

ASYMPTOMATIC MALARIA AMONG PREGNANT WOMEN IN EDO STATE, NIGERIA

FREDERICK OLUSEGUN AKINBO¹,
BABATUNDE OSANYINBI¹, RICHARD OMOREGIE²,
ADEDAPU BABATUNDE ANIBABA ANDE³

Abstract

Malaria is a serious public health problem in tropical and subtropical regions of the world with far reaching medical, social and economic consequences. Malaria during pregnancy is a major cause of fetal and maternal morbidity and mortality. This study was conducted to determine the prevalence of asymptomatic malaria in pregnant women as well as the risk factors in acquiring asymptomatic malaria in Benin City, Nigeria. A total of 539 patients were recruited for this study. They consisted of 439 pregnant women attending clinics and 100 non-pregnant apparently healthy women served as controls. The age of the study participants ranged from 21 years to 45 years. Blood specimen was collected from each participant to detect malaria parasite and to determine haemoglobin concentration using standard techniques. Pregnancy was significantly associated with asymptomatic malaria (OR=2.442 95%; CI= 1.496, 3.987; P=0.0004). Multiparous pregnant women and those who use only insecticide had significantly higher prevalence of asymptomatic malaria (P<0.0001 and P=0.0092, respectively). Age, gestational age, level of education, marital status, occupation, use of antimalarial, type of antimalarial and source of insecticide-treated bed nets had no significant effect on the prevalence of asymptomatic malaria among pregnant women (P>0.05). Pregnant women have a 1 to 4-fold increased risk of developing anaemia than non-pregnant women. Anaemia was associated with asymptomatic malaria among pregnant women (OR=2.268; 95%; CI=1.414, 3.637; P=0.0009). The prevalence of asymptomatic malaria among pregnant women was 44.87% with multiparous women and those that use only insecticide as preventive measure having higher prevalence of asymptomatic malaria. Measures to reduce asymptomatic malaria among pregnant women are advocated.

INTRODUCTION

Malaria is recognized as a serious public health problem in tropical and subtropical regions of the world with far reaching medical, social and economic

consequences.¹ Each year in sub-Saharan Africa, where 80 - 90% of world malaria cases occur, approximately 19 - 24 million women are at risk of malaria and its adverse consequences during pregnancy.^{2,3} Malaria potentially affects about 50% of the world's population majority of who live in sub-Saharan Africa. Pregnant women and the under-fives form the bulk of its worst victims in endemic areas.^{4,5}

Malaria and pregnancy are mutually aggravating conditions. The physiological and pathological changes in pregnancy due to malaria have a synergistic effect on the course of each other. The complications arising from malaria in pregnancy include

KEYWORDS:

1. Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, Benin City, Nigeria. fjbongang@yahoo.com; Tbl: +2348033796874

2. School of Medical Laboratory Sciences, University of Benin Teaching Hospital, Benin City, Nigeria. richyamos@yahoo.com; Tbl: +2348105543053

3. Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital, Benin City, Nigeria. Anibaba15@yahoo.co.uk; Tbl: +2348023522257

*Corresponding Author

Frederick O. Akinbo
Tbl: +2348033796874, E-mail addresses: fjbongang@yahoo.com

febrile illnesses, hypoglycaemia, cerebral involvement, pulmonary edema and puerperal sepsis.⁶ Malaria during pregnancy is a major cause of foetal and maternal morbidity and mortality.⁷ The vast majority of women with malaria infections during pregnancy remain asymptomatic, and this increases the risk of maternal anaemia and delivering a low-birth-weight (LBW) baby.⁸ In high-transmission settings, where levels of acquired immunity tend to be high, *P. falciparum* infection is usually asymptomatic in pregnancy. Yet, parasites may be present in the placenta and contribute to maternal anaemia even in the absence of documented peripheral parasitaemia. Both maternal anaemia and placental parasitaemia can lead to low birth weight, which is an important contributor to infant mortality.⁹

Anaemia is the most common haematological manifestation of Plasmodium infection. It is defined by the World Health Organization as haemoglobin concentration < 11g/dl in pregnant women.¹⁰ Anaemia, which can be mild to severe, acute or chronic, is one of the multitudes of complications associated with parasitic infections.¹¹ The relationship between parasitic infection and anaemia is a pathogeno-physiologic type¹² where it is recognized that certain factors play important roles. The factors may include the strain and number of the parasites, the size and site, metabolic processes of the parasite, age and level of immunity at the time of infection, presence of co-existing diseases or conditions which reduce immune responses, malnutrition, and the life style of the person infected.¹³ Anaemia is said to be the commonest medical condition in pregnancy with a prevalence of 50% worldwide.¹⁴ Omigbodun¹⁴ and Komolafe et al.¹⁵ put the prevalence of anaemia in developing countries including Nigeria at 60% in pregnancy out of which 7% are said to be severely anaemic.

Malaria is known to cause increased haemolysis of parasitized red blood cells of which the degree of haemolysis depends on the burden of parasites.^{16,17} The association of anaemia and asymptomatic malaria in pregnancy in Benin City is still being studied. The paucity of data on the risk factors associated with malaria in pregnancy with the current reality of massive malaria interventions necessitated this study. Against this background, this study aimed at determining the prevalence of asymptomatic malaria in pregnant women in Benin City, Nigeria.

MATERIALS AND METHODS

Study area

The study was conducted at the University of Benin Teaching Hospital, Benin City, Nigeria between January and June 2013. It is located in the South-South geopolitical zone of Nigeria. It serves as a referral hospital to Edo, Delta, Ondo, Anambra, and Kogi States.

Study population

A total of 539 patients were recruited for this study. They consisted of 439 pregnant women attending antenatal clinics and 100 non-pregnant apparently healthy women served as controls. The age of the study participants ranged from 21 years to 45 years. Patients that refused consent and those with signs and symptoms (fever, chills, rigor, nausea, vomiting, headache, body aches and pains, malaise and generalized body weakness) of malaria were excluded. The controls were recruited from the surrounding community. The study participants were selected by serial sampling technique. The protocol for this study was approved by the Ethical Committee of the University of Benin Teaching Hospital, Benin City. Informed consent was obtained from each participant prior to specimen collection. A structured questionnaire bothering on the

demographic characteristics was administered to each participant. Information obtained included age, parity, marital status, level of education, and occupation amongst others.

Specimen collection and processing

About five milliliters of blood was obtained from each patient, dispensed into ethylene diamine tetra-acetic acid (EDTA) container and mixed. Malaria was diagnosed by using a previously described method.¹³ Briefly, thick blood films were made from each blood sample and allowed to air-dry. Slides were stained in 3% Giemsa stain for 30 minutes, rinsed in tap-water and allowed to air-dry. The stained films were examined for malaria parasites by microscopy. A total of 200 fields per film were examined.¹

Haemoglobin estimation was determined using a Sysmex KX - 21 haematology analyzer (Sysmex Corporation, Kobe, Japan). Anaemia was defined as a haemoglobin concentration less than 11.0 g/L.¹⁰

Statistical analysis

The data obtained were analyzed using the Chi square (X^2) test and odd ratios (OR) analysis using the software INSTAT® (Graph Pad Software Inc, La Jolla, CA, USA).

RESULTS

Pregnancy is a risk factor for acquiring asymptomatic malaria (OR=2.442; 95% CI= 1.496, 3.987; P=0.0004). With the exception of parity, where multiparous pregnant women had significantly (P<0.0001) higher prevalence of asymptomatic malaria, other demographics - age, gestational age, level of education, marital status and occupation, had no significant (P>0.05) effect on the prevalence of asymptomatic malaria among pregnant women (Table 1).

The effect of antimalarial usage and other preventive measures on the prevalence of asymptomatic malaria is shown in Table 2. Only pregnant women that use insecticide-treated bed nets have significantly lower prevalence of asymptomatic malaria (P=0.0092). Use of antimalarial, type of antimalarial used and source of insecticide-treated bed nets did not affect the prevalence of asymptomatic malaria (P>0.05).

Pregnant women have a 1 to 4- fold increased risk of developing anaemia than non-pregnant women. In non-pregnant women, asymptomatic malaria was not associated with anaemia, while among pregnant women asymptomatic malaria was associated with anaemia (OR=2.268; 95% CI=1.414, 3.637; P=0.0009) (Table 3).

DISCUSSION

Malaria can cause severe disease in pregnancy.¹⁹ The vast majority of women with malaria infection during pregnancy remain asymptomatic.⁹ Asymptomatic malaria in pregnant women has been reported to cause maternal anaemia and low birth weight.²⁰

An overall prevalence of 44.87% of asymptomatic malaria was observed among pregnant women in this study. This is higher than the 24% observed in Ouagadougou, Burkina-Faso²¹ and 3.1% in Sokoto, Nigeria.¹ However, it is lower than that observed by Onyenekwe et al.²² Nwagha et al.⁷ and Agan et al.¹⁷ in which the reported prevalence ranged from 58.4% to 95.4%. The observed difference could be due to geographical location even within the same country. Petri et al.²³ had reported among children with diarrhea that the prevalence of infection varies with geographical locations, regions within the same country, and even overtime in the same location and population. Indeed, in

Table 1: Effect of demographics on the prevalence of asymptomatic malaria

Characteristic	No. Tested	No. infected (%)	OR	95% CI	P value
Pregnant women	439	197(44.87)	2.442	1.496, 3.987	0.0004
Non-pregnant women	100	25(25.00)	0.410	0.251, 0.669	
Age (year) of pregnant women					
≤25	53	22(41.51)			0.6296
26-35	324	144(44.44)			
≥36	62	31(50.00)			
Gestational age					
First trimester	73	34(46.58)			0.7814
Second trimester	262	114(43.51)			
Third trimester	104	49(47.12)			
Level of education					
Primary	19	8(42.11)			0.2628
Secondary	170	68(40.00)			
Tertiary	250	120(48.00)			
Parity					
Nulliparous	119	57(47.90)			<0.0001
Primiparous	182	55(30.22)			
Multiparous	138	85(61.59)			
Marital status					
Single	8	4 (50.00)	1.233	0.304, 4.997	0.7686
Married	431	193 (44.78)	0.811	0.200, 3.286	

Occupation			
Civil servant	183	79(43.17)	0.4680
House wife	42	21(50.00)	
Business woman	177	77(43.50)	
Student	21	9(42.86)	
Applicant	12	8(66.67)	
Banker	2	2(100.00)	
Lawyer	2	1(50.00)	

OR=Odd ratio; CI=Confidence interval; * $P<0.05$

Table 2: Effect of antimalarial usage and other preventive measures on the prevalence of asymptomatic malaria

Characteristic	No. Tested	No. infected (%)	OR	95% CI	P value
Use of antimalarial					
Yes	423	186(43.97)	0.357	0.122, 1.045	0.0891
No	16	11(68.75)	2.803	0.957, 8.211	
Type of antimalarial used					
Artemisinin BC	270	130(18.15)			0.2457
Chloroquine	128	50(39.06)			
Proguanil	30	11(36.67)			
Pyrimethamine	11	6(54.55)			
Malaria preventive methods					
Insecticide	17	10(58.82)			0.0092
Insecticide treated bed nets	199	74(37.19)			
Door & window netting	152	84(55.26)			
Use of antimalarial	49	19(38.78)			
Combined preventive methods	22	10(45.45)			
Source of treated nets					
Pharmacy	15	7(46.67)			0.7484
Private hospital	46	15(32.61)			
Government hospital	109	40(36.70)			
Patent medicine store	29	12(41.38)			

* $P<0.05$

Table 3: Effect of asymptomatic malaria on the prevalence of anaemia

Subjects	No. tested	No. with anaemia (%)	OR	95% CI	P value
Pregnant women	439	336(76.54)	2.563	1.630, 4.030	<0.0001
Non-Pregnant	100	56(56.00)	0.390	0.248, 0.613	
Pregnant women					
With malaria	197	166(84.26)	2.268	1.414, 3.637	0.0009
Without malaria	242	170(70.25)	0.441	0.275, 0.707	
Non-pregnant women					
With malaria	25	16(64.00)	1.556	0.611, 3.960	0.4853
Without malaria	75	40(53.33)	0.643	0.253, 1.637	

* $P < 0.05$

terms of asymptomatic malaria, this has also been noted.¹

Asymptomatic malaria is significantly associated with pregnancy in the study (OR=2.442; 95% CI=1.496, 3.987; $P=0.0004$). Pregnancy has been reported to lower immunity as a result of general immunosuppression, sustained by elevated level of serum cortisol, which allows fetal allograft retention but renders the women susceptible to various infectious diseases.²⁴ This may explain the finding in this study,

In endemic areas, such as Nigeria, immunity to malaria is acquired in an exposure-related manner such that the greatest burden of the disease falls on younger people.²⁵ However, the prevalence of asymptomatic malaria was not significantly ($P=0.6296$) affected by the age of the pregnant women. A similar picture was observed for non-pregnant women (data not shown).

A recent study in Benin City among pregnant women attending a traditional birth home did not also find any significant difference in the prevalence of malaria parasitaemia in relation to age.²⁶

The finding that gestational age did not significantly affect the prevalence of asymptomatic malaria agrees with a previous report.²¹ Similarly, level of education, marital status and occupation of pregnant women did not affect the prevalence of asymptomatic malaria.

In this study, asymptomatic malaria was significantly more prevalent in multiparous pregnant women than their primiparous and nulliparous counterparts. This finding is not in agreement with the findings of Douamba et al.²¹ where parity had no effect on the prevalence of asymptomatic malaria. It has been reported that *Plasmodium falciparum* may get sequestered in the placenta.²⁷ With

successive pregnancies, women are exposed to variety of strains of malaria parasite, and may develop efficient mechanism to control infection and prevent disease.^{26, 29} Thus, multiparous pregnant women may develop more efficient mechanism to tolerate the parasite without developing signs and symptoms of illness compared to primiparous and nulliparous pregnant women.

It has been reported that prophylactic use of antimalarial reduces the prevalence of asymptomatic malaria among pregnant women.¹⁷ The type of antimalarial and the interval between antimalarial use and diagnosis of asymptomatic malaria will determine the efficacy of prophylactic antimalarial usage amongst other factors. In this study, use of antimalarial and type of antimalarial used did not affect the prevalence of asymptomatic malaria. We were unable to accurately determine the interval between consumption of antimalarial and diagnosis of asymptomatic malaria. It is possible that resistance to the used antimalarial are present in the parasite as over the counter sales of antimicrobial agents are rife in our community and have been implicated as possible reasons for increased antimicrobial resistance observed in the country.^{30, 31} However, further studies are needed to verify this.

Pregnant women who use insecticide-treated bed nets as malaria preventive measures had the least prevalence of asymptomatic malaria (37.19%) compared with those that use other methods. Use of insecticide-treated bed net is a recognized effective means of preventing malaria infection. Thus, insecticide treated bed nets should be made available to pregnant women to reduce the prevalence of asymptomatic malaria. The insecticide-treated bed nets may be obtained from any source as the source of insecticide-treated bed nets did not significantly ($P=0.7484$) affect the prevalence of asymptomatic malaria among pregnant women.

The prevalence of anaemia is significantly higher in pregnant women compared with non-pregnant women and anaemia is associated with pregnancy. This agrees with previous reports of Oladeinde et al.³² The cause of anaemia in pregnancy is multifactorial and includes haemodilution, infections, inadequate erythropoiesis, amongst others.^{17, 32} Malaria has been reported as the leading cause of anaemia among pregnant women in our environment.¹⁹ This was observed in this study where asymptomatic malaria was significantly associated with anaemia among pregnant women and agrees with previous reports.^{1, 17, 21} Among non-pregnant women, the prevalence of anaemia was higher in those with asymptomatic malaria, though the difference was not significant. This may indicate that asymptomatic malaria is not a significant contributor of anaemia among apparently healthy non-pregnant women. Anaemia has been observed among apparently healthy Nigerians and worsening economy was suggested as a possible reason.³³

CONCLUSION

The prevalence of asymptomatic malaria among pregnant women was 44.87% with a 1 to 4-fold increased risk of acquiring it. Prevalence of asymptomatic malaria was higher among multiparous women and those who use only insecticide as preventive measures. Anaemia was associated with asymptomatic malaria. Measures to reduce asymptomatic malaria and associated sequelae are advocated.

Acknowledgement

We thank the management of University of Benin Teaching Hospital, Benin City, Edo State for providing specimens used in this study.

REFERENCES

1. Isah, A. Y., Amanabo, M. A. and Ekele, B. A. (2011) Prevalence of malaria parasitaemia amongst asymptomatic pregnant women attending a Nigerian teaching hospital. *Ann Afr Med.* 10(2), 171-174

2. Steketee, R. W., Wirima, J. J., Slutsker, L., Hymann, D. L. and Breman, J. G. (1996). The problem of Malaria and Malaria Control in pregnancy in sub-Saharan Africa. *Am. J. Trop. Med. Hyg.* 55, 2-7.
3. Guyatt, H. L. and Snow, R. W. (2001). The epidemiology and burden of *Plasmodium falciparum* related anaemia among pregnant women in sub-Saharan Africa. *Am. J. Trop. Med. Hyg.* 55, 1-106.
4. Enato, E., Okhamafe, A., Okpers, E. and Oseji, F. (2007). Prevalence of Malaria during Pregnancy and Antimalarial Intervention in an Urban Secondary Health Care Facility in Southern Nigeria. *Med. Princ. Pract.* 16(3), 240-243.
5. Menendez, C., D'Alenassandro, U. and O Ter Kuile F (2007). Reducing the burden of malaria in pregnancy by preventive strategies. *Lancet infect. Dis.* 7(2), 126-35. 9.
6. Erhabor, O., Adias, T. C. and Hart M. L. (2010). Effects of falciparum malaria on the indices of anaemia among pregnant women in the Niger Delta of Nigeria. *J. Clin. Med. Res.* 2(3), 35-41.
7. Nwagha, U. L., Ugwu, V. O., Nwagha, T. U. and Anyaehie, B. O. (2009). Asymptomatic *Plasmodium* parasitaemia in pregnant Nigerian women: almost a decade after Roll Back Malaria. *Trans. R. Soc. Trop. Med. Hyg.* 103(1), 16-20.
8. Guyatt, H. L. and Snow, R. W. (2004). Impact of malaria during pregnancy on low birth weight in sub-Saharan Africa. *Clin. Microbiol. Rev.* 17,760-769
9. WHO (2008). Technical Expert Group meeting on intermittent preventive treatment in pregnancy (IPTp). World Health Organization, Geneva
10. Aimakhu, C. O. and Olayemi, O. (2003). Maternal haematocrit and pregnancy outcome in Nigerian women. *West Afr. J. Med.* 22(1), 18-21.
11. Agiomea, K. (2003) Anaesthetic considerations in patients with parasitic diseases and anaemia: <http://www.nda.ox.ac.uk/wfsa/al/html/papers/pap021.html>;1-8
12. Stephenson, L. S., Latham, C., Kurz, K. M., Kinoti, S. N., Oduori, M. L and Crompton D/ W. T. (1985). Relationships of *S. haematobium* hookworm and malarial infections and metrifonate treatment on haemoglobin level in Kenyan school children. *Am. J. Trop. Med. Hyg.* 34, 519-528.
13. Cheesbrough, M. (1999) *Parasitological Tests.* Cambridge University Press.
14. Omigbodun, A. O. (2004). Recent trends in the management of anaemia in pregnancy. *Trop. J. Obst. Gynaecol.* 21(1), 1-3.
15. Komolafe, J. O, Kuti, O., Oni O. and Egbewale B. E. (2005). Socio-demographic characteristics of anaemic gravidae at booking: A preliminary study at Ilesha, western Nigeria. *Nig. J. Med.* 14(2), 151-154.
16. Steketee, R. W., Nahlen, B. L., Parise, M. E. and Mendez, C. (2001). The burden of malaria in pregnancy in malaria endemic areas. *Am. J. Trop. Med. Hyg.* 64, 28-35.
17. Agan, T. U., Ekabua, J. E., Iklaki, C. U., Oyo-Ita, A. and Ibanga, I. (2010). Prevalence of asymptomatic malaria parasitaemia. *Asian Pacific J. Trop. Med.* 2, 1-5.
18. Omoregie, R., Adedotun, B. B., Ogefero, H. O., Iduh, P., and Duru, M. (2007). Comparison of the efficacy of malaria PF rapid test device, Giemsa-stained thick blood film and QBC in the diagnosis of malaria in Benin City, Nigeria. *Mary Slessor J. Med.* 7, 1-4.
19. Anorlu, R. I., Odum, C. U. and Essien, E. E. (2001). Asymptomatic malaria parasitaemia in pregnant women at booking in a primary health care facility in a periurban community in Lagos, Nigeria. *Afr. J. Med. Sci.* 30, 39-41.
20. Uneke, C. J., Sunday-Adeoye, I., Iyare, F. E., Ugwuja, E. I. and Duhlińska, D. D. (2007). Impact of maternal *Plasmodium falciparum* malaria and haematological parameters on pregnancy and its outcome in Southeastern Nigeria. *J. Vector Borne Dis.* 44, 285-290.
21. Douamba, F. Z., Bisseye, C., Djigma, F. W., Compaoré, T. R., Bazie, V. J. T., Pietra, V., Nikiema, J. B. and Simporé, J. (2012). Asymptomatic Malaria Correlates with Anaemia in Pregnant Women at Ouagadougou, Burkina Faso. *J. Biomed. Biotech.* doi:10.1155/2012/198317.
22. Onyenekwe, C. C., Meludu, S. C., Dioka, C. E. and Salimonu, L. S. (2002). Prevalence of asymptomatic malaria parasitaemia amongst pregnant women. *Indian J Malariol.* 39(3-4), 60-65.

23. Petri, Jr W. A., Miller, M., Binder, H. J., Levine, M. M., Dillingham, R. and Guerrant, R. L. (2008). Enteric infections, diarrhea, and their impact on function and development. *J. Clin. Invest.* 118(4): 1277-1290.
24. Meeusen, E. N., Bischof, R. J., Lee, C. S. (2001). Comparative T-cells response during pregnancy in large animals and humans. *Am. J. Repro. Immunol.* 46, 169-179.
25. McGregor, I. A. (1986). The development and maintenance of immunity to malaria in highly endemic areas. *Clin. Trop. Med. Comm. Dis.* 1, 1-29.
26. Oladeinde, B. H., Omoregie, R., Odi, I. and Oladeinde, B. O. (2012). Prevalence of malaria and anaemia among pregnant women attending a traditional birth home in Benin City, Nigeria. *Oman Med. J.* 27 (3), 232-236.
27. Fried, M. and Duffy, P. E. (1996). Adherence of *Plasmodium falciparum* to chondroitin sulfate A in the human placenta. *Science.* 275, 1502-1504.
28. Beck, S., Mockenhanpt, F. P., Bunzle, U., Egglete, T. A., Thompson, W. N. and Stark, K. (2001). Multiplicity of *Plasmodium falciparum* infection in pregnancy. *Am. J. Trop. Med. Hyg.* 65(5), 631-636.
29. Beeson, J. G., Rogerson, S. J., Cooke, B. M., Reeder, J. C., Chai, W., Lawon, A. M., Molyneux, M. E. and Brown, C. V. (2000). Adhesion of *Plasmodium falciparum* infected erythrocytes to hyaluronic acid in placenta malaria. *Nat. Med.* 6, 86-90.
30. Okeke, I. N., Lamikanra, A. and Edelman, R. (1999). Socio-economic and behavioural factors leading to acquired bacterial resistance to antibiotics in developing countries. *Emerg. Infect. Dis.* 5(1), 18-27.
31. Omoregie, R. and Eghafona, N. O. (2009). Urinary tract infection among asymptomatic HIV patients in Benin City, Nigeria. *Br. J. Biomed. Sci.* 66(4), 190-193.
32. Oladeinde, B. H., Omoregie, R., Olley, M. and Anunibe, J. A. (2011). Prevalence of HIV and anaemia among pregnant women. *North Am. J. Med. Sci.* 3(12), 548-551.