3%) of them were males and 480 (85.4 %) were treated on out patients basics.

Table 1: Malaria treatment outcome

Variable	Frequency	%
Treatment outcome (N = 562)		
Good	413	73.5%
Poor	149	26.5%

4.2.0 The resources available for the provision of malaria treatment services Human:

The key informant interviews with the heads of the selected PHC facilities showed that they were all female and their mean age was 44.0±1.4 years. Their minimum qualification was Staff nurse midwife and the maximum was B.Sc from (Table 2). Meanwhile the LGA PHC coordinator was also a female and holds an M.sc degree.

Though the LGA operates the Integrated Management of Childhood Illness (IMCI) only 10 of the heads of the 31 PHCs in the LGA were trained on the use of this strategy which was aimed at improving the child health services rendered at the Primary health care level. Of the four selected PHC heads, only two including the PHC coordinator had been trained on the use of IMCI (about 4 years ago) and all of them including the PHC coordinator again had also received training on malaria treatment protocol by the State ministry of health in the last one year (Table 2). Though there was provision for in-service training, none of the health staff had undergone any major training programme or had been re-trained on the Use of IMCI in the last one year.

Table 2: Demographic characteristics of the PHC Facility heads/PHC coordinator and trainings relevant to malaria treatment in the last five years

Variable	Response by respondents and the facility they head				
	Amaogwugwu	**WBHE**	**Ojike**	**Umuawa-Alaocha**	**Umuahia North LGA PHC coordinator**
Rank	ACNO	ACNO	DDNS	NO	DNS
Age (Yrs)	44	45	45	42	48
Highest qualification	B.sc	NM	B.sc	NM	M.sc
Gender	Female	Female	Female	Female	Female
IMCI training	Yes	No	Yes	No	Yes
How long ago was IMCI training?	4 yrs	NA	4 yrs	NA	5 yrs
Malaria training in last I year	Yes	Yes	Yes	Yes	Yes

***ACNO Assistance chief nursing officer; DDNS Deputy director of nursing services; NM Nurse midwife and DNS Director nursing services**

The LGA PHC coordinated reported that the health department is forced to carry out quarterly supervisory visits to the various PHC facilities instead of the stipulated twice monthly visits due to inadequate staff and funds. However these supervisions were done without written protocols.

4.2.1 Material resources available for rendering malaria treatment services at the PHCs:

The Umuahia North LGA PHC coordinator also stated that the health department has never distributed the IMCI guidelines as well as the National malaria treatment protocol to its PHC facilities since these guidelines were published. She also reported that, three years ago, the LGA health department gave anti malaria drugs for under-five children to all its health facilities which were used in treating malaria freely without extra charges to the patients. However, no new stock or other drugs have been given in recent times apart from the vaccines used for routine immunization which WHO and UNICEF are coordinating and supporting. It was also noted that

the LGA gave free Insecticide treated nets (ITN) to the various PHC facilities for distribution about two years ago to pregnant/nursing mothers as part of her effort to reduce the incidence of malaria in the locality.

Part of the challenges facing the health department that was identified were, poor funding, inadequate staff, poor infrastructures and lack of staff training and re-training programs. It was observed that World Bank Housing Estate (WBHE) PHC had the highest number of staff with the ability to diagnose malaria although Ojike street PHC sees the highest proportion of children with malaria every day. Also of the four PHC facilities visited, it was only Ojike street PHC facility that does not have the ability to admit patients for observation (Table 3).

It was also observed that prior to presentation at the four PHCs visited all the children would have been given chloroquine anti malaria drugs by their caregivers at home apart from Ojike street PHC where some of the children where equally given the recommended anti malaria drugs Artemisinin based combination therapy (ACT) (Table 4).

Table 3: Staff strength/work load at the four facilities

Variables	Amaogwugwu	WBHE	Ojike	Umuawa-Alaocha
Reported № of staff with capacity to attend to malaria cases (x/n)	2/3	7/9	4/7	4/5
Reported average № of children seen in the facility per day (N)	8	10	30	20
Proportion of children treated for malaria daily (X/N)	6 (75%)	8 (80%)	10 (33.3%)	5 (25%)
Availability of facility for admission	Yes	Yes	No	Yes

x = number of staff with the capacity to treat malaria and n = total number of staff in the PHC facility

Table 4: Treatments reportedly given to the children by the caregivers at home before they are brought to the health facility

Variables	Amaogwugwu	WBHE	Ojike	Umuawa-Alaocha
Type of treatment given by caregivers before coming to the facilities				
Concoctions	No	No	No	No
PCM	Yes	Yes	Yes	Yes
CQ	Yes	Yes	Yes	Yes
ACT	No	No	Yes	No
Nil treatment given before coming to the facility	No	No	No	No

From the assessment of the visited health facilities, it was observed that though the oldest and newest facilities were 72 years and 11 years respectively only three years records were available in each of the four facilities. Apart from WBHE health centre, all the others still prescribe chloroquine as part of malaria treatment. It was also observed that when prescribed anti malaria drugs are not available, apart from Umuawa - Alaocha health centre that would prefer to ask the patients to go and purchase these drugs themselves the other three facilities would rather restock these drugs immediately to ensure it is handed over to the patients there and then. All the facilities visited made malaria diagnosis presumptively without using rapid diagnostic test kits or microscopy. Umuawa – Alaocha was the only facility that had at least a supervisory visit from either the LGA health department or the State ministry of health in the last five months (Table 5).

Table 5: Assessment of the health facilities from inception till date and malaria treatment/control activities

Variables	Amaogwugwu	WBHE	Ojike	Umuawa-Alaocha
Year of establishing PHC	1948	1999	1991	1996
Availability of complete record from inception at the facilities	No	No	No	No
№ of years with complete records since inception	3 yrs	3 yrs	4 yrs	3 yrs
Type of drugs used in the treatment of malaria at the facilities				
PCM	Yes	Yes	Yes	Yes
CQ	Yes	No	Yes	Yes
SP	Yes	No	No	No
ACT	Yes	Yes	Yes	Yes
Blood syrups/tabs	Yes	Yes	Yes	Yes
Antibiotics	No	No	Yes	Yes
If above drugs are always available at the facilities	No	Yes	Yes	Yes
Receipt of free ACT/ITN for distribution in the last one year	No	No	No	No
Where there occasions when prescribed anti-malaria drugs were not available at the facility in the last 3 months	Yes	Yes	No	No
What facilities would do in situations where anti-malaria drugs are not available?				
Buy from a chemist to restock	Yes	Yes	Yes	No
Prescribe for patients to go and buy	No	No	No	Yes
Reported № of supervisory visits from the LGA in the last 5 months	1	1	4	6
If malaria diagnosis are presumptively made	Yes	Yes	Yes	Yes

4.3.0 Factors affecting under – five years children malaria treatment outcome in PHC facilities in Umuahia

4.3.1 Descriptive analysis

The mean age of the caregivers was 32.6±6.6 years. Most of the caregivers 478 (85.0%) were married and 130 (23.1%) were civil servants, majority (23.1%) were secondary school leavers and 13 (2.3%) had no formal education. The 25 – 39 years age group was in the majority 423 (75.3%) and Christians {Pentecostal 297 (52.8%) as well as Orthodox 260 (46.3%)} were also in the majority. Among the caregivers that brought their sick children to the clinic, majority 528 (94.0%) were the mothers (Table 6).

The median cost of treating a child at the chemist was ₦300 (range = 20 - 1,500), if the child was taken to a private clinic, the median cost was ₦1,300 (range = 110 - 6,000). Meanwhile the median cost of treating the child at the PHC facility, was ₦700 (range = 270 - 1,600). (Table 7)

Table 6: Socio-demographic characteristics of caregivers

Variable	Frequency	%
Age (Years)		
<20	4	0.7
20-24	54	9.6
25-29	152	27.0
30-34	141	25.1
35-39	130	23.1
40-44	52	9.3
45 and above	29	5.2
Total	**562**	**100.0**
Marital Status		
Single mother	42	7.5
Married	478	85.0
Divorce	22	3.9
Widow	20	3.6
Total	**562**	**100.0**
Occupation		
Housewife	78	13.9
Farmer	25	4.5
Hairdresser	47	8.4
Trader	193	34.3
Tailor	21	3.7
Student	13	2.3
Teacher	52	9.3
Paramilitary	3	0.5
Civil servant	130	23.1
Total	**562**	**100.0**
Level of education		
Nil	13	2.3
Primary	55	9.8
Secondary	364	64.8
Tertiary	130	23.1
Total	**562**	**100.0**
Religion		
Islam	4	0.7
Orthodox church	260	46.3
Pentecostal church	297	52.8
Traditional	1	0.2
Total	**562**	**100.0**
Relationship with the sick child		
Father	25	4.4
Mother	528	94.0
Relatives	9	1.6
Total	**562**	**100.0**

Table 7: The mean/median cost of treating an under-five child presumed to have malaria at various locations (₦)

Characteristics	Mean	(S.D)	Median	(Range)
Cost of treating a child in a chemist	347.5	192.6	300	20 – 1,500
Cost of treatment in the health centre	729.6	348.0	700	100 – 3,000
Cost of treatment in the private clinic	1,637.0	933.5	1,300	110 – 6,000
Total cost of present treatment in the facility	734.4	263.9	700	270 – 1,600

Using the centile poverty scale (Table 8) to grade the caregivers and their households, majority 231 (41.1%) of them from their earnings were observed to be on the 60th poverty centile scale (middle class) followed by the upper middle class with 176 (31.3%) 80th poverty centile (Tables 9). It was also observed that the upper class (from the social classification in Table 8), had the most proportion of children with good treatment outcome (82.1%) and the lower class had the least (50%). There wasn't much difference in the proportion of children with good treatment outcome between the middle and upper middle social classes both having 72.3% and 72.2% respectively (Table 10).

Table 8: Social classification of caregiver's household using their average monthly income

Household income per month	Poverty grade (centile)	Social classification
< ₦5,000	20	Lower
₦5,000 – ₦10,000	40	Lower middle
₦11,000 – ₦30,000	60	Middle
₦31,000 – ₦50,000	80	Upper middle
> ₦50,000	100	Upper

Table 9: Average income earned by the caregiver household in a month (N = 562)

Amount earned by household in a month	Frequency	%
< ₦5,000 (Lower class)	2	0.4
₦5,000 – ₦10,000 (Lower middle class)	47	8.4
₦11,000 – ₦30,000 (Middle class)	231	41.1
₦31,000 – ₦50,000 (Upper middle class)	176	31.3
> ₦50,000 (Upper class)	106	18.9

Table 10: The effect of social classification of the caregivers on good treatment outcome

Social class	% of children with good treatment outcome	% of children with bad treatment outcome
Lower (N=2)	50.0	50.0
Lower middle (N=47)	66.0	34.0
Middle (N=231)	72.3	27.7
Upper middle (N=176)	72.2	27.8
Upper (N=106)	82.1	17.9

It was observed that more than half of the caregivers 304 (54.1%) came alone with their children for treatment at the health centres, while the rest were either accompanied by relative 127 (22.6%) or their husbands 75 (13.3%) (Fig 6).

Also about half of the caregivers 287 (51.1%) had two under – five years children in their household followed by those with one under – five years child in their household 217 (28.6%) (Fig 7).

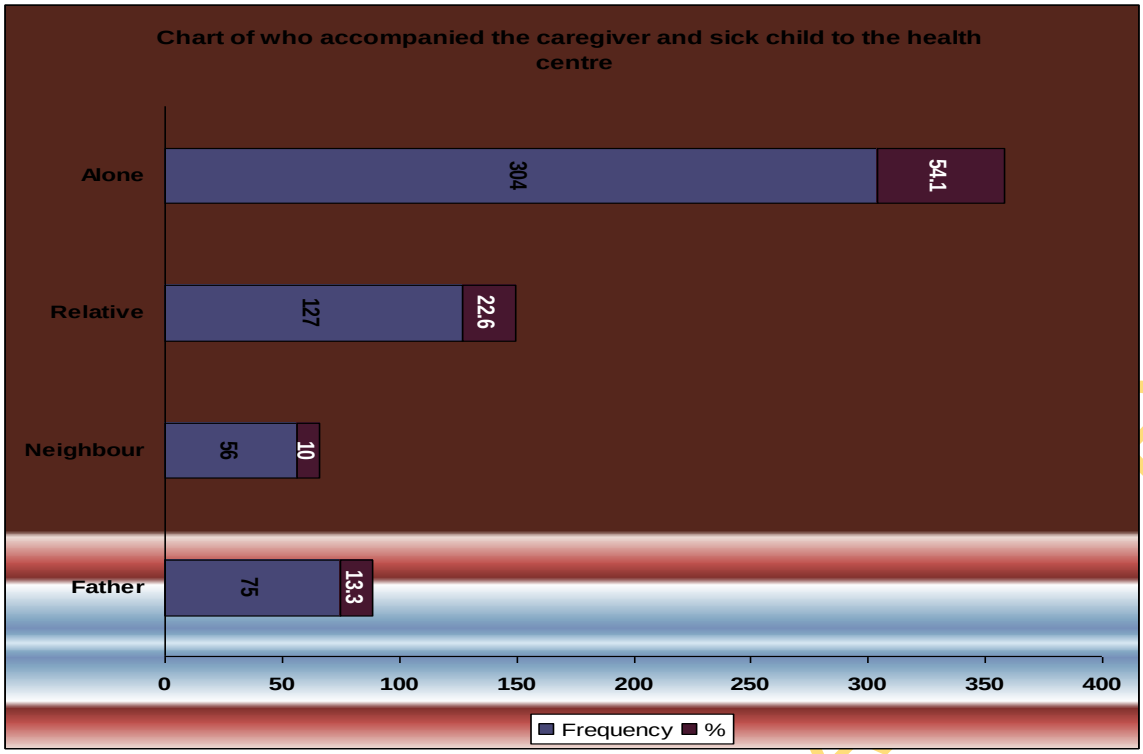

Fig 6: A graph of weather the caregiver was accompanied to the clinic and who did

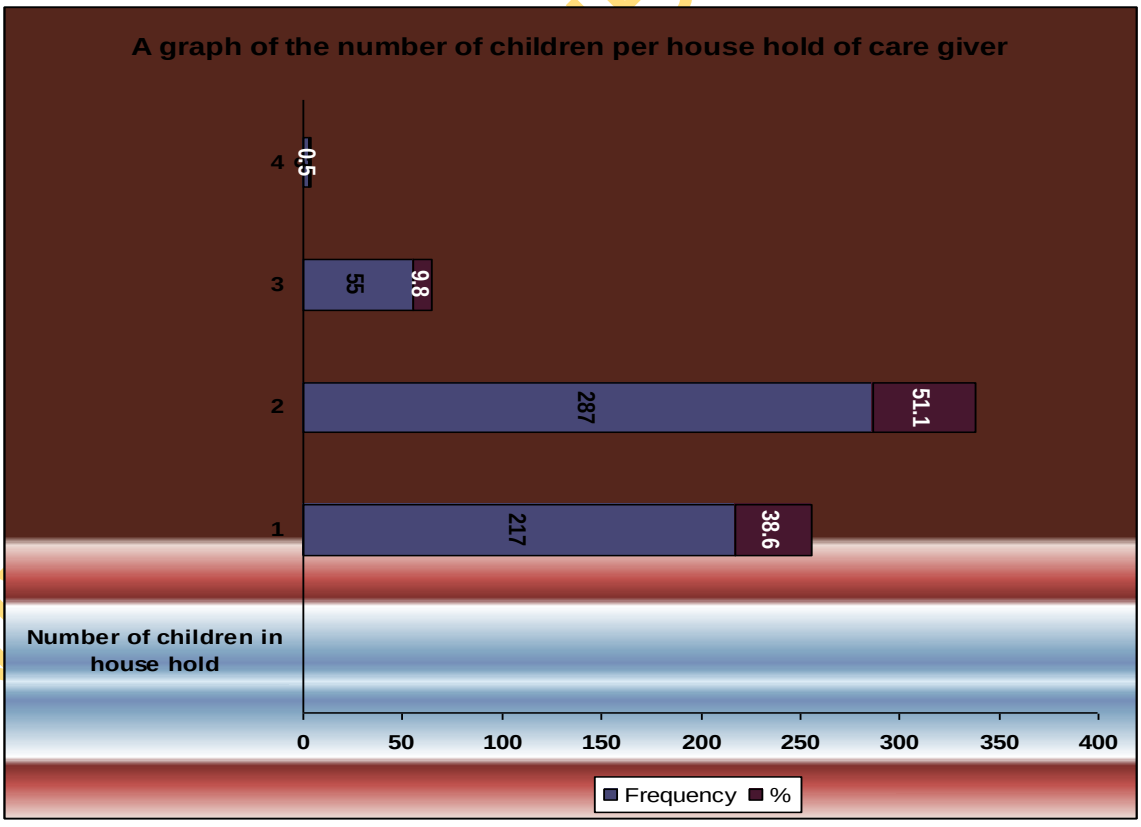

Fig 7: A graph of the number of under five – years children in each caregiver household

Also from the descriptive analysis of the data on the 562 under – five children enrolled into the study, it was observed that the median age of the children was 24 months (Range 2 – 59). One fifth 118 (21.0%) of the children were under 12 months old and 305 (54.3%) were male, (Table 11).

Table 11: Demographic information on the sick children (N=562)

Variables	Frequency	%
Age (Months)		
< 12	118	21.0
12 – 17	75	13.3
18 – 23	78	13.9
24 – 29	83	14.8
30 – 35	55	9.8
36 – 41	57	10.1
42 – 47	32	5.7
48 – 53	42	7.5
54 – 60	22	3.9
Total	**562**	**100**
Gender		
Male	305	54.3
Female	257	45.7
Total	**562**	**100**

It was also observed that majority of the children 480 (85.4%) were treated on outpatient basis and 82 (14.6%) were admitted for observation. From their baseline status before treatment was given, all 562 children had fever (measured with a thermometer ≥ 38°C) at the start of the study and 383 (68.1%) were vomiting. Some had the following signs of severe malaria, convulsion 57 (10.1%), anaemia 48 (8.5%) and jaundice 17 (3.0%) (Table 12).

Table 12: Baseline clinical information of the children before treatment was started (N=562)

Variables	Frequency	%
Signs & symptoms on presentation apart from fever		
Vomiting	383	68.1
Chills & rigor	132	23.5
Convulsion*	57	10.1
Dull not active	349	62.1
Anaemia *	48	8.5
Jaundice *	17	3.0
Sunken eyes*	33	5.9
Drowsy*	49	8.7
Spleenomegaly	12	2.1

* Associated with severe malaria

It was observed that after 48hrs post anti-malaria treatment, 146 (26.0%) still had fever, 16 (2.8%) had jaundice, 17 (3.0%) were still vomiting and they were all referred while about 413 (73.5.0%) responded well to treatment without requiring further treatment (good outcome). (Table 13)

Table 13: Clinical information of the sick children 48 hrs after treatment was started (n=562)

Variables	Frequency	%
Signs & symptoms 48 hrs after treatment		
Fever	146	26.0
Jaundice	16	2.8
Vomiting	17	3.0
Chills & rigor	-	-
Febrile convulsion	-	-
Sunken eyes	3	0.5
Drowsy	12	2.1
Dull & not active	29	5.2
Non of the above signs /symptoms	413	73.5
Outcome of treatment after 48 hrs		
Satisfactory (good)	413	73.5
Poor	149	26.5
Total	**562**	**100**

The number of episodes of fever the children had suffered in the two months preceding the study was observed to be 31.0%, 34% and 29% for those that had suffered one episode, two or three episodes of fever respectively (Table 14).

Table 14: Number of episodes of fever experienced by the children in the last two months

Variable	Frequency	%
Number of episodes of fever in the last 2 months		
Once	174	31.0
Twice	191	34.0
Thrice	162	28.8
Four times	35	6.2
Total	**562**	**100**

Most of the children 394 (70.1%) was observed would have been taken to a chemist shop for treatment before they were eventually brought to the health centre, while 114 (20.3%) were brought straight to the health centres (Table 15).

Table 15: Treatment sought by caregivers before coming to the health centre

Variables	Frequency	%
Traditional healer	9	1.6
Church	45	8.0
Chemist	394	70.1
Sort no treatment	114	20.3
Total	**562**	**100.0**

One hundred and ninety eight (35.2%) of the caregivers were observed to first notice fever in a child <12hrs as of the time of presentation at the health facilities while 364 (64.8%) first noticed fever after 12hrs. It was again observed that about 107 (19.0%) of the children had stopped having fever about 2 hrs after anti-malaria drugs were administered and 250 (44.5%) and 56 (10%), stopped having fever ≤24hrs and 24-48hrs respectively, after treatment was given and these were the children that were classified as having good treatment outcome (Table 16). For the remaining 149 (26.5%), in which the fever persisted leading to referral, they were the ones referred to as having poor outcome and they are the group of interest i.e. what were those factors that made the other 413 to recover from the fever and they did not. Efforts were made to identify these factors in the analytical section that will soon follow.

Table 16: Time interval between when drugs were administered and when the fever stopped

Variables	Frequency	%
About 2 hrs after treatment	107	19.0
≤ 24 hrs	250	44.5
24 – 48	56	10.0
Fever persisted	149	26.5
Total	**562**	**100.0%**

Anti – malaria drugs were administered on about half (49.0%) of the children immediately after consultation while 51.0% had their drugs <24hrs after consultation and non got beyond 24hrs (Fig. 7). Most of the time 540 (96.1%) a caregivers would notice a child to be having fever when the body is hot to touch, while 354 (63.0%) of the time it is when the child is restless.

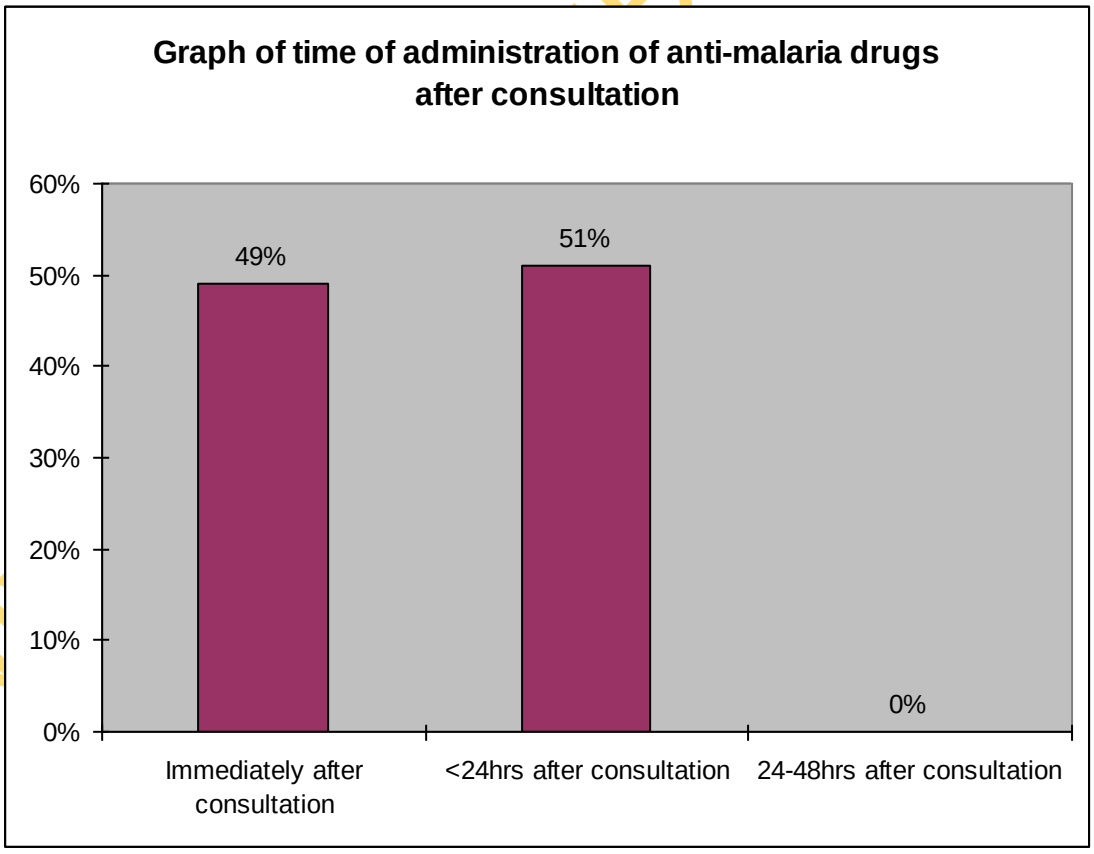

Fig 7: Time interval between consultation and administration of drugs

When a child is noticed to have fever 45% of the caregivers would give home treatment ≤24hrs after the fever is first noticed and 55% of them would give treatment after 24hrs (Fig 8).

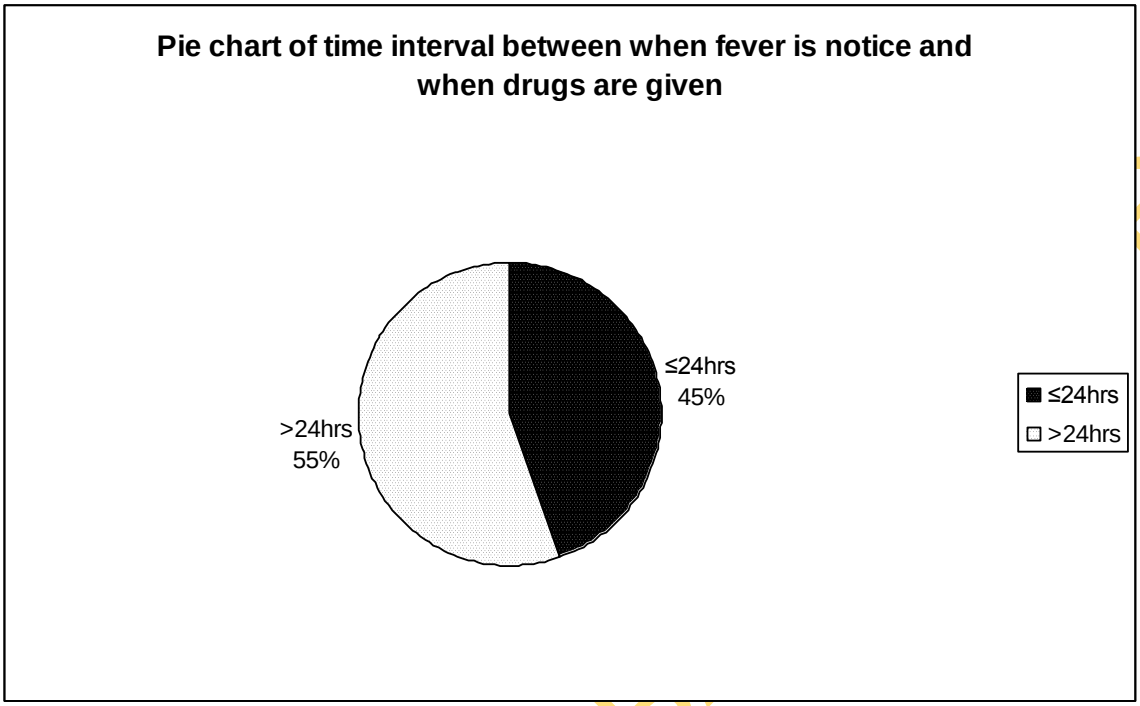

Fig 8: Time interval between when fever is noticed and drugs are given during home treatment of malaria

Immediately after noticing fever in a child (Table 17), 523 (93.1%) of the caregivers would give PCM, 255 (45.4%) of them would take the sick child to the health centre and 346 (61.6%) would tepid sponge the child to bring down the temperature.

Table 17: Activities of the caregiver when a child develop fever at home (N = 562)

Variables	Frequency	%
Wait till it is serious	17	3.0
Give PCM immediately	523	93.1
Give malaria treatment immediately	43	7.7
Take a child to the health centre	255	45.4
Tepid sponge	346	61.6

It was observed that when the caregivers do home treatment of malaria (Table 18), nearly all the caregivers 523 (98.9%) would give paracetamol (PCM) while 190 (33.8%) would give chloroquine and 93 (16.5) of them would give left over drugs used in previous treatment irrespective of the type of drugs.

Table 18: Drugs used by caregivers when they do home treatment of malaria (N = 562)

Variable	Frequency	%
PCM	556	98.9
Chloroquine	190	33.8
Camoquine	43	7.7
Artesunate	73	13,0
ACT	24	4.3
Blood syrups/tablets	343	61.0
Herbs	3	0.5
Left over drugs	93	16.5

It was observed that a good number of caregivers know about activities that could prevent them and their children from having malaria. Majority of them 517 (92.0%) believed sleeping under ITN and 490 (87.2%) cutting bushes around the houses would prevent malaria in the household (Table 19).

Table 19: Frequency of caregivers perceived knowledge of malaria prevention (N = 562)

Variables	Frequency	%
Clearing bushes	490	87.2
Covering open water containers	348	61.9
Draining blocked gutters	345	61.4
Sleeping under ITN	517	92.0
Spraying homes with insecticides	402	71.5
Taking prophylactic treatment	386	68.7

Also the caregivers carried out the following malaria prevention activities at home 248 (44.1%) of them agreed that their children were sleeping under ITN and 310 (55.2%) sprayed their rooms regularly in the evenings with insecticide (Table 20)

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Table 20: Malaria prevention efforts by the caregivers

Prevention effort	Frequency	%
Child sleeps under ITN	248	44.1
Doors & windows have nettings	398	70.8
Child usually treated prophylacticaly	352	62.6
Rooms are sprayed with insecticides	310	55.2
Family staying outside in the evenings	381	67.8
Burning mosquito coil while outside in the evenings	106	18.9

Malaria prevention activities during the antenatal period by mothers while the child was been conceived were reported/observed to be 213 (37.9%) mothers slept under ITN while pregnant, 508 (90.4%) took Intermittent Preventive Treatment (IPT) (Table 21).

A high proportion of the caregivers 352 (62.6%) agreed that either parents decides when a sick child should be taken to the health centre (Fig 9).

Table 21: Antenatal period malaria prevention activities when the child was been conceived

Antenatal activities	Frequency	%
Mothers slept under ITN		
Yes	213	37.9
No	349	62.1
Total	**562**	**100.0**
Mothers took IPT		
Yes	508	90.4
No	54	9.6
Total	**562**	**100.0**

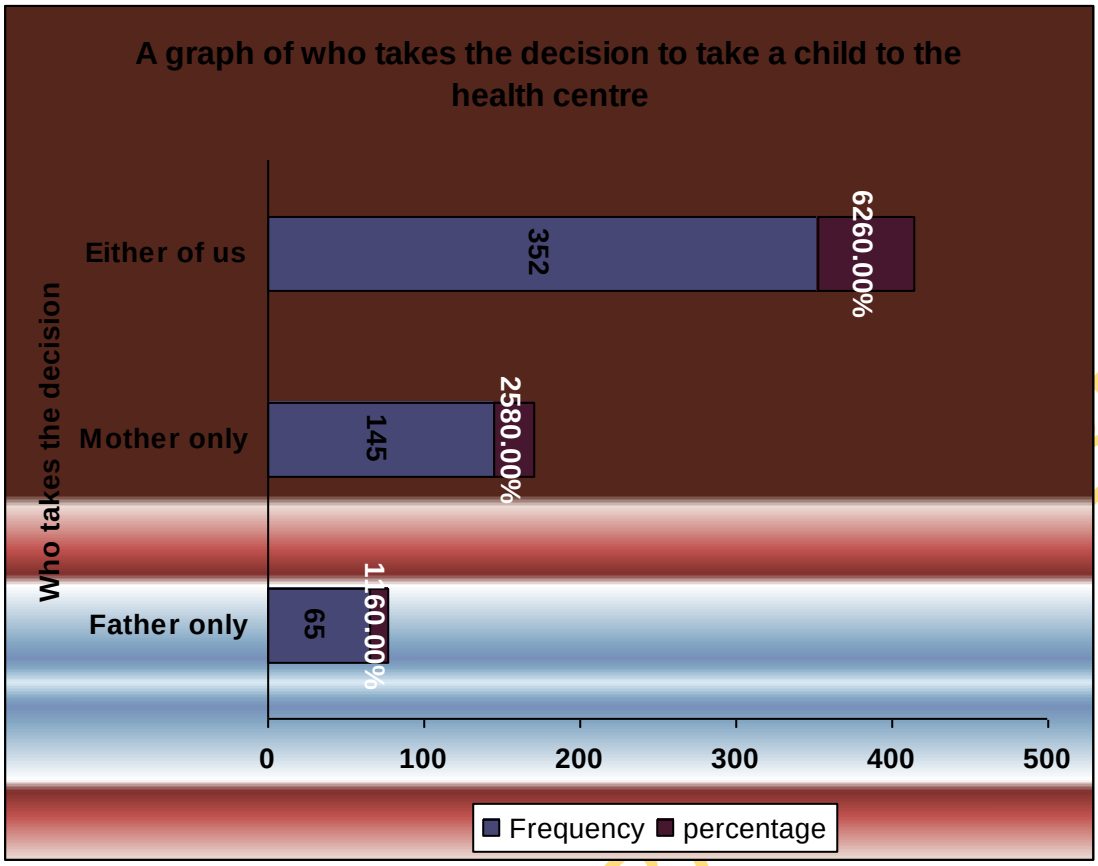

Fig 9: A bar chart of who decides when a child should be sent to the health facility

It was observed from post natal information obtained from mothers/caregivers that, 100 (17.8%) of the sick children were small for age at birth, 335 (59.6%) were exclusively breastfed, 511 (90.9%) were fully immunized for age (Table 22). Also it was observed that 355 (63.2%) of mothers were taught home treatment of malaria during ANC and 238 (42.3%) were equally taught what to do when a child develop fever as shown in (Tables 23).

Table 22: Postnatal information concerning the sick child from mothers/caregivers

Variables	Frequency	%
Child small for age at birth		
Yes	100	17.8
No	462	82.2
Total	**562**	**100.0**
Did exclusive breastfeeding		
Yes	335	59.6
No	227	40.0
Total	**562**	**100.0**
Child fully immunized		
Yes	511	90.9
No	51	9.1
Total	**562**	**100.0**

Table 23: What mothers were taught during ANC

Variable of interest	Frequency	%
Taught home treatment of malaria during ANC		
Yes	355	63.2
No	207	36.8
Total	**562**	**100.0**
Taught ORS during ANC		
Yes	549	97.7
No	13	2.3
Total	**562**	**100.0**
Taught what to do when child is febrile		
Yes	238	42.3
No	324	57.7
Total	**562**	**100.0**
Taught tepid sponging		
Yes	110	19.6
No	452	80.4
Total	**562**	**100.0**

Majority 482 (85.8%) of the caregivers believed the services rendered at the four health facilities used in this study was good (Table 24).

Table 24: Impression about the services rendered at the health facility

Variables	Frequency	%
Feelings about services in the clinic		
Good	482	85.8
Not good	80 5	14.2
Total	**562**	**100**

Majority 440 (78.3%) of the caregivers interviewed, live greater than 1 km from the health centre while few of them about 122 (21.7%) lives about 1km from the health centre.

Asked how government could curtail the malaria menace in the community, most of the caregivers 462 (82.2%) agreed that the provision of free anti-malaria drugs will improve the fight against malaria in the communities. While 480 (85.4%) of them believed free ITN would be vital in curbing malaria menace in their community (Table 25).

Table 25: Suggestions by caregivers on how government can curtail the menace of malaria in the community

Variable	Frequency	%
Provision of free anti-malaria drugs	462	82.2
Provision of free ITN	480	85.4
Clearing of bushy environment	45	8.0
Provision of health centers in the community	4	0.7
Educating mothers on the need for ITN	40	7.1
Avoiding stagnant water	15	2.7
Provision of free laboratory	13	2.3

4.3.2 Bivariate analysis

After carrying out an initial univariate analysis, some variables were identified that were considered to be capable of influencing the malaria treatment outcome among the under-five years children observed in this study. So it was decided that a Bivariate/multivariate analysis on them would be carried out. Variables like who decides when a sick child should be sent to the hospital had no association with the treatment outcome of malaria noticed among under – five children in Umuahia North LGA of Abia State (Table 26).

Table 26: Association between who decides when a child is taken to the clinic when sick and good treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Who decides when to take a child to the clinic?			
Father alone decides			
Yes (n = 65)	44 (67.7)		
		0.953	0.329
No (n = 497)	269 (74.2)		
Mother alone decides			
Yes (n =145)	110 (75.9)		
		0.413	0.520
No (n = 417)	302 (72.7)		
Either parent decides			
Yes (n =352)	259 (73.6)		
		0.001	0.972
No (n = 210)	154 (73.3)		

However there was an association between a mother sleeping under ITN while pregnant and good treatment outcome among the sick children as it was significant at a p<0.003 (Table 27). The significance at p<000 noticed between mothers been taught home care of malaria during ANC and good treatment outcome was also a sign of an association between them (Table 27).

Table 27: Association between the various ANC activities by mothers and good treatment outcome among the children

Variable of interest	Good outcome x(%)	X^2	P = value
Mothers took prophylactic malaria treatment during ANC			
Yes (n = 508)	375 (73.8)		
		0.147	0.701
No (n = 54)	38 (70.4)		
Mothers slept under ITN during ANC			
Yes (n = 213)	172 (80.8)		
		8.698	0.003**
No (n =349)	241 (69.1)		
Mothers taught home care of malaria during ANC			
Yes (n = 355)	291 (82.0)		
		34.437	0.000**
No (n = 207)	122 (58.9)		
Mothers taught preparation of ORS during ANC			
Yes (n = 549)	404 (73.6)		
		0.467	0.973
No (n = 13)	9 (69.2)		
Mothers taught what to do when child is febrile			
Yes (n = 238)	178 (74.8)		
		0.253	0.615
No (n = 324)	235 (72.5)		

**** Significant at p< 0.05**

There was neither an association between a sick child been less than or greater than 12 months old and good treatment outcome nor the gender of the sick child and good treatment outcome (Table 28)

Table 28: Demographic information of the sick children and its association with good treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Age group of the children			
≤ 12 months (n = 118)	81 (68.6)		
		1.498	0.221
> 12 months (n = 444)	332 (74.8)		
Gender of the sick child			
Male (n = 305)	220 (72.1)		
		0.487	0.485
Female (n = 257)	193 (75.1)		

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An association was observed between a caregiver having formal education and having good treatment outcome i.e. the proportion of the educated caregivers to those without formal education was 407 (74.1%) to 6 (46.8%) at p<0.05. Also obtaining good treatment outcome had no association with who accompanied the caregiver to the clinic (Table 29).

Table 29: Association between caregiver's level of education or who accompanied them to the health centre and good treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Is caregiver educated			
Yes (n = 549)	407 (74.1)		
		3.77	0.05**
No (n = 13)	6 (46.8)		
Child's father accompany caregiver to the H/C			
Yes (n = 75)	56 (74.8)		
		0.012	0.913
No (n = 487)	357 (73.3)		
Neighbors accompany caregiver to the H/C			
Yes (n = 56)	39 (69.6)		
		0.278	0.598
No (n = 506)	374 (73.9)		
Relatives accompany caregiver to the H/C			
Yes (n = 127)	101 (80.2)		
		3.282	0.070
No (n = 437)	312 (71.6)		
Caregiver was alone			
Yes (n = 304)	212 (70.7)		
		2.327	0.127
No (n = 258)	201 (76.7)		

**** Significant at p< 0.05**

It was observed that among all the baseline signs and symptoms that the children presented with at the health facility (Table 30), a sick child having signs of severe malaria like febrile convulsion, anaemia, jaundice, sunken eyes, drowsy and spleenomegaly were all significant predictor of poor treatment outcome as they were significant at p<0.00, p<0.00, p<0.00, p<0.00, p<0.00 and p<0.00 respectively. A child having chills & rigor where however a predictor of good treatment outcome and was significant at p<0.03.

Table 30: Association between the various signs and symptoms of the sick child at the time of presentation in the clinic and good treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Vomiting			
Yes (n = 383)	273 (71.3)	2.664	0.103
No (n = 179)	140 (78.2)		
Chills & rigor			
Yes (n = 132)	107 (81.1)	4.582	0.032**
No (n = 430)	306 (71.2)		
Fébrile convulsion			
Yes (n = 57)	19 (33.3)	50.227	0.0000**
No (n = 505)	394 (78.0)		
Child dull & not active			
Yes (n = 349)	256 (73.4)	0.000	0.995
No (n = 213)	157 (73.7)		
Anaemia			
Yes (n = 48)	19 (39.6)	29.091	0.0000**
No (n = 514)	394 (76.7)		
Jaundiced			
Yes (n = 17)	4 (23.5)*	0.000	0.0000**
No (n = 545)	409 (75.0)		
Drowsy			
Yes (n = 49)	22 (44.9)	20.941	0.0000**
No (n = 513)	391 (76.2)		
Had sunken eyes			
Yes (n = 33)	12 (36.4)	22.816	0.0000**
No (n = 529)	401 (75.0)		
Spleenomegaly			
Yes (n = 12)	3 (25.0)*	0.000	0.0004**
No (n = 550)	410 (75.5)		

*** Fisher s exact test**
**** Significant at p< 0.05**

An association was also observed between when the duration of fever was <48hrs or >48hrs before presentation and good treatment outcome as it was significant at p<0.05 (Table 31).

Table 31: Association between duration of fever and treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Fever started <48hrs before presentation (n=462)	348 (75.3)	3. 983	0.046**
Fever started >48hrs before presentation (n=100)	65 (63.0)		

**** Significant p< 0.05**

An association was not observed between the number of episodes of fever in the last two months preceding the study and good treatment outcome (Table 32).

Table 32: Association between number of episodes of fever in the last two months before presentation and treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
≤ 3 episodes of fever in the last 2 months (n = 527)	384 (72.9)	1.208	0.272
> 3 episodes of fever in the last 2 months (n = 35)	29 (82.9)		

There was no observable association between when a caregiver detects fever in a child through direct touch and good treatment outcome while there was an association between good treatment outcome and when fever is elicited in a child when he/she is observed to be restless as it was significant at p<0.00 (Table 33).

Table 33: Association between how a caregiver detects fever in her sick child and good treatment outcome at the health facilities

Variable of interest	Good outcome x(%)	X^2	P = value
Detect fever through touch			
Yes (n = 540)	398 (73.3)	0.108	0.742
No (n = 22)	15 (68.2)		
Detect fever when child is restless			
Yes (n = 354)	277 (78.3)	10.478	0.001**
No (n = 208)	136 (65.4)		

**** Significant at p< 0.005**

Giving treatment to a sick child within or >24hrs of detecting fever and good treatment outcome had no association (Table 34).

Table 34: Association between when treatment was given after detecting fever and good treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Treatment given within 24 hrs of detecting fever (n = 311)	220 (70.7)	2.392	0.122
Treatment given > 24 hrs of detecting fever (n = 251)	193 (76.9)		

On comparing the type of home treatment given to a child when he/she is noticed to be febrile and good treatment outcome, it was observed that there were significant degree of association between good treatment outcome and when a child is taken immediately to a health centre as soon as fever is noticed and also when tepid sponging is done on a child with fever as they were both significant at a p< 0.00 and p<0.00 respectively (Table 35). Also giving a sick child chloroquine by caregivers during home treatment of malaria was significant at p<0.00 showing that it was a predictor of good treatment outcome (Tables 36).

Table 35: Association between the type of home treatment and good treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Give PCM when a child develops fever			
Yes (n = 523)	388 (74.2)	1.412	0.235
No (n = 39)	25 (64.1)		
Usually give full malaria treatment			
Yes (n = 43)	35 (81.4)	1.087	0.297
No (n = 519)	378 (72.8)		
Take a child to the H/C immediately			
Yes (n = 255)	205 (80.4)	10.783	0.001**
No (n = 307)	208 (67.8)		
Tepid sponge as soon as fever is detected			
Yes (n = 346)	277 (80.1)	19.078	0.000**
No (n = 216)	136 (63.0)		

**** Significant at p< 0.05**

Table 36: Association between the drugs used by caregivers during home treatment of malaria and good treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Give CQ during home treatment			
Yes (n = 190)	157 (82.6)		
		11.620	0.000**
No (n = 372)	256 (68.8)		
Give ACT during home treatment			
Yes (n = 24)	21 (87.5)		
		1.831	0.179
No (n = 538)	393 (72.9)		
Give other left over drugs			
Yes (n = 93)	62 (66.7)		
		2.258	0.133
No (n = 469)	251 (74.8)		

**** Significant at p< 0.05**

It was equally observed that when a child was made to sleep under ITN was positively associated with good treatment outcome as it was significant at p<0.02, however having mosquito nets on the doors and window as well as treating a child prophylactically had no association with the treatment outcome (Table 37).

Table 37: Association between malaria prevention practices by caregivers and treatment outcome

Variable of interest	Good outcome x(%)	X^2	P = value
Child usually sleep under ITN			
Yes (n = 248)	195 (78.6)		
		5.559	0.018**
No (n = 314)	218 (69.4)		
Doors/windows in the house are netted			
Yes (n = 398)	294 (73.9)		
		0.046	0.830
No (n = 164)	119 (72.6)		
Child is treated prophylacticaly			
Yes (n = 352)	263 (74.7)		
		0.571	0.450
No (n = 210)	150 (71.4)		

**** Significant at p< 0.05**

Though there was no direct association between treating a sick child in either the urban or rural health centre and treatment outcome however, treating a sick child in Ojike-street PHC as oppose

to World Bank housing estate PHC both of which are in the urban area was associated with good treatment outcome as it was significant at p<0.04 (Tables 38).

Table 38: Association between good treatment outcome and location of the health centre

Variable of interest	Good outcome x(%)	X^2	P = value
Child treated in an urban health centre (n = 315)	234 (74,3)		
		0.150	0.70
Child treated in a rural health centre (n = 247)	179 (72.5)		
Child treated at Ojike road H/C (n = 221)	172 (77.8)		
		4.26	0.04**
Child treated at WBHE H/C (n = 94)	62 (66.0)		
Child treated at Amaogwugwu H/C (n = 77)	51 (66.2)		
		1.75	0.19
Child treated at Umuawa-Alaocha H/C (n = 170)	128 (75.3)		

Significant at p, 0.05

It was observed that treating a child on out patient basis, was a good predictor of good treatment outcome at a p<0.00 as opposed to admitting a child for observation (Table 39).

Table 39: Association between treatment outcome and how a sick child was treated

Variable of interest	Good outcome x(%)	X^2	P = value
Child admitted for observation (n = 82)	39 (47.6)		
		31,584	0.0000**
Child was treated on outpatient basics (n = 480)	374 (77.9)		

Significant at p< 0.05

Though there was no association between caregivers taking malaria prophylactic treatment during pregnancy and good treatment outcome, it was however observed that, there was

significant degree of association between a mother taking prophylactic malaria treatment during pregnancy and a child been treated prophylacticaly for malaria at p<0.00 (Table 40).

Table 40: Association between a mothers taking prophylactic treatment during pregnancy and she treating her child prophylacticaly for malaria after birth

Variable of interest	Child treated prophylacticaly x(%)	X^2	P = value
If mother took prophylactic malaria treatment during her pregnancy			
Yes (n = 508)	341 (67.1)		
		43.62	0.000**
No (n = 54)	11 (20.4)		

**** Significant at p< 0.05**

In the same vain, there was significant association between a mother sleeping under ITN during her ante natal (ANC) period and her child using same after birth at p<0.00 (Table 41).

Table 41: Association between a caregiver sleeping under ITN during ANC and her child using same as malaria preventive method after birth

Variables	Child using ITN x(%)	X^2	P = value
If mothers used ITN during ANC (while pregnant of the sick child)			
Yes (n = 213)	147 (69.0)		
		84.54	0.0000**
No (n = 349)	101 (28.9)		

**** Significant at p<0.05**

4.3.3 Multivariate analysis

The 18 variables that were significantly associated with good treatment outcome were further subjected to multivariate analysis by carrying out logistic regression modeling and the following models came out (Table 42).

(1) A child having signs of severe malaria would negatively affect the good treatment outcome i.e.

  (a) A child having febrile convulsion {OR 0.1562 (C.I = 0.0797 – 0.3064)} p<0.000

  (b) A child having anaemia {OR 0.3027 (0.1319 – 0.6589)} p<0.003

  (c) A child having jaundice {OR 0.1801 (0.0490 – 0.6624)} p<0.010

  (d) A child been severely dehydrated {OR 0.2806 (0.1184 – 0.6651)} p<0.004

(2) When mothers of the children were educated during ANC

  (a) On home treatment of malaria {OR 2.5603 (1.6312 – 4.0185)} p<0.000

(3) Practices by caregivers when a child develop fever at home

  (a) Taking a child to a health centre {1.9530 (1.2257 – 3.1117)} p<0.005

  (b) Carrying out tepid sponging {1.5475 (0.9801 – 2.4434)} p<0.061

  (c) Giving chloroquine {1.9348 (1.1779 – 3.1780)} p<0.009

(4) Malaria prevention activities at home by caregivers

  (a) Caregiver sleeping under ITN

  While pregnant of the sick child {2.2285 (1.3741 – 3.6139)} p<0.001

Table 42: Logistic regression modeling result of those variables that were significant from bivariate analysis of factors associated with good treatment outcome

Variable of interest	Odds ratio	95% Confidence interval	P = value
Signs of severe malaria			
Febrile convulsion	0.1562	(0.0797 – 0.3064)	0.000**
Anaemia	0.3027	(0.1391 – 0.6589)	0.003**
Jaundice	0.1801	(0.0490 – 0.6624)	0.010**
Sunken eyes	0.2806	(0.1184 – 0.6651)	0.004**
What mothers were taught during ANC			
Taught home care of malaria	2.5603	(1.6312 – 4.0185)	0.000**
Practices when a child develops fever			
Takes a child to a health centre	1.9530	(1.2257 – 3.1117)	0.005**
Tepid sponge	1.5475	(0.9801 – 2.4434)	0.061**
Give chloroquine	1.9348	(1.1779 – 3.1780)	0.009**
Malaria prevention activities			
Mothers slept under ITN while pregnant of the sick child	2.2285	(1.3741 – 3.6139)	0.001**

**** Significant at p< 0.05**

CHAPTER FIVE

5.0 Discussion

In this analysis of the study on "Malaria treatment outcome among under-five children attending primary health care centres in Umuahia North LGA of Abia State Nigeria, a prevalence of good treatment outcome of 73.5% was recorded. This prevalence is lower than 79% that was found in a pilot study that had earlier been carried out few weeks preceding this study at two primary health centres in Umuahia North LGA that were excluded from this study. Tangpukdee *et al.*, 2007 reported a prevalence of uncomplicated malaria progressing up to severe malaria after admission of 3 – 5% (poor outcome) making a good treatment outcome of about 95% which was quite higher than what was observed in this study. At the selected Primary health care (PHC) centres, the facility heads had the necessary trainings to carry out malaria treatment in children and they uses presumptive diagnosis to arrive at the diagnosis of malaria in under-five years children in line with the WHO IMCI Guideline for malaria. However, with poor record keeping at the facilities, lack of access to the IMCI guideline and the National malaria treatment protocol and poor supervision by the LGA health department, quality health care/services cannot be guaranteed. This may be one of the reasons while some of the facilities still prescribe chloroquine contrary to the National policy on the treatment of malaria. Krause and Sauerborn had in 2000 observed in their work in rural Burkina Faso that health care services/intervention utilization by most community is dependent on availability of quality services by the health care providers among others. It was observed that a child getting treatment at ojike street PHC have a better outcome than if treated at World bank housing estate PHC both of which are in the urban area. The only remarkable thing about Ojike street PHC is that it had the highest number of supervisory visits in the last five months preceding the study as well as been the only PHC studied that does not have the capability to admit patients for observation. Malaria is known to

be the major cause of mortality and morbidity in the tropical and subtropical regions in the world. However, mortality can be reduced by effective use of standard treatment procedures such as the National treatment protocol and the IMCI guideline. Patients who require hospitalization and those who need intensive care can be identified promptly and treated before they develop complications. About 10% of cases of *falciparum* malaria can be classified as severe malaria, among which the mortality is 10% but may rise to as high as 50% (Pasvol, 2005). It is well established that the prognosis of acute uncomplicated falciparum malaria patients who might progress to severe malaria vary depending on the early diagnosis, prompt management and the presence of any of the complications associated with malaria disease (Marsh *et al.*, 1995, White, 2003 Mishra *et al.*, 2006).

In this study, 94% of the caregivers bringing children with fever to the health facilities were mothers which is in line with Tarimo *et al*, 2000 work in Tanzania of 89%, Njama *et al.*, 2003 in Uganda of 95% and Yewhalaw *et al.*, 2010 in Ethiopia of 97.4%. The findings in this study also showed that only 45.4 % of caregivers would go to a health facility as first line of care for a febrile child as opposed to Yewhalaw *et al.*, 2010 value of 71.5%. Very few caregivers (1.6%) from this study would seek treatment from traditional healer whereas Njam *et al.*, 2003 in his study in Uganda reported that none of the caregivers sort helps from the traditional healers. Most of the children in this study were <24 months (48.2%) while the findings by Snow *et al.*, 2005 in Mozambique was about 50% of the same age group. This study also noted that majority of the caregivers would seek care at the patent medicine dealers first (70.1%) compared to (20.3%) that would go straight to the health centre. This is a major challenge to attaining the Roll back malaria strategy of prompt access to health care services by children with fever in Sub Sahara Africa region that need to be addressed urgently and this will also help to protect poor households from double spending accessing the same health care services twice that would impoverished them. Biritwum *et al.*, 2000 in their work in Ghana had reported similar findings where 82% of the care givers would have patronize the patent medicine stores before going to

the clinic. Although treating a child at the chemist looks cheaper, when one consider the sub standard treatment that could be given and the associated consequences of delayed access to prompt care as well as the eventual cost of getting retreated on the long run, accessing prompt services at the health facility obviously appeared to be the best thing to do. The observation in this study that the proportion of children with good treatment outcome increases as one goes up the social classes of the caregivers is collaborating the argument by international health care partners that there should be a strong advocacy at all levels for a pro – poor approach to the provision of health care services. Gwatkin and Guillot, 2000 in there work had observed the relationship between poverty and health; poverty leading to ill health, and ill health leading to increased poverty. Treating the children as outpatient was associated with good treatment outcome and this could be as a result of the fact that children with severe malaria or presumed malaria complication would most likely be admitted for observation during treatment than those with no complications. Those mothers that would discover that there children have fever when they are restless are more likely to seek help immediately than those who elicits fever by touching as the former would consider restlessness as a sign of severity of the illness while the later would want to observe the child in case the fever subsides and this is consistent with Yewhalaw *et al.*, 2010 findings that in Ethiopia caregivers would wait until the child is seriously sick before seeking care at the health facility. The use of chloroquine during home management of malaria was associated with good treatment outcome as compared to the ACT , this also may be as result of the fact that majority of the caregivers are familiar with the dosage of chloroquine as compare to the newer drugs which even if they give they are likely to give wrong doses. This is consistent with the findings of Salako *et al.*, 2001, who *carried* out a study in Nigeria and found that 77.5% of their respondents who had taken chloroquine as self administered first line of treatment were satisfied with the outcome, and this is also an indication that some strains of the *falciparum* malaria may have retained some form of sensitivity to chloroquine.

Majority of the caregivers were knowledgeable about the efficacy of ITN in the prevention of malaria which is similar to the findings by Tarimo *et al.,* 2000 in Tanzania and Nuwaha, 2001 in Ugadan. This study also found that taking a child promptly to the health centre as soon as fever is noticed is a strong predictor of good treatment outcome of children presenting with signs of malaria in the health centres which is in line with the findings of other workers in Africa such as Ibadin *et al.,* 2000 in Benin, Dzeing-Ella *et al.,* 2005 and Mishra *et al.,* 2006. The use of ITN by mothers during pregnancy was a predictor of good treatment outcome and this may have been influenced by the strong association that existed between a mother using ITN during her ante natal periods and her child using same as was observed in this study. The use of ITN is believed to reduce the level of parasitaemia in the blood of individuals and this is thought to in turn reduce the level of haemolysis and subsequently the incidence of anaemia and thus the severity of the illness (Mathanga *et al*., 2010). Guinovart *et al.,* 2008 had earlier observed in their study that the level of parasitaemia is significantly associated with the development of anaemia in children with malaria. When caregivers are taught home management of malaria or other form of malaria prevention technique, it had significant impact in predicting positive treatment outcome of under – five children with malaria and this is also supported by the work of Ajayi *et al.,* 2008 which showed that when mothers or caregivers were taught a new malaria control technique it was largely embraced by the community and this led to an improvement of the health of children in the community. It was also observed that the presence of signs of severe malaria like anaemia, febrile convulsion etc led to poor treatment outcome and this in effect mean that a child not presenting with them is likely to have a good treatment outcome. This is collaborated by the findings of Mishra *et al.,* 2006 who had earlier documented that the presence of signs of complication of malaria disease can actually lead to the progression of uncomplicated malaria to the severe form. Tangpukdee *et al.,* 2007 while working with adults that had malaria in trying to develop predictive score of uncomplicated falciparum malaria patients turning to severe malaria found dehydration (sunken eyes in children in this study) to be associated with progression of un

complicated malaria to the severe form a fact that was also collaborated by Ibadin *et al.,* in their earlier study in 2000. Also (Dzeing *et al.,* 2005) also reported that anaemia, was the frequent features of children patient with severe malaria followed closely by hypoglycaemia and then cerebral malaria (we did not investigate both). However having chills & rigor was a predictor of good outcome in this study with a proportion of 107 (81.1%) to 306 (71.2%) of not having chills & rigor at a statistical significance of P<0.03 and the reason for this might be the fact that when a child develops chill and rigors it is mistaken for convulsion and as such help is immediately sort at the health facilities. It has already be stated that as part of the findings of this study, it was observed that when a sick child is taken to the clinic <48hrs after fever had started there was a strong associated with good treatment outcome at p<0.046 which is in essence supporting one of the Roll back malaria strategies to promptly treat any child with malaria.

The observation in this study that when a caregiver uses prophylactic anti malaria drugs or slept under an ITN while pregnant she is likely to treat her own child prophylacticaly or made him or her sleep under ITN after birth further collaborated Ajayi *et al.,* 2008 findings in their work. They had observed as earlier stated above that mothers or caregivers could actually during their ANC period be made a useful means of introducing a new malaria control technique into the community as a means of improving the health of children. Though it was observed in this study that when a child sleeps under an ITN and when the mother had earlier used an ITN too during her ANC periods were initially both predictors of good treatment on bivariate analysis. However when both were subjected to logistic regression modeling, only mother using ITN during pregnancy was significant showing that the later was actually a confounding variable. The lessons one can draw from here is that the uptake of those health care interventions that are shared by mothers and their children alike can be enhanced by encouraging/enforcing their practices among mothers. The importance of this finding is further strengthened by the fact that mother taking intermittent preventive treatment (IPT) during her ante natal period was a strong predictor of the child benefiting from same at P<0.00.

5.1 Conclusion

In conclusion this study has shown that effective management of malaria in children under the ages of five years requires mothers to be knowledgeable about causes and early signs of malaria such as fever that has been proven to be the interactive clinical indicator of malaria infection. They should then seek, obtain, and use medication appropriately as early as possible through timely decision, accessibility and correct use of the drugs and follow-up. When a child presents with signs and symptoms of severe malaria at the health centre, there is a high tendency that the illness would deteriorate or the child will not recover within 48hrs (WHO manual for CHW). Therefore the child would need extra medical care either in a secondary facility or a tertiary facility. If and when the caregiver cannot afford this treatment the life of the child would be in danger. It is therefore pertinent that the incidence of mothers who sort care elsewhere before coming to the health facility should be reduced as this does not only cause unnecessary delays of treatment but also waste the meager resources at the disposal of the affected households. Behavioral change communication is an important method that can be employed so that the incidence of malaria can be reduced drastically in the community. As mothers can be trained during ANC (as was observed in this study as well as in works done by Ajayi *et al*., 2008 and Anumudu et al., 2007) and be made to be agents of change and positive influence on other members of the community especially fellow mothers. In this way, the home care practices for the sick child would be strengthened, early presentation of children with fever at the health centres would improve, majority of under – five years children in the community would be sleeping under an ITN in line with the Roll back malaria strategy and there would be lower level of parasitaemia in children leading to fewer cases of signs of severe malaria such as anaemia among under – five children in the community. If the government can empower health care workers especially those at the community level, to go into the communities and communicate these various behavioral changes to the mothers, then avoidable mortalities due to malaria among under – five years children would be greatly reduced. This strategy could even be further

strengthened to include all the malaria control and prevention measures targeting other members of the community. Finally if we enforce health care service interventions shared by mother and child alike on mothers either during the ante natal or post natal periods, then there are higher chances of the intervention getting to the child.

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APPENDIX

MALARIA TREATMENT OUTCOME AMONG UNDER-FIVE CHILDREN AT PRIMARY HEALTH CARE CENTRES IN UMUAHIA NORTH LOCAL GOVERNMENT AREA, ABIA STATE

[CARE GIVERS QUESTIONNAIRES]

Section A

Identification

1. Questionnaire number _____ 2. Interviewer code_____
3. Interview date (dd/mm/yyyy) _____

Section B

Demographics of Household/caregivers

4. Marital status: Married ☐ **Single mother** ☐ **Divorce** ☐ **Widow** ☐

5. Age in yrs _____

6. Occupation: _____

7. Level of education: Ni☐ Primary ☐ Secondary ☐ Tertiary ☐

8. Relationship with sick child
Mother ☐ Father ☐ Relative ☐ Neighbour ☐

9. Who accompanied the care giver and the sick child to the health center? (Check as appropriate)

(a) Child's father ☐
(b) Neighbor(s) ☐
(C) Relatives ☐
(d) Was alone ☐
(d) Others specify _____

10. Residence

LGA: _____ Ward: _____

Village: _____

11. Religion: Pentecostal ☐ Orthodox church ☐ Islam ☐
Traditional ☐ Others specify _____

12. Number of children < 5 years in the house hold _____

13. How much does your household earn in a month? _____

14. Approximately how much does your house hold spend in a month (housing, feeding, health etc? _____

Section C

ASSESSMENT OF THE SICK CHILD

15. Age of the sick child (Yrs) _____

16. Gender of the sick child: Male ☐ Female ☐

17. The child is: Admitted for observation ☐ Outpatient ☐

Baseline information (condition of the child on presentation at the clinic)
(History taken from the mother)

18. Which of these symptoms was your child having before bringing him/her for treatment? (Check as appropriate)
(a) Fever ……
(b) Vomiting ……..
(c) Chills & rigor ……
(d) Convulsion …….

(e) Child was dull not active ……..

(From physical examination of the sick child)

19. These signs were found from examination of the sick child (Check as appropriate)
    (a) Temperature ºC …….. (Check with a clinical thermometer)
    (b) Anaemia ……..
    (c) Jaundice ……..
    (d) Sunken eyes ……
    (e) Drowsy ……
    (f) Spleenomegaly ……

History of the illness

20. Number of episodes of fever in the last two months?
    One ☐ Two ☐ Three ☐ Four ☐ Others_____

21. When did this current episode of fever start?

    <12 hrs ago ☐ 2 – 48 hrs ago ☐ 8 hrs ago ☐ xact time) ……:…… Hrs

22. Where else was this child taken to before bringing him/her to the health center?

    Chemist shop ☐ Traditional healer ☐ Church ☐

23. How much does it cost you to treat an < 5 yrs child fever in the
    (a) Chemist shop ……..
    (b) Using traditional medicine……
    (c) Health center……..
    (d) Private hospital……

24. How much does it cost you to treat your <5 child with malaria in the health facility?
    (a) Registration/card ……..
    (b) Admission per day ……..
    (c) Anti pyretic ……
    (d) Artemisinin combination therapy ……
    (d) Chloroquine ……..
    (e) Haematinics ……..
    (f) Transportation to the clinic…….
    (g) Others Specify_____ ……

Post treatment information/assessment (condition of the child 48hrs later)

25. 48 hours after treatment, child is having (Check as appropriate)
    (a) Fever ……

(b) Jaundice …….
(c) Vomiting …….
(d) Chills & rigor …….
(e) Febrile convulsion ……
(f) Sunken eyes ……..
(g) Drowsy ……
(h) Child is dull and not playing ……
(i) Non of the above

26. When was anti-malaria drug given to the sick child?

Immediately after consultation ☐ 24 hrs after consultation ☐
> 24 hrs after consultation ☐ Exact time of administration ……Hrs

27. When did the fever stop 48 hours after treatment?
(a) Immediately after treatment was started …….
(b) < 24 hrs after treatment was started ……..
(c) 24 - 48 hrs after treatment was started …….
(d) Exact time fever stopped …… Hrs

28. Classification of treatment 48 hrs after treatment was commenced

☐ ☐

Good **Bad**

Section D

Care giver's ability to carry out home care of a child with fever

29. How do you recognize fever in your child? (Check as appropriate)
(a) When body was hot to touch ……..
(b) When child became restless ……

30. When a child is noticed to be febrile, how long does it take before treatment is given?

<24 hrs ☐ 24 – 48 hrs ☐ >48hrs ☐

31. Which of these do you normally do when this child develop fever? (Check as appropriate)

(a) Wait until it gets serious ☐
(b) Give Paracetamol immediately ☐
(c) Give full malaria treatment immediately ☐
(d) Give treatment the next day ☐
(e) Take child to a chemist ☐
(f) Take child to health centre ☐
(g) Tepid sponge ☐

32. Which of these drugs do you give when you do home treatment on your child with fever.

(a) Give Paracetamol ……..
(b) Give Chloroquine ……
(c) Give camoquine ……
(d) Give Artesunate ……
(e) Give Artesunate combination therapy ……
(f) Give blood tablet ……..
(g) Herbs …….
(h) Other left over drugs from previous treatment ……..

Section E

Care givers' general awareness about causes of malaria and its prevention

33. Malaria is transmitted by: Mosquitoes bite ☐ Cockroach bite ☐
Houseflies bite ☐ others specify_____

34. Which of these is/are correct, malaria can be prevented by (Check as appropriate)
(a) Clearing the bushes around our homes ……..
(b) Covering all open water containers ……
(c) Draining all blocked gutters …….
(d) Sleeping under ITN ……
(e) Spraying our homes with insecticides ……..
(f) Taking prophylactic treatment ……

35. Care givers malaria causing/prevention activities at home
(a) Child sleep under mosquitoes net Y N
(b) Doors/windows at home has protective nettings Y N

(c) Child is usually treated prophylactically for malaria Y N
(d) Rooms are sprayed with insecticide Y N
(e) Family staying outside in the evenings for fresh air? Y N
(f) When you stay outside do you burn mosquitoes coil? Y N

Section F

Antenatal/postnatal activities

36. Did you sleep under ITN when you were still pregnant of this sick child?
Y N

37. Did you take prophylactic malaria treatment while pregnant of this sick child?
Y N

38. Number of times you were treated for malaria while pregnant of this sick child _____

39. Was your child small for age at birth? Y N

40. Did you do exclusive breastfeeding for your baby? Y N

41. If yes for how long? _____months

42. Is your child fully immunized for age? Y N

43. If no, how many visits did he/she misses? _____

44. Were you ever taught child's health promotion activities in the clinic? Y N

45. If yes which of these were you taught? (Check as appropriate)
(a) Home treatment of malaria ……..
(b) How to prepare ORS ……
(c) What to do when a child has fever at night in the home ……..
(d) Others specify _____

46. Who decides weather to take a sick child to the clinic? (Check as appropriate)
(a) Father only …….
(b) Mother only …….
(c) Either of us ……

Section G

Satisfaction with the services at the health facility

47. What is your opinion about the attitude of the health staff?

Good ☐ Fair ☐ Poor ☐

48. Would you like to come back to this clinic if your child was ever sick?

Y N If yes why? _____-

49. Did you get all the drugs you need to treat the child in the clinic? Y N

If yes which did you get? (Check as appropriate)

a. Paracetamol …….
b. Chloroquine ……..
c. Camoquine ……..
d. Artesunate ……..
e. Artesunate combination therapy ……
f. Blood tonic …….

50. How far is the clinic from your home?

< 1 km ☐ 1 -2 km ☐ 2 -5 km ☐ > 5km ☐

51. What do you think can be done to improve on the malaria care of <5 yrs in your community?

_____
_____
_____
_____
_____
_____
_____

MALARIA TREATMENT OUTCOME AMONG UNDER FIVE CHILDREN AT PRIMARY HEALTH CARE CENTRES IN UMUAHIA NORTH LOCAL GOVERNMENT AREA, ABIA STATE

[UMUAHIA NORTH PHC COORDINATOR STRUCTURED KII]

Section A

Identification

1. Questionnaire number _____ 2. Interviewer code_____
3. Interview date (dd/mm/yyyy) _____

Section B

Demography/training

4. Rank;
DSNO ☐ PNO ☐ SNO ☐ NO ☐ CHW ☐
Others specify_____

5. Qualification;_____

6. What are the various units that make up the LGA health dept?
_____
_____
_____
_____
_____

7. What is the level of training of the various unit head?
_____
_____
_____

_____
_____

8. Does the LGA operate the IMCI strategy? Y N

9. Number of staff heading the various PHC facility in the LGA that are trained on IMCI _____

10. Level of training of the various health facility heads in the LGA?
_____
_____
_____
_____
_____
_____

11. Is there any arrangement for in service training for the health staff?
Y N

12. Number of training on IMCI conducted for the staff of the department in the last one year? _____

Section C

Material /drugs

13. Did the department distribute IMCI guidelines/National malaria treatment protocol to the various health facilities in the LGA? Y N

14. Does the LGA have enough drugs for the PHC facilities? Y N

15. Which are the anti-malaria drugs that are in stock?
_____
_____
_____
_____
_____

16. How often are these drugs supplied to the various health facilities?

weekly ☐ monthly ☐ yearly ☐

17. Are drugs given freely to the under five been treated for malaria in the health facilities? Y N

18. Are there any extra charges on these drugs by the health facility?
Y N if yes, how much?_____

19. On the average what is the cost of treating malaria in the health facility?
(a) Registration/card ……..
(b) Admission per day ……..
(c) Anti pyretic ……
(d) ATC ……
(d) CQ ……
(e) Haematinics ……
(f) Others Specify_____

20. How often does the LGA health department carry out supervisory visit to the various health facilities? _____

21. Does the LGA have a protocol of systematic supervision of its health workers at the various health facilities? Y N

22. Does the department have enough staff to carry out its activities?
Y N

23. Have the department receive any ITN for distribution this year?
Y N

24. What are some of the malaria control activities carried out by the department?
_____
_____
_____
_____
_____
_____

25. Are these activities well funded?
Y N

26. What is the immunization coverage of the LGA? _____

27. What are some of the challenges faced by the department?

_____
_____
_____
_____
_____
_____

MALARIA TREATMENT OUTCOME AMONG UNDER-FIVE CHILDREN AT PRIMARY HEALTH CARE CENTRES IN UMUAHIA NORTH LGA, ABIA STATE

[PHC FACILITY HEAD KII]

Section A;

Identification

1. Questionnaire number _____ 2. Interviewer code_____
3Interview date (dd/mm/yyyy) _____

Section B;

Demography and training

4. Age: (Yrs) _____

5. Gender: Male ☐ **Female** ☐

6. Rank:
DSNO ☐ PNO ☐ SNO ☐ NO ☐ CHW ☐
Others specify_____

7. Level of training;
PGD ☐ B.Sc ☐ Sch of Nurs ☐
Sch of Health tech ☐ Others specify_____

8. Where you ever trained on use of IMCI? Y N If yes how long ago_____

9. Did you receive any training on the management of malaria in the last one year? Y N

10. How many staff in this clinic can attend to patients with malaria? _____

11. On the average, how many patients come to this clinic in a day? _____

12. How many of them were treated for malaria? _____

13. How many other support staff do you have in this clinic? _____

Section C:

Materials

14. Do you have the IMCI guideline?
Y N If yes sight……..

15. Do you have the National treatment protocol for malaria?
Y N If yes sight ……..

16. Does this facility have any provision for patient admission?
Y N If yes, how many beds? _____

17. Does this facility have the following materials?

(a) Thermometer? Y N If yes sight……..
(b) Weighing scale? Y N If yes sight…….
(c) Water? Y N If yes sight tap or water/container….
(d) Mosquitoes nets for patients on admission? Y N If yes sight…
(e) Stethoscope? Y N If yes sight…….
(f) Monitoring chart? Y N If yes sight ……..

18. Number of hours the clinic is open for service
<24 hrs ☐ 24 hrs ☐

Section D;

Patronage

19. Average Number of patients seen per day (from treatment book record)_____

20. From your observation, what proportion of mothers would have commenced treatment for their sick child before coming to the clinic?

< 30% ☐ 30 – 50% ☐ 50 – 80% ☐ >80% ☐

21. What form of treatment do mothers normally give at home before coming to the health centre?

(a) Gave concoctions/herbal medicine Y N
(b) Gave PCM Y N
(c) Gave Chloroquine Y N
(d) Gave Artesunate Y N
(e) Gave nothing Y N

Record keeping

22. What year did this facility become fully operational_____

23. Does this facility have complete record of all its activities since inception?
Y N If yes confirm…

24. How many years' records are available? .....

25. How many children where immunized in this facility last year? _____
Check the immunization register……..

Availability of anti malarial drugs/ITN

26. What drugs do you normally use in the treatment of malaria in this facility?

_____
_____
_____
_____
_____
_____
_____
_____

Are these drugs available in this clinic? Y N
Sight to confirm which are available……..

27. Have this facility received any ACT from the LGA this year?
Y N

28. If yes are they still in stock? Y N

29. Have this facility given ITN for distribution this year? Y N

30. If yes, are they still in stock? Y N

31. Have you been out of stock of drugs? Y N If yes how long_____

32. When out of stock of drugs what do you advice patients to do?

(a) Buy drugs in a chemist shop? Y N
(b) Refer patients to other clinics? Y N

33. Number of times supervisors from the LGA visited this facility in the last two months_____

34. On the average what is the cost of treating malaria in this health facility?
(a) Registration/card ……..
(b) Admission per day ……..
(c) Anti pyretic ……
(d) ATC ……
(d) CQ ……..
(e) Haematinics ……..
(f) Others Specify_____ ……

35. How do you make diagnosis of malaria in the health center?

(a) From laboratory results? Y N
(b) Clinical examination? Y N
(c) From the complaints? Y N

Map of Abia State with the study area marked in green