

THE IMPACT OF PLACENTAL MALARIA ON THE NEONATE: A CASE CONTROL STUDY FROM A HIGH MALARIA TRANSMISSION AREA IN GHANA.

MATE SIAKWA¹, DZIGBODI KPIKPITSE², AZANU WISDOM³, ASAMOAH ISAAC⁴.

1. School of Nursing, University of Cape Coast, Cape Coast, Ghana.

2. School of Nursing, Garden City University College Kumasi, Ghana.

3. Department of Obstetrics and Gynaecology, Komfo Anokye Teaching Hospital, Kumasi, Ghana.

4. St Michael Hospital Pramso, Ghana.

*Correspondence: Mate Siakwa, School of Nursing, University of Cape Coast, Ghana.

Telephone: +233 0509181687. E-mail: msiakwa@yahoo.co.uk

ABSTRACT

Neonatal mortality is high in Ghana and among the major causes infection is second to preterm birth. The contribution of malaria infection to neonatal mortality desire more rigorous investigation considering the fact that Ghana lies in the high malaria transmission zone. The aim of this study was to determine the adverse effects of placental malaria on neonatal outcomes. This case-control prospective study was conducted during the period of July 2007 and March 2012. Two hundred and twenty (220) neonates of women with positive placental malaria (cases) and 200 neonates of healthy women who were negative for placental malaria participated in the study. Both groups were assessed for gestational age, live/stillbirth, birth weight, birth asphyxia, Apgar score at one minute and five minutes. Placental malaria is associated with low birth weight ($p<0.001$), birth asphyxia ($p<0.001$) low Apgar score ($p<0.001$), stillbirth ($p=0.0013$) and preterm delivery ($p<0.001$). The WHO intervention for PM strategies must be given priority attention to minimize adverse neonatal outcomes. Also screening and treatment of neonates with such birth outcomes for malaria is recommended.

Keywords: placental malaria, neonatal outcome, preterm delivery, stillbirth, asphyxia.

INTRODUCTION

There seems to be the need for more studies into various aspects of malaria in pregnancy (Hartman et al 2010), especially the impact of placental malaria on the neonate. Placental malaria could have devastating effects on the foetus in utero and on the new born (Rogerson et al 2007, Tobon-Castano et al 2011, McDonald et al 2015) and create health problems later in life (Christensen et al 2011, Morrison et al 2010). It has been reported that malaria infections during pregnancy is responsible for 75,000 to 200,000 infant deaths per year in sub-Saharan Africa (Steketee et al 2001) due to the subsequent adverse health outcomes including; intrauterine growth retardation, low birth weight, prematurity, intrauterine death and still birth (Desai

et al 2007; Faladel et al., 2010 & Orimadegun, 2010). Women living in malaria endemic areas are at high risks for malaria infections and they might acquire significant clinical immunity before pregnancy, and placental malaria though often asymptomatic could have harmful effects on the foetus (Rogerson et al 2007).

During pregnancy, especially in first pregnancies women are more susceptible to *Plasmodium falciparum* infections and experience a higher frequency and density of parasitaemia than their non-pregnant counterparts (Brabin 1983, Akanbi et al 2005) the mechanism underlying this susceptibility is not definitive. It has been suggested that despite the acquired antimalarial immunity of these pregnant women, the uteroplacental vascular space apparently

provided a site for parasite sequestration and development (van Geertruyden et al 2004). It therefore follows that the parasite replication will reduce nutrient transport across the placenta and allow for passage of parasitized red blood cells to the fetus that may retard fetal growth (van Geertruyden et al 2004, Kidima 2015) and infant survival. The aim of this study was to determine the adverse effects of placental malaria on neonatal outcomes.

PATIENTS AND METHODS

Design: Descriptive case-control prospective study conducted during the period of July 2007 and March 2012.

Sampling: Four hundred and twenty (420) neonates of pregnant women seen in antenatal clinic of the St Michael Hospital Pramso, Ghana during the study period were purposively selected and enrolled in the study after mothers' informed consent had been obtained. These comprised two hundred and twenty (220) neonates of women with positive placental malaria (cases) and 200 neonates of healthy pregnant women who were negative for placental.

Placental Malaria Determination: The fixed placental biopsy samples which were embedded in paraffin wax were prepared and (Giemsa haematoxylin) eosin and periodic acid Schiff stained in the histopathology laboratory. An experienced consultant clinical microbiologist examined the slides for the presence of malaria parasites, malaria pigments, placental morphology and signs of infection other than malaria. We defined placental malaria as the presence of parasites and/or pigment in the red blood cells or the presence of pigment in the monocytes in the intervillous space of the placenta according to Bulmer et al (1993) was classified as active placental malaria.

Outcome of pregnancy: Neonates born to participants in both case and control groups were assessed for gestational age, live/stillbirth, birth weight, Apgar score at one minute and five minutes. Conditions indicative of the general health status of the neonates were also noted.

Ethical consideration: Institutional Review Board of the University of Cape Coast approved the study and ethical clearance was obtained from the Central Regional Hospital. Participants' also signed informed consent and participation was voluntary.

Data analysis: Data was analyzed with SPSS 21. For the univariate analysis of categorical variables, Pearson's Chi square or Fisher's exact test was used. For continuous variables, we used the Independent sample t-test after checking Normality and equality of the variance on the basis of Levine's test at 5% significant level.

RESULTS

This prospective case-control study identified 220 cases exposed to placental malaria and 200 controls not exposed. Gestational age of neonates who were exposed to placental malaria was significantly less than that of neonates who were unexposed to placental malaria ($p < 0.001$). This could mean that placental malaria adversely affected gestational age contributing to premature babies. Birth weight was This study is also limited in design in that it did not consider cord parasitemia of the neonates. However, it is widely recognized that neonates exposed to malaria infected placentas are likely to be malaria-infected (Mukhar et al 2005).

lower among neonates in the case group than neonates in the control group. Again, the difference was statistically significant ($p < 0.001$) and indicated that placental malaria had adverse effects on birth weight. Apgar scores at 1 minute and 5 minutes between the groups was statistically significant ($p < 0.001$). 56/8 at 1 minute and 34/2 at 5 minutes in the case/control groups respectively, suggesting that placental malaria affected Apgar score. There was a higher risk for stillbirth among exposed neonates than among unexposed neonates to placental malaria. A statistically significant difference was reported ($p = 0.0013$). Asphyxia was more common among exposed cases than in the control group, the difference was once more statistically significant ($p < 0.001$), revealing that placental malaria caused asphyxia in the neonate (table 1).

Table: 1 Neonatal Characteristics of Infants Born to Mothers

Parameters	Variables	Case (n=220)	Control (n=200)	Chi Square	P-Values
Gestational Age	Preterm	60	22	16.6355	0.0000
	Term	160	178		
Birth Weight	<2500g	124	36	23.9124	0.0000
	≥2500g	96	164		
Apgar Score at 1 min	< 7	56	8	35.6919	0.0000
	≥ 7	164	192		
Apgar Score at 5 min	< 7	34	2	26.1164	0.0000
	≥ 7	186	198		
Birth Outcome	Live	200	197	10.2416	0.0013
	Still Birth	20	3		
Asphyxia	Present	42	6	23.6082	0.0000
	Absent	188	194		

DISCUSSION

This case-control study determined the association between placental malaria and adverse neonatal outcomes. It was observed that exposure to placental malaria carried the risk for prematurity, low birth weight, low Apgar scores at 1 minute and 5 minutes, still birth, and asphyxia at birth.

In this study a significant number of neonates who were exposed to placental malaria were less than 37 weeks of gestation at birth compared to neonates who were not exposed to placental malaria. Studies conducted early on have shown that malaria in pregnancy affected gestational age (Desai et al 2007, Tobon-Castano et al 2011). Numerous studies demonstrate that parasite specific adhesions in placental intervillous spaces contribute to placental insufficiency (Suguitan et al 2003, Muehlenbachs et al 2006, Diouf et al 2007, Mens et al 2010, Hvild 2011, Umber et al 2011, Boeuf et al 2013). It has been suggested that placental insufficiency by sequestration of malaria parasites could directly or indirectly lead to intrauterine growth retardation and premature birth. These two mechanisms are thought to be responsible for low birth weight (Brabin et al 2004, Nosten et al 2007, Rogerson et al (2007).

Placental malaria was significantly associated with low birth weight in this study. This finding is consistent with several studies which have focused on low birth weight as an adverse neonatal outcome of placental malaria. It has been reported that having

just an incident of malaria which may be treated during pregnancy lowers birth weight (Nosten et al 1999, Desai et al 2007). Many more studies have demonstrated that malaria which is one of the most common parasitic infections in pregnancy (Price et al 2007, Rijken et al 2012) lowers birth weight whether it is symptomatic or asymptomatic (Nosten et al 2007). Low birth weight is identified as carrying the highest risk factor for neonatal mortality thereby increasing infant mortality (Guyatt & Snow 2001, Luxemburger et al 2001, van Geertruyden et al 2004, Kassam et al 2006). However, this study was limited by its design and did not cover neonatal or infant deaths resulting from low birth weight.

Previous studies indicate that MiP has also been reported to be associated with low Apgar scores in the neonate (Ticconi, et al., 2003).

A previous study reported an association between placental malaria and increase in risk for stillbirth (van Geertruyden et al 2004), which is confirmed by the presented data.

CONCLUSION.

In conclusion, PM contribute to adverse neonatal outcome such prematurity, stillbirth low birth weight asphyxia and low Apgar score. A difficulty in prevention of these adverse neonatal outcomes arises as the infection remains asymptomatic in the mother and could only be detected after the birth of the neonate. It is therefore imperative that neonates with

such outcome are screened and treated for malaria. This study is limited in design, because it did not consider cord parasitemia of the neonates but then it is generally known that neonates exposed to malaria infected placenta are likely to be malaria infected. Malaria infection should not be ruled out when ever neonatal sepsis is suspected because it is difficulty to make distinction between the symptomatology of malaria and other infections in the neonates

REFERENCES

1. Ananth CV, Vintzileos AM (2006). Epidemiology of Preterm Birth and its clinical Subtypes. *J Matern Fetal Neonatal Med* 19: 773-782
2. Akanbi OM, Odaibo AB, Afolabi KA, Ademowo OG (2005) Effect of self-medication with antimalarial drugs on malaria infection in pregnant women in South Western Nigeria. *Med Princ Pract.* 14: 6-9.
3. Brabin BJ (1983) An analysis of malaria in pregnancy in Africa. *Bulletin of the world Health Organization* 61, 1005-1016.
4. Christensen DL, Kapur A, Bygbjerg IC (2011). Physiological adaptation to maternal malaria and other adverse exposure: low birth weight, functional capacity, and possible metabolic disease in adult life, *international journal of gynecology and obstetrics*, 115 suppl 1 16-19
5. Desai M, ter Kuile FO, Nosten F et al (2007). Epidemiology and burden of malaria in Pregnancy. *The Lancet infectious Diseases* 7: 93-104
6. Guyatt HL, Snow RW (2001). Malaria in pregnancy as an indirect cause of infant mortality in sub-Saharan Africa. *Trans R Soc Trop Med Hyg* 95 569-576
7. Kassam SN, Nesbitt S, Hunt LP, Oster N, Soothill P, Sergi C (2006). Pregnancy Outcomes in Women with or without malaria. *Int J Obs Gynecol* 93: 225-232
8. Kidima W (2015) Syncytiotrophoblast Functions and fetal growth restriction during placental Malaria: Updates and Implication for future interventions. *biomed Research international*
9. Luxemburger C, McGready R, Kham A, Morison L, Cho T, Chongsuphajasiddhi T, White NJ, Nosten F (2001). Effects of Malaria during pregnancy on infant mortality in an area of low malaria transmission. *Am J Epidemiol* 154: 459-465
10. McDonald CR, Cahill LS, Ho KT, Yang J, Kim H, Silver KL et al (2015). Experimental Malaria in Pregnancy induces neurocognitive injury in Uninfected Offspring via C5a-C5a Receptor Dependent Pathway. *PLoS Pathog* 11(a): e1005140.doi:10.1371/journal.ppat.1005140
11. Morrison JL, Duffield JA, Muhlhausler BS, Gentili S, McMillen IC (2010). Fetal growth restriction, catch-up growth and the early origins of insulin resistance and visceral obesity *Pediatric Nephrology*, 25: (4) 669-677.
12. Mukhar MY, Lesi FE, Iroba EU, Egri-Okwaji MTC, Mafe AG (2005) Congenital Malaria among babies at a Tertiary Centre in Lagos, Nigeria. *J Trop Ped.* 52 19-23
13. Rogerson SJ, Mwapasa V, Meshnick SR (2007). Malaria in Pregnancy: Linking immunity and pathogenesis to prevention. *AmJ Trop Med Hyg* 77: 14-22
14. Tobon-Castano A, Solano MA, Sanchez LG, Trujillo SB (2011). Intrauterine Growth Retardation, Low Birth Weight and Prematurity in Neonates of Pregnant Women with Malaria in Columbia. *Rev Soc Bras Med Trop* 44: 364-370
15. Van Geertruyden JP, Thomas F, Erhart A, D'Alessandro U (2004). The contribution of Malaria in Pregnancy to Perinatal Mortality. *Am J Trop Med Hyg* 71(suppl 2) 35-40