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Full Length Research Paper

Does placental malaria infection impairs the passage of measles antibodies from mothers to their newborn infants?

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Infants are protected from measles by maternal measles antibodies (MMA). The level of these antibodies in infants at birth depends on maternal levels and the extent of placental transfer, which can be impaired by placental malaria. The efficiency of transplacental transfer of MMA was assessed in relation to placental malaria in Maiduguri. A hospital based cross-sectional descriptive study was carried out on 104 mother-infant pairs. Subjects were selected using systematic random sampling and tested for MMA at delivery. Placental tissues for the diagnosis of placental malaria infection were also obtained. Correlation coefficient was used to investigate the relationship of MMA of mother-infant pairs and Student t test was used to test for significance of means. Fifty eighty (55.8 %) newborn infants had mothers diagnosed with placental malaria. Of these, nine (8.7 %) newborn infants had unprotective levels of MMA. Correlation of MMA in mother-infant pairs was significant (p = 0.003). Overall mean (SD) MMA of newborn infants was 208.81 (75.46), 95 CI (194.13 – 223.48). While mean (SD) MMA of newborn infants of mothers with placental malaria was 194.60 (83.42), 95 CI (172.67 – 216.54), those whose mothers were uninfected was 226.72 (60.28), 95 CI (208.82 – 244.61), and comparison of these means was significant (p = 0.030). Placental malaria infection was associated with reduction of MMA in our newborn infants.

Keywords: Placental malaria, maternal measles antibodies, newborn infants, Maiduguri.

INTRODUCTION

Despite the availability of measles vaccine worldwide, measles is still associated with high mortality rates in children especially those residing in developing countries. In 2006, Owen et al in the Gambia reported a yearly mortality figure of measles in children to be approximately one million. Maternal measles antibodies (MMA) are passed actively from mothers to their foetus via the placenta in most cases from third trimester of gestation (Caceres et al, 2000). These antibodies protect infants

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from measles and at the same time may interfere with successful response to measles vaccination later in infancy (Owen et al, 2006 and Caceres et al, 2000). Brair et al, in 1994 has indicated that one-tenth of babies whose mothers were diagnosed with placental malaria had unprotective levels of tetanus antibodies, despite adequate maternal levels. One would expect placental malaria to also impair the passage of MMA in mother-infant pairs; nonetheless however, this has not been fully resolved. Scott et al, (2005) in Kenya further documented conflicting report on the effect of placental malaria on MMA transfer in mother-infant pair. Therefore, there is the need for more studies on this subject.

Not only are MMA transfer from mother to foetus impaired, nutrient transfer to the foetus could also be impaired if the placenta is severely damaged by placental malaria (Brabin et al, 2004). This could result to the following complications: 1) intrauterine growth retardation, 2) low birthweight and still birth among others. Mothers who lack sufficient immunity to malaria or are having severe immunosupression are worst hit by these complications (Brabin et al, 2004). Understanding the interactions between placental malarial infection and MMA is important, since placental malaria can impair the levels of MMA in newborn infants. Because of the existing gap in knowledge coupled with lack of data on this subject in most Sub-Saharan African nations especially North-East sub-region of Nigeria; we assessed the efficiency of transplacental transfer of MMA in relation to placental malaria in mother-infant pairs in Jere local government area of Maiduguri, Borno state, Nigeria.

MATERIAL AND METHODS

Study Area

The study was carried out at the Department of Paediatrics, Obstetrics unit, immunology and histopathology of the University of Maiduguri Teaching Hospital, (UMTH), Nigeria. Apart from being the largest health facility in the area, UMTH serves as a referral centre for the six North-Eastern States and neighboring countries of Chad, Cameroon and Niger Republics.

Ethical Considerations

The study protocol was reviewed and authorised by the Medical Research and Ethics Committee of the UMTH. The approval was on the agreement that patient anonymity must be maintained, best clinical practice be 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 internatio-nal guidelines for human experimentation in clinical research (World Medical Association Declaration of Helsinki, 2000). Informed consent from parents was also obtained. Parents had unlimited liberty to deny consent or opt out of the study without any consequences.

Sample Size/subject selection

The minimum sample size was determined using the Browner's formula (Browner 2001), which detects differences between two means when using paired sampling units: the effect size was set at 0.2, alpha level at 0.05 and power at 80%. However, 30% of the calculated minimum sample was added to maximize power. Therefore, the sample size for this study was one hundred and four mother-infant pairs. Consenting women who delivered vaginally at the UMTH were enrolled between 10th January and 21st March 2010. Demographic and retrospective antenatal data were obtained by questionnaire and from the antenatal health card. Hypertensive women, those delivering stillborns, infants with congenital abnormalities and mothers who received blood transfusion during pregnancy were excluded. The subjects were selected using systematic random sampling method where the first of every three mothers was picked as they presented to the labour ward. Where the first mother did not fulfil the inclusion criteria, the immediate next mother that qualified was selected.

Collection of specimens

Three milliliters (ml) of venous blood was obtained from the mother on admission to the labour ward, and from the umbilical cord of their neonates at delivery using sterile disposable five (ml) syringe under aseptic technique. These blood samples were placed in sterile plain bottles and serum was separated after centrifuging the blood samples at 5000 revolutions per minute (rpm) for five minutes. The serum obtained was stored in a refrigerator at -20°C until the time of measles IgG assay by enzyme linked immunosorbent assay (ELISA) in units per millilitre (U/ml).

Placental biopsy specimen was obtained from maternal side of the placenta and stored in 10% formaldehyde. Paraffin embedded sections of the placental tissues were stained with Giemsa solution and examined by light microscopy under polarised light. Placental malaria infection was defined by the presence of parasites and malaria pigment (Owen et al 2006, Brabin et al 2004, and Burns et al 1980).

The levels of MMA were measured by ELISA (Demeditec diagnostic Gmbh Kiel Germany) in accordance with standard laboratory practice (Caceres et

Table 1. Relationship between placental malaria and levels of maternal measles antibody of newborn infants

Placental malaria	Maternal measles antibodies of newborn infants		
	Protective n (%)	Unprotective n (%)	Total n (%)
Positive	49 (47.1)	9 (8.7)	58 (55.8)
Negative	43 (41.4)	3 (2.8)	46 (44.2)
Total	92 (88.5)	12 (11.5)	104 (100)

Table 2. Mean maternal measles antibody distribution of mother-infant pairs

Mother-infant pairs	Maternal measles antibodies (U/ml)	
	Mean ± SD	95% CI*
Mothers	136.71 ± 96.01	118.04 – 155.38
Newborn infants	208.81 ± 75.46	194.13 – 223.48
p value	p < 0.0001	-

**CI = confidence interval*

Table 3. Placental malaria and mean maternal measles antibody profiles of newborn infants

Placental malaria	Mean maternal measles antibody of newborn infants (U/ml)	
	Mean ± SD	95% CI*
Negative	226.72 ± 60.28	208.82 – 244.61
Positive	194.60 ± 83.42	172.67 - 216.54
p value	0.030	-

**CI = confidence interval*

al, 2000). The ELISA well plates were coated with Edmonston MV strain and results were presented in units per millilitre (U/ml). The MMA Levels < 8 U/ml were classified as negative, equivocal with levels of 8 -12 U/ml and positive when levels are >12 U/ml. On the basis of these recommendations, protective titres for MMA were defined as the levels of MMA >12 U/ml, and unprotective titres as levels of MMA ≤ 12 U/ml similar to another publication elsewhere (Caceres et al, 2000 and Milagritos et al 2005).

Data analysis

Statistical analyses was performed by use of statistical package for social science (SPSS) statistical software version 16, Illinois, Chicago USA. Values were expressed as mean ± standard deviation (SD) and their 95% confidence intervals (CIs) were calculated. The mean coefficients of MMA were compared using the Student t test. Correlation coefficient was used to compare levels of MMA of mother-infant pairs at birth. A p- value < 0.05 was considered significant. Tables were used appropriately for illustrations.

RESULTS

A total of 104 newborn infants were enrolled in this study out of which 55 (52.9 %) were males and 49 (47.1 %) females, giving an approximate male to female ratio of 1.1:1. Fifty eight (55.8 %) of the newborn infants had their mothers diagnosed with placental malaria. Of these, nine (8.7 %) of the newborn infants were found with unprotective levels of MMA (Table 1).

The overall mean (SD) of mother's age was 23.86 (5.25), 95% CI (22.84 - 24.88) years. Mean (SD) age of mothers diagnosed with placental malaria was 23.63(5.66), 95% CI (21.95-25.31), and that for uninfected mothers was 24.03(4.94), 95 CI (21.74-25.33). Levels of MMA in mother-infant pairs had significant correlation (p = 0.003) for both placental malaria infected and uninfected groups. Table 2 shows mean MMA profiles of mother-infant pairs which has a ratio of 1:1.5. The comparison of mean MMA of mother-infant pairs was significant (p < 0.0001).

Mean MMA was lower in newborn infants whose mothers had placental malaria as shown in Table 3. Mean maternal measles antibody comparison between newborn infants whose mothers had placental malaria

and those of mothers without placental malaria was significant (p = 0.030).

DISCUSSION

Significant proportion of mothers that participated in this study had placental malaria. This may not be surprising because Maiduguri, Borno state, Nigeria, is located in holoendemic region for malaria (Ogala 2007). Similar finding was made by researchers in Kenya (Scott et al, 2005). Milagritos et al, (2005) in Kagamba, Lyke et al, (2003) in Bandigiara and Bouvier et al, (1997) in Bougoula have reported high endemicity of malaria in Sub-Saharan Africa. If these are considered, there wouldn't be any contradiction between our study group and that of Kenya. Malaria being stable in our population that is to say the transmission of malaria is all year round could be one reason for this observation (Milagritos et al 2005, and Ogala 2007). Savannah ecological belt that formed our geographical vegetation may also constitute a favorable breeding ground for mosquitoes (Ogala 2007, and Bouvier et al, 1997). Thirdly, access to health care delivery services, which includes prompt diagnosis and treatment of malaria in our locale still remains a challenge rendering ineffective management of malaria (Bouvier et al, 1997). In this regard, Scott et al, (2005) in Kenya argued that cases of placental malaria might be more in younger age mothers. Their argument was consistent with findings of current work. These mothers have just begun their childbearing career and most of them could be naïve on the need for proper antenatal care services (ANC). Considering the effect of pregnancy on the immune physiology of prospective mothers, failure to adhere to intermittent malaria prophylaxis as part of ANC would favor the development of placental malaria.

Almost all the newborn infants in present study were having protective levels of MMA similar to those of their mothers. This was consistent with observation made in other studies (Caceres et al, 2000 and Scott et al, 2005). Measles being endemic in our environment would cause the up regulation of its placental receptors leading to passage of more MMA to foetus; this was also evident in this study (Caceres et al 2000, Scott et al 2005, and Sarvas et al 1993). Of note is that only (8.7 %) of newborn infants whose mothers had placental malaria were having unprotective MMA. Mothers of these newborns had high malarial parasitaemia of their placental (+2 to +3). By interpretation the malaria parasitaemia on the placenta were up to 1-10 per high power field, and damage to the placenta occurs mostly at high density of malaria parasitaemia (Owen et al 2006, Scott et al 2005, Burns et al 1980, Milagritos et al 2005, and Ogala 2007). With this, most of the placentas of our study population have MMA receptor sites preserved for effective MMA transfer, as such most newborns in this study started out with high levels of MMA. Another explanation that could be advanced for the high levels of MMA observed in newborn infants in recent study could be the efficient placental transfer of MMA in mother-infant through an active pathway (Caceres et al, 2000). More so, majority of the mothers in present study were in their early child bearing age, and are expected to have normal placenta in terms of structure that would support active transfer of MMA to their fetuses.

Eventhough the overall mean MMA of newborn infants in this study was high; mean MMA of newborn infants of mothers with placental malaria was lower compared to those whose mothers were uninfected. Colleagues elsewhere made similar observation and they reported that, the reduced placental transfer of MMA to fetuses was due to the damages incurred by the placenta by malaria parasites (Owen et al 2006, Scott et al 2005, and Brabin et al 2004). Such newborn infants could start out at birth with low levels of MMA. Reports have indicated that MMA are lost rapidly in infancy (Caceres et al, 2000 and Sarvas et al, 1993). Therefore, if these newborns have low MMA at birth, coupled with rapid loss of MMA in infancy, they become highly prone to measles (Caceres et al 2000, Milagritos et al 2005, and Yamaguchi et al 2002). This could have been the reason for one–fifth and half cases of measles recorded in infants less than six and nine months of age respectively (Yamaguchi et al, 2002).

Contrastingly, other workers did not establish significant relationship between placental malaria and MMA of newborn infants in a population of a West African district (Milagritos et al, 2005). This might not be unconnected to the recent success credited to better control of malaria during pregnancy (Owen et al, 2006). Mothers in that study had antenatal care services (ANC) and were given routine ANC drugs which contained antimalarials. The administration of intermittent preventive therapy for malaria during ANC could have led to the insignificant effect of placental malaria on MMA transfer that was reported.

CONCLUSION

Placental malaria infection was associated with reduced MMA of newborn infants that formed our study population.

LIMITATION

Caution may be needed in generalizing the results of this work since only a small cohort of mother-infant pairs participated in recent work at the UMTH.

RECOMMENDATION

Future studies of this kind should include larger number of mother-infant pairs from multiple health centers so as to obtain a representative cross-section of the study population.

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