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REVIEW ARTICLE

The Prevalence of Congenital Malaria: Nigerian Experience

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ABSTARCT

This study was aimed at highlighting on the prevalence of malaria among pregnant women in Nigeria within the last ten years. The prevalence of congenital malaria in Nigeria varies and it affects every geopolitical zone in Nigeria. This is because Nigeria like other countries in the tropics and subtropics has factors which favour the survival of mosquito. Although the World Health Organization (WHO) recommends the use of insecticide treated nets and effective case management of uncomplicated malaria as a feasible and cost-effective control strategy, Nigeria remains one of the worst affected countries in the world with malaria among pregnant women and neonates. This paper recommends more programs to the menace of this infection among pregnant women and neonates in Nigeria.

Keywords: Malaria, Nigeria, *Plasmodium*, Pregnancy

1 Introduction

Malaria is a serious public health challenge and a major cause of maternal and infant morbidity and mortality in malaria–endemic countries [1]. Malaria in pregnancy is associated with higher rates of parasitemia, severe anemia, hypoglycemia, and acute pulmonary edema than malaria in non–pregnant women [2]. Also, *Plasmodium falciparum*–infected red cells sequester in the placenta, disrupting nutritional exchange between mother and fetus and causing intrauterine growth retardation, abortion, stillbirth, and low birth weight may occur [3]. In a World Malaria Report, Nigeria accounts for a quarter of all malaria cases in the 45 malaria–endemic countries in Africa clearly showed the challenge of malaria in Nigeria [4].

The main strategy of malaria control is the effective case management of malaria which involves proper clinical assessment, laboratory confirmation of the disease by using light microscopy or rapid diagnostic technique (RDT) before treatment with an effective antimalarial therapy [5]. Most cases of malaria cases in Nigeria are caused by *Plasmodium falciparum* and it is the most virulent of all the species mostly causing malaria–related morbidity and mortality in the country [6]. This study was aimed at highlighting on the prevalence of malaria among pregnant women in Nigeria from 2007 to 2017; factors contributing to the prevalence of the infection and the needed efforts for control.

2 Epidemiology of Malaria

Epidemiology of malaria among pregnant women in Nigeria Malaria is a zoonetic disease transmitted through female mosquito vector of *Anopheles funestus*, *Anopheles moucheti*, *Anopheles gambiae* and *Anopheles arabiensis*. It is caused by parasitic protozoans of the genus *Plasmodium* with species *falciparum*, *vivax*, *malariae*, *ovale* and *knowlese* [1,7,8]. Of all the species of human plasmodia, *Plasmodium falciparum* is the most pathogenic as it presents malignancy in the type of malaria associated with it. In non–immune subject, this type of malaria usually run an acute course and terminates fatally if not quickly treated with specific drugs [8]. According to WHO [9], malaria parasite is generally with the tropical and

subtropical regions because the development in the mosquito is greatly retarded when the temperature is below 20°C.

Malaria in pregnancy is a major contributor of maternal and neonatal mortality [10]. According to WHO, there were more than 200 million malaria cases in 2012. An estimated 627,000 people died from malaria in 2012 and 90% of them were in Sub–Saharan Africa. Nigeria, the Democratic Republic of Congo, Uganda, Ethiopia and Tanzania account for 50% of the global deaths and 47% of all malaria cases (WHO, 2015). The greater percentage of cases occurs in children under the age of five years and pregnant women [11].

According to Table 1 presenting malaria prevalence among pregnant women in Nigeria between 2007 and 2017, there is a variation in congenital malaria prevalence and it affects all the geopolitical regions in Nigeria. This highlights the health importance of malaria as a major public health issue in Nigeria. Apart from being the underlying cause of most mother and child death, it also causes serious complications in pregnant women which result to low birth weight in neonates, high placental plasmodia burden and foetal complications [12,13]. Malaria transmission in Nigeria occurs all year round with a major peak during the rainy season and the rains are longer in the south and shorter in the drier northern parts of the country [14].

Table 1: *Malaria prevalence among pregnant women in Nigeria between 2007 and 2017*

Source	Year	Geographical zone	Prevalence of malaria in pregnancy	Study design
[15]	2007	South West	72.0%	Cross sectional
[16]	2007	South South	10.0%	Cross sectional
[17]	2007	North East	22.1%	Cross sectional
[18]	2007	South East	15.0%	Cross sectional
[19]	2008	South East	19.7%	Cross sectional
[20]	2009	South West	7.7%	Cross sectional
[21]	2009	South East	58.4%	Cross sectional
[22]	2009	South East	16.0%	Cross sectional
[23]	2010	South South	95.4%	Cross sectional
[24]	2010	South West	52.0%	Cross sectional
[25]	2010	North Central	42.3%	Cross sectional
[26]	2011	North Central	71.6%	Cross sectional
[27]	2011	South East	20.0%	Cross sectional
[28]	2012	South South	78.9%	Cross sectional
[29]	2013	North West	36.0%	Cross sectional
[30]	2013	South South	74.0%	Cross sectional
[31]	2013	South South	26.0%	Cross sectional
[32]	2014	South South	42.0%	Cross sectional
[33]	2015	North Central	88.0%	Cross sectional
[34]	2015	South South	40.6%	Cross sectional
[35]	2015	North West	41.6%	Cross sectional
[36]	2015	South East	99.0%	Cross sectional
[37]	2016	South West	60.6%	Cross sectional
[38]	2016	South West	49.8%	Cross sectional
[39]	2016	South East	73.1%	Cross sectional
[40]	2017	South South	31.3%	Cross sectional
[41]	2017	South East	41.0%	Cross sectional
[42]	2017	South South	31.3%	Cross sectional

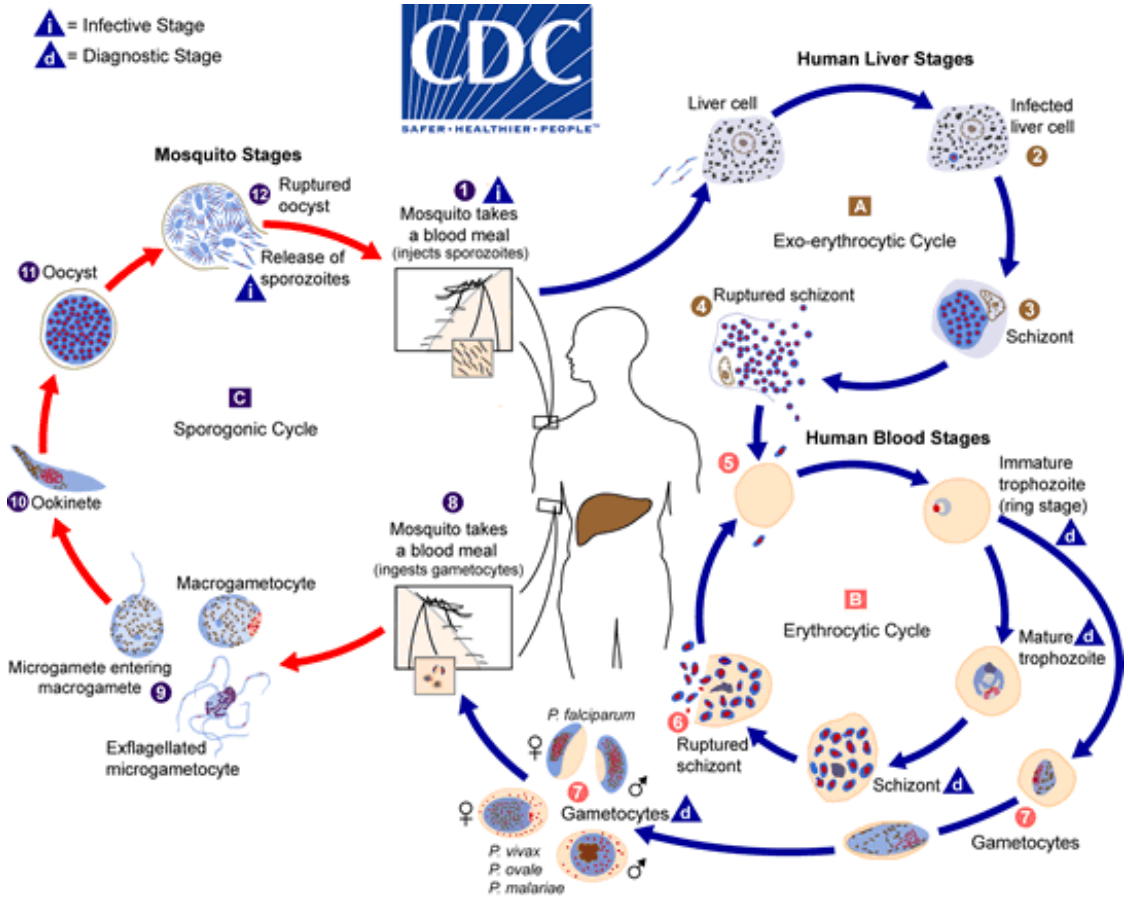

Figure 1: *Generalized life cycle of malaria parasite [44]*

3 Life Cycle of Malaria Parasites

Although the life cycles of the four species of human malaria parasites are not identical, they are sufficiently alike to permit a general description [43]. The life cycle of Plasmodium parasites can be divided into three stages; the exo–erythrocytic or pre–erythrocytic stage which usually occurs in the liver, the erythrocytic stage which occurs in the erythrocytes, and the sexual stage which occurs in the mosquito as shown in Figure 1.

In exoerythrocytic schizogony, an infected female anopheline mosquito introduces sporozoites into man during feeding. These sporozoites are taken up by the blood stream and within thirty minutes, they disappear from the blood stream. The sporozoites are elongate bodies measuring about 11µm in length, with a central nucleus. The sporozoites enter the liver cells (hepatocytes) and develop into cryptozoites giving rise to metacryptozoites. This rapid multiplication by schizogony is referred to as pre–erythrocytic schizogony [45]. The metacryptozoites divide several times over a period of six to nine days to produce thousands of merozoites which are released into the blood circulation and this marks the end of the pre–erythrocyte stage. In *Plasmodium vivax* and Plasmodium ovale, some injected sporozoites may differentiate into dormant forms called hypnozoites which may remain in the liver cells for sometimes before it undergoes schizogony to cause relapse of infection when the red cells are invaded [45].

In the erythrocytic schizogony, the merozoites enter into the bloodstream through the process of endocytosis (recognition and attachment of the merozoites to the erythrocyte membrane). On entry into the red blood cell (erythrocyte), a merozoite assumes the appearance of a small chromatin mass situated at the periphery of a larger mass of cytoplasm, in which a vacuole appears. Because of its characteristic appearance, this early trophozoite stage is referred to as a

"signet ring". As it grows into maturity, it assumes an amoeboid shape as its nucleus divides to form up to 20 or more merozoites, depending on the Plasmodium species. The dividing stage is called a schizont. The mature schizont often called a segmenter causes the infected erythrocyte to rupture to produce more merozoites which are released within 48 to 72 hours due to the destruction of the red blood cells for the manifestation of human malaria depending on the species and which then immediately invade additional erythrocytes. This schizogony cycle often continues until it is controlled by the immune response or chemotherapy or until the patient dies in the case of *Plasmodium falciparum* [45, 46].

The schizont also releases pigments and waste products in addition to the merozoites attack are responsible for the feverish condition shown by high temperature. Merozoites of some Plasmodium species selective attack erythrocytes of certain age. For instance, merozoites of *Plasmodium vivax* attack young immature red blood corpuscles called reticulocytes, those of *Plasmodium malariae* attack the older erythrocytes while those of *Plasmodium falciparum* attack any available erythrocyte [47].

Some merozoites after several generations of erythrocytic schizogony differentiate into sexual stage called gametocytes. The male cells (microgametocytes) and the female cells (macrogametocytes) circulate in the blood until they either perish or are ingested by a female anopheline mosquito. The stage in the mosquito begins after a blood meal by a female anopheline mosquito, ingesting all the Plasmodium stages present in the blood stream but only the gametocytes survive to establish the sporogony cycle in the mosquito. The male gametocyte is called microgametocytes while the female gametocyte is called macrogametocyte. In the midgut of the mosquito, the macrogametocyte develops a small amount of chromatin, and is thus transformed into a macrogamete. Equally in the mosquito midgut, the microgametocyte develops four to eight hair–like flagella (exflagellation) and is transformed into microgamete. The microgametes detach themselves and swim freely about in the fluid filled lumen of the midgut until they contact a macrogamete where penetration is quickly accomplished. The fertilized macrogamete called a zygote develops into a mobile ookinete. The ookinete within 24 hours penetrates the stomach wall of the mosquito between the cells and develops as an oocyst and attaches to the motile midgut wall to encyst on the basal lamina, the extra cellular matrix layer separating the haemocoel from the midgut. The oocyst gradually matures producing a spherical mass within which sporozoites develop mitotically. The oocyst usually matures within 10 to 20 days depending on the external environmental conditions, Plasmodium species and physiological characteristics of the anopheline mosquito, attending a body size of 50–60μm [48]. On rupture of the mature sporocyst by the oocysts, the sporozoites are released and they migrate through the haemocoel (body cavity) to the salivary glands to complete the cycle approximately 7 to 18 days after ingestion, depending on host parasite combination and external environmental condition. On feeding, the sporozoites are injected into the tissues or directly into the blood stream of the new host (man) to initiate a new schizogony cycle. All stages in the life cycle are thought to be haploid, apart from the diploid zygote, which immediately after fertilization undergoes a two–step cycle meiotic division, the resulting cell containing a nucleus with four haploid genomes. The sexual process and meiotic division following fertilization allow genetic makeup of the sporozoites and together with mutations provides the raw material upon which selective pressures such as antimalarial drugs can work [46, 48].

4 Transmission of Malaria

Malaria is transmitted in various ways by mosquito injection of sporozoites; by the transfer of erythrocytic stages other than gametocytes; and in a blood transfusion. Furthermore, blood donation from semi–immune persons without clinical symptoms may contain malarial parasites. In congenital malaria, infected mothers transmit parasites to their children before or during birth [49].

There are several factors which promote the transmission of malaria. These factors include the status of the parasite, the vector and the human host which interacts with one another and also with the biological and physical environment [50]. Malaria transmission in an area may be stable or unstable [51]. Stable malaria occurs when a population is continuously exposed to a fairly constant rate of malarial inoculation, while unstable malaria occurs seasonally with marked changes in transmission from one season to another and from one year to the other [52]. Carter & Mendis [52] noted that the differences in stability of malaria transmission, notably between tropical Africa and most other malarious regions are largely due to the behaviour and other biological characteristics of the regional species and subspecies of Anopheles vectors and their environments [53,54]. The climatic conditions are also the determining factor to the transmission of malaria. This supports longevity of the vector mosquitoes and rapid development of the parasites within them [55]. All of these features enable stable and indeed, generally intense malaria transmission in the tropics, notably Africa [52].

5 Immunity to Malaria

Those in malarious areas have developed immunity for malaria while immunity is unable to reach a high level in unstable malaria area [54]. There are two types of clinical immunity in malaria. They are immunity which reduces the risk of death from malaria and the immunity which reduces the intensity of clinical symptoms. A third type is antiparasitic immunity which directly reduces the numbers of parasites in an infected individual [52]. The number of infected malaria parasites and the intervals between them are all important to determining the malaria immune status of an individual. In the case of acute attacks of *Plasmodium falciparum* malaria, it is possible that a degree of immunity to some aspects of severe life–threatening disease may be achieved after only one or two infections [56] and clinical immunity to other non life–threatening clinical effects of malaria requires more and frequent infections by malaria parasites [57]. Due to the time taken to achieve effective immunity to malaria under conditions of endemic infection, antimalarial immunity is often said to be "age dependent". Very young children appear to have a poor capacity to acquire effective protective antimalarial immunity of any sort, while older children and adults may do so more readily [58].

6 Symptoms of Malaria

Symptoms of *Plasmodium falciparum* infection may include fever, chills, sweats, cough, diarrhea, respiratory distress and headache [59]. The symptoms of other species of malaria parasite infections may begin with indefinite malaise and a slow rising fever of several days in duration, followed by shaking chills and rapidly rising temperature, usually accompanied with headache and nausea, and ending with profuse sweating. After a period free of fever, the cycle of chills, fever and sweating is repeated every one to three days [59, 60].

7 Diagnosis of Malaria

The gold standard in the diagnosis of malaria is microscopy. This involves the demonstration of the malaria parasites in blood films, which could be either thick or thin [61]. Other supportive techniques include sophisticated indirect fluorescent antibody (IFA) test, immunoglobulin values and haemagglutination tests and molecular techniques [48]. In recent years, several malaria rapid test kits have been developed for the detection of specific malaria antigen–antibody [62].

8 Control Strategies of Malaria in Nigeria

Malaria in pregnancy is a major preventable cause of maternal morbidity and poor birth outcomes. To prevent the adverse outcomes of malaria in pregnancy, WHO [1] recommends the use of insecticide treated mosquito nets and effective case management of malaria and anaemia in pregnant women. In areas of moderate to high malaria transmission of sub–Saharan Africa, WHO [1] also recommends intermittent preventive treatment in pregnancy with sulfadoxine pyrimethamine (SP). In recent years, an alternative preventive strategy consisting of intermittent screening and treatment in

pregnancy using rapid diagnostic tests (RDTs) during antenatal care visits has been evaluated in several countries. Moreover, multiple studies have assessed the safety of using artemisinin–based combination therapies (ACTs) in the first trimester of pregnancy WHO [1]. FMOH [63] focuses on the following main strategies:

i. Management of cases
ii. Prevention of malaria with insecticide–treated nets (ITN), and
iii. Use of intermittent preventive treatment (IPT) during pregnancy.

According to Mazumdar & Mazumdar [64], the first strategy entails diagnosis to ensure that at least 80% of the people at risk of malaria take prompt and effective treatment within 24 hours of start of illness due to malaria. Under this scheme, the children under five will receive free Artmether–Lumefantrine (AL) through public sector and faith based health facilities.

A home based case management strategy has been planned especially for the children less than 5 years of age. The second intervention strategy is called the Integrated Vector Management system. This process is designed to ensure that at least 80% of the population at risk of malaria sleeps under insecticide treated nets. Other programs meant for children such as Immunization Plus Days and Measles campaigns had been used as an opportunity to reach a larger number of children in the country. Under this scheme it is proposed that the Long Lasting Insecticide Nets be given to pregnant women attending first ante natal care [64].

The third intervention strategy was formulated due to the emergence of multi–drug resistance of malaria parasites to Chloroquine (CQ) and Sulfadoxine–pyrimethamine (SP) which were first–and and second–line treatment respectively for uncomplicated malaria in Nigeria, a review of the antimalarial treatment policy was enacted [65,66]. In line with WHO recommendation for treatment of uncomplicated malaria using Artemether–lumefantrine and Artesunate–amodiaquine which showed more efficacy than CQ or SP, the Federal Government of Nigeria reviewed the treatment policy of uncomplicated malaria to the treatment policy for uncomplicated malaria to ACT in 2005 [67].

9 Conclusion

Malaria infections are highly prevalent in Nigeria and a leading cause of maternal neonatal morbidity. *Plasmodium falciparum* which is the most pathogenic Plasmodium species accounts for most cases of these infections in Nigeria. The effectiveness of interventions through effective management of uncomplicated malaria and sleeping under insecticide treated nets has been demonstrated to be cost–effective and feasible. There is therefore need to intensify awareness on the appropriate management of uncomplicated malaria and the advantages of using the long lasting insecticide nets to minimize and possibly eliminate the adverse effects of malaria in pregnant women and newborns.

10 Competing Interests

The author declared that no conflict of interest exists in this publication.

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