Evaluation Of Maternal Malaria At Childbirth Using Rapid Diagnostic Test And Its Relationship With Birth Weight And Fetal Hemoglobin Levels In Nigeria

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Abstract

The prevalence of maternal malaria at childbirth was determined using a rapid malaria diagnostic test (RDT) that detects Plasmodium. falciparum histidine-rich proteins 2 (HPR2) and its relationship with birthweight and fetal hemoglobin levels was evaluated. Apparently healthy pregnant women were enrolled shortly before childbirth at Abakaliki south-eastern Nigeria. Of the 300 women screened 59(19.7%) were positive for malaria infection. The prevalence of low birth weight LBW (<2.5kg) was 24.6% and the prevalence was significantly higher among babies born by mothers with malaria infection (30.4%) than those uninfected (23.0%) (P<0.05). The mean birth weight was lower among babies from malaria infected mothers than those from uninfected mothers (2.45kg vs. 2.80kg). The prevalence of fetal anemia (Hb<12.5g/dl) was 65.1% and was slightly higher among newborns from malaria infected mothers (65.8%) than those from uninfected mothers (64.9%). Early diagnosis is an indispensable requirement to appropriate case management of malaria in pregnancy.

INTRODUCTION

Malaria is described as a disease of poverty and underdevelopment and undoubtedly the most complex and severe public health challenge in the vast majority of tropical and sub-tropical regions of the world, with 300 to 500 million cases and 2 to 3 million deaths per year [1]. The sub-Saharan Africa still remains the worst affected region and records about 90% of all malaria deaths in the world today [2]. This is because majority of infections are caused by Plasmodium falciparum, the most dangerous of the four human malaria parasites (P. falciparum, P. ovale, P. vivax, P.malariae), accounting for an estimated 1.4 to 2.6 million deaths per year in this region [2,3]. In malaria endemic regions of the sub-Saharan Africa, pregnant women are highly susceptible to malaria with an estimated 24 million pregnant women affected [4]. This has a great implication for maternal, fetal and infant health. For instance, each year between 75,000 and 200,000 infant deaths are attributed to malaria infection in pregnancy globally [4,5]. This is in addition to the contribution of malaria to adverse pregnancy outcomes including low birthweight (LBW)(through prematurity or interuterine growth retardation IUGR) which is known to be the single greatest and most important risk factor for neonatal and infant mortality [6,7]. Furthermore, in several areas where malaria in pregnancy is common a severe degree of fetal anemia is reported [8]. Fetal anemia has been described as an important public health issue because it is one of the major risk factors for infant anemia which is a life threatening condition and an important cause of hospital admission in many developing countries [9,10].

The adverse perinatal outcomes associated with malaria in pregnancy, makes early and accurate diagnosis of malaria absolutely imperative. Early and accurate diagnosis as well as appropriate case management are essential to addressing the malaria burden in pregnancy and its outcome, and have been advocated consistently by the World Health Organization (WHO) [1,2]. Late and inaccurate diagnoses are major contributors to malaria mortality and to mortality from non-malaria illnesses, especially bacterial diseases, that malaria symptoms can resemble [11,12]. Thus the diagnosis of malaria in endemic areas of the tropics is considered an enormous challenge particularly in the sub-Saharan Africa [1,13]. Two major factors responsible for this are; first, most diagnosis of malaria, and decisions on the subsequent management of the disease, continue to be based on symptoms and signs that are poorly specific across a range

of epidemiological settings [11,14]. Secondly, microscopic examination of blood smears still remains the only laboratory technique used for malaria diagnosis in most settings and this is labor intensive, requires significant skills and time, which can cause therapeutic delays [15,16]. In most African health centers for instance, microscopy standards are sub-optimal and sensitivity is notoriously low due to the lack of high quality equipment, the use of low quality stains and other reagents, and lack of supervision and trained staff [17].

The importance of early, less cumbersome and yet accurate diagnosis of malaria particularly in high risk groups as pregnant women necessitated the introduction of rapid malaria diagnostic tests (RDTs) [16,17]. The WHO has recognized the RDTs as potential solution to improve malaria diagnosis because they can be used at the periphery of health services where laboratory equipment, electricity, and personnel with minimal training may be absent and they have lower capital and maintenance costs, and require less training than microscopy [18]. Most of the RDTs are immuno-chromatographic dipstick assays that detect either histidine-rich proteins-2 (HRP2) produced by infected red blood cells or parasite lactate dehydrogenase, an enzyme present in the glycolytic pathway of the parasite and the RDTs produced by a variety of manufacturers have been evaluated as diagnostic tests for malaria [13]. In this study the RDT that detects P. falciparum HRP2 was used to evaluate maternal malaria at childbirth and its relationship with birth weight and fetal hemoglobin levels.

MATERIALS AND METHODS
STUDY AREA

This study was conducted at the Ebonyi State University Teaching Hospital (EBSUTH), located in Abakaliki the capital of Ebonyi State in South Eastern Nigeria, from June 2006 to December 2006. The climatic condition of the area is characterized by two distinct seasons, the wet and the dry seasons, the former takes place between April and October, while the latter occurs from November to March. Malaria transmission in the area is perennial but usually at the peak towards the end of the rainy season.

ETHICAL CONSIDERATIONS

The study protocol was approved by Department of Medical Microbiology/Parasitology, Faculty of Clinical Medicine, Ebonyi State University, Abakaliki, Nigeria. Ethical approval was obtained from the Ethical Committee of the EBSUTH, Abakaliki. The approval was on the agreement

that patient anonymity must be maintained, good laboratory practice/quality control ensured, and that every finding would be treated with utmost confidentiality and for the purpose of this research only. All work was performed according to the international guidelines for human experimentation in clinical research [19].

STUDY POPULATION/SAMPLING TECHNIQUE

Pregnant women at full term who were admitted at EBSUTH for childbirth and who fulfilled the following study inclusion criteria were enrolled into the study: (i) attended the antenatal clinic at EBSUTH, (ii) had an uncomplicated singleton pregnancy 32 weeks' gestation (based on the fundal height estimation), (iii) reside in Abakaliki or neighbouring local government areas, (iv) had no obvious clinical evidence of malaria (asymptomatic), and (v) had no known underlying chronic illness.

Following informed consent and shortly before child birth, about 5ml of the maternal peripheral blood was obtained from each participant by venepuncture technique into sterile EDTA container for laboratory analysis. Immediately after childbirth, about 5ml of cord blood was obtained into sterile EDTA container for laboratory analysis and the birth weight of each baby was determined using an electronic weighing machine.

LABORATORY ANALYSIS

A rapid diagnostic test kit, the Smart Check Malaria P.f cassette (Globalemed, 1101 King St. Suite 370, Alexandria, VA 22314 USA), was used. The kit is a type of immuno-chromatographic dipstick assay that detects histidine-rich proteins produced by P. falciparum in whole blood specimens. The manufacturer's instructions were strictly followed to determine the P. falciparum malaria status of each maternal blood specimen.

The fetal haemoglobin concentration (HbC) was determined using the cyanmethaemoglobin method described previously [20]; reading was done using a spectrophotometer (Bayer RA 50). Fetal was anemia defined by Hb<12.5 g/dl [9,21].

All the analysis was done at the Research Laboratory of Department of Medical Microbiology, Ebonyi State University, Abakaliki and all participant identified with malaria infection were treated at the hospital before they were discharged.

STATISTICAL ANALYSIS

Difference between proportions were evaluated using the chi-square tests while differences in means where evaluated using one-way analysis of variance ANOVA. Statistical significance were achieved at P<0.05.

RESULTS

A total of 300 women were enrolled in this study and of these 59(19.7%, 95%CI., 15.2-24.2%) were positive for malaria infection as indicated by the RDT. The birth weight values of 211 and fetal hemoglobin levels of 192 newborns were determined, the rest could not be assessed due to logistic problems at the labor ward of the hospital. The prevalence of LBW (<2.5kg) was 24.6% and the prevalence was significantly higher among babies born by mothers with malaria infection (30.4%) than those uninfected (23.0%) (F-ratio=14.8, df_1/df_2=2/3, P<0.05). The mean birth weight was lower among babies from malaria infected mothers than those from uninfected mothers (2.45kg vs. 2.80kg) (Table 1).

Figure 1

Table 1: Association of maternal malaria infection at childbirth with birthweight in Abakaliki, Nigeria.

Maternal malaria infection	Birth weight (kg)			Overall Total	Mean Birth weight(kg)
	< 2.5	2.6-3.5	≥ 3.6		
Positive	14(30.4)	28(60.9)	4(8.7)	46	2.45
Negative	38(23.0)	113(68.5)	14(8.5)	165	2.80
Total	52(24.6)	141(66.8)	18(8.5)	211	

The prevalence of fetal anemia (Hb<12.5g/dl) was 65.1% and was slightly higher among newborns from malaria infected mothers (65.8%) than those from uninfected mothers (64.9%). Statistically no significant difference was found in the trend (?2 =0.01, df=1, P>0.05). The mean fetal hemoglobin concentration of newborns from malaria infected mothers was 11.05g/dl, while that of newborns from uninfected mothers was 11.87g/dl (Table 2).

Figure 2

Table 2: Association of maternal malaria at childbirth with fetal haemoglobin (Hb) concentration in Abakaliki, Nigeria

Maternal malaria infection	Fetal Hb concentration (g/dl)		Overall Total	Mean Fetal Hb concentration (g/dl)
	Number(%) with Hb<12.5	Number(%) with Hb≥12.5		
Positive	25(65.8)	13(34.2)	38	11.05
Negative	100(64.9)	54(35.1)	154	11.87
Total	125(65.1)	67(34.3)	192	

DISCUSSION

Improved diagnosis of malaria in pregnancy in endemic regions of low income setting would continue to be an indispensable requirement to the roll back malaria initiative of the WHO. In this study we recognize the importance of the RDT and attest to its usefulness in rapid and less cumbersome maternal malaria diagnosis. A maternal malaria prevalence of 19.7% was obtained in this study using the Smart Check P.f RDT. This is comparable to the prevalence rates ranging from 2.6% to 81.1% obtained from various malaria endemic regions using various kinds of RDTs [22,23,24,25,26].

It is suggested that RDTs in the nearest future would become major epidemiologic tools in the assessment of the impact of malaria during pregnancy.

In this study LBW was significantly associated with maternal malaria infection at childbirth (P<0.05). Although there is paucity of information on the use of RDT as an epidemiologic tool to evaluate maternal malaria and its relationship to birthweight, information however abounds on the use of malaria microscopy technique in various maternal malaria-birthweight related studies. And findings from these studies have consistently indicated that malaria infected mothers had higher prevalence rates of low birth weight newborns compared to those of the uninfected mothers [7,23,27]. In fact falciparum malaria during pregnancy has long been recognized as an important determinant of low birth weight [6,7]. A number of randomized controlled trials of preventive antimalarial measures during pregnancy have confirmed this causal effect by showing that preventing malaria increases birth weight [28,29].

Findings from this present study indicated that the prevalence of fetal anemia was slightly higher among babies born by malaria infected mothers compared to those of the uninfected mothers, and of course the difference was not statistically significant (P>0.05). As with maternal malaria-birthweight studies, there is also paucity of information on the use of RDTs in maternal malaria-fetal anemia related studies. However available studies in which the microscopy technique was used to assess maternal malaria in relation to fetal anemia showed conflicting outcomes. In Kisumu, Kenya, and southern Malawi, babies born to mothers with detectable P. falciparum parasitemia on a peripheral blood film at delivery had a lower mean Hb level at birth compared with babies children born to mothers free of parasitemia at delivery [9,30]. On the contrary, in a similar study conducted in Blantyre, Malawi, even though malaria was associated with a reduction in maternal hemoglobin, no reduction in cord hemoglobin and no significant relationship between

maternal and cord hemoglobin levels were found, furthermore authors noted that cord blood markers of hematological and hypoxic statuses did not differ between malaria-infected and uninfected women [31]. Since the etiology of fetal anemia is complex and multifactorial further studies that will incorporate the assessment of other possible causes of fetal anemia are advocated.

In conclusion it is pertinent to state that a major drawback of this study was the lack of quantification of parasitemia which is a limiting factor associated with all RDTs [13]. Also the possibility of false positive and false negative results cannot be completely overruled as a result of cross-reactivity. Nevertheless, the urgency and importance of obtaining results quickly from the examination of blood samples from pregnant women with suspected acute malaria makes RDTs absolutely imperative. This is because early diagnosis is an indispensable requirement to appropriate case management of malaria in pregnancy in order to avert its associated adverse perinatal outcomes.

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