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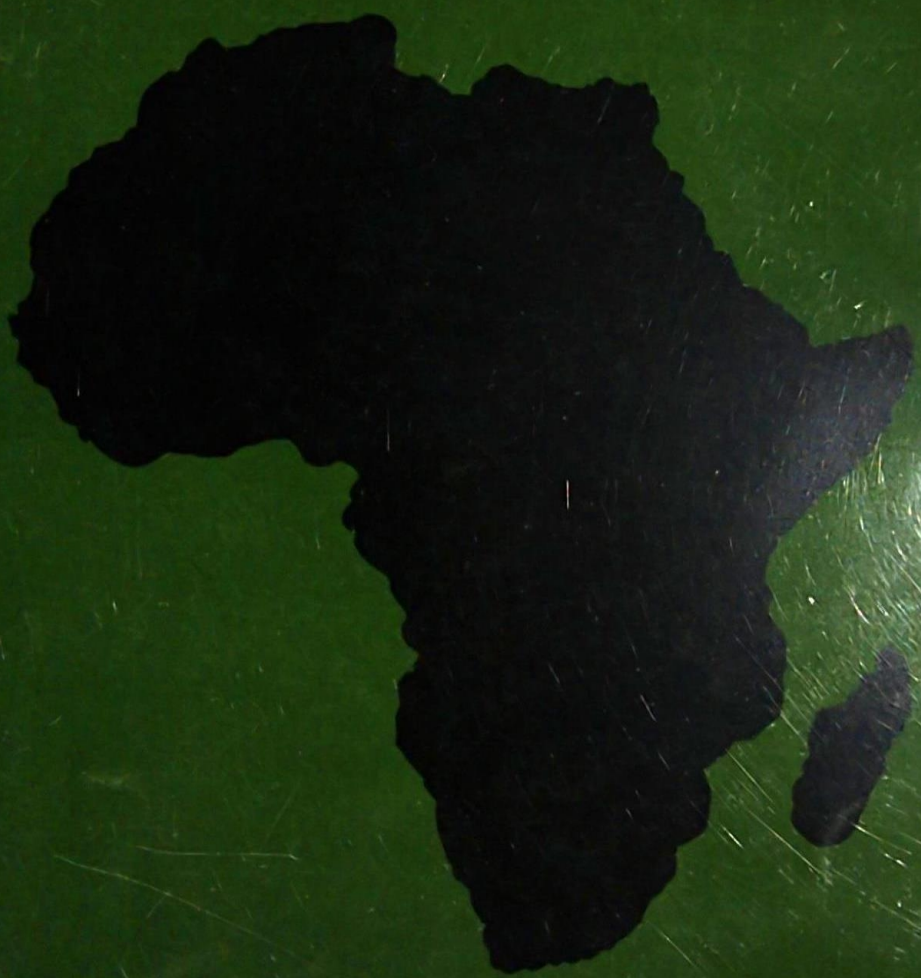

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Congenital malaria in a hyperendemic area: a revisit

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Summary

Screening of 104 mother-baby pairs for *P. falciparum* malaria revealed that 29% of mothers from low socio-economic group and 11% of their babies had malaria parasitaemia. The corresponding figures for middle and high socio-economic groups were 15% and 7%, respectively. The parasite densities in the babies were not proportional to maternal load and were generally low, although higher in the low socio-economic group. Maternal pyrimethamine prophylaxis did not appear to protect babies from parasitisation and there was no demonstrable beneficial effect on the babies' birth-weights.

Keywords: *Malaria: congenital, maternal prophylaxis; socio-economic levels.*

Résumé

L'examen de 104 pairs mére – enfant pour le P. falcipa um a montré que 29% des mamans ressostissants des basses conches socio-économiques et 11% de leurs exfants sruffrent de la parrassitaemia (taux élere de parasites du paludisme). Les figures correspondents des classes socio-économiquement moyennes et élévées ont été de 15% et 17%, respeitivement. La densité des parasites ches les enfants n'éfait pas proportionnelle au farolean maternal et étout généralement bas, beim qu' elevée dams les basses conihes socio - économiques. La prophylaxie pyrimethamine n'a pas été un agent protector des enfants du la parrasitibation and il n' ya pas eu d'effet bénéficiuire démontrble sur le poids de nuissance des enfants.

Introduction

Although pregnancy has been associated with an increased susceptibility to malaria, especially in primigravidae [1,2], earlier reports (four decades ago) concluded that the transfer of malaria transplacentaly was unlikely because of the placental barrier function [3, 4]. However, during the course of this decade, various reports have indicated a change in the pattern of this transfer in areas endemic for malaria, thus leading to more cases of congenital malaria [5-8]. Deleterious effects of gestational malaria include fetal wastage, early neonatal deaths, low birth-weight and preterm delivery. The contributing effects of placental parasitisation to the delivery of light-for-dates babies have previously been documented; the effect being more pronounced in primigravidae [9]. For these reasons and because of the risk of severe maternal anaemia that can result from maternal disease, the use of chemoprophylaxis was advocated and has been used widely in endemic malarious areas. Various chemoprophylatic drugs have been studied, for example, chloroquine, pyrimethamine, mefloquine and malorprim to mention a few [10-12]. The efficacy and safety of these drugs in protecting mothers and their babies have been questioned. For example, studies have suggested that pyrimethamine is not an effective prophylactic agent [13], and that chloroquine, though still an effective antimalarial drug, has had its use curtailed owing to the emergence of chloroquine-resistant *P. falciparum* infection in both *in vivo* and *in vitro* studies [11]. Mefloquine is relatively well tolerated and has the advantage of single day regimen and ideal properties for prophylactic use; however, although rare, serious adverse reactions do occur and resistance has already emerged in some parts of the world [10].

The present report is designed as a comparative study between two hospitals attended by patients from different socio-economic levels, to determine a) the level of maternal parasitisation at delivery in relation to neonatal parasitisation, (b) the influence of maternal pyrimethamine prophylaxis on neonatal parasitisation and (c) the possible influence of socio-economic factors on the incidence of congenital malaria.

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Materials and methods

This prospective study was undertaken during a 2-month period of the rainy season, August and September, 1993. The study took place at two hospitals located in Ibadan, southwest Nigeria: the University College Hospital (which cares for high - risk pregnancies and women of predominantly middle to high socio-economic status) and Adeoyo Maternity Hospital (which cares for low risk pregnancies and women mostly from low socio-economic status). Ethical clearance was given for the study jointly from the Ethical Committees of the two hospitals concerned. Informed consent was also obtained from the mothers. Mother-baby pairs were recruited consecutively into the study; the only inclusion criterion being a baby's age of less than 48 hours. Maternal data collected included the gestational age and the type and regularity of malarial prophylaxis received during pregnancy. Infant data collected included the gestational age by date (in weeks) and by Ballard's scoring [14] and the postnatal age (in hours), gender, anthropometric measurements, comprising birth-weights (kg), the occipito-frontal circumference (cm) and the crown-heel length (cm); the rectal temperature was recorded in °C.

Duplicate thick and thin blood films were made from blood obtained by a finger prick from each mother after skin preparation with alcohol swab, and by a heel prick in each baby after adequate skin preparation; haemostasis was ensured by digital pressure with a dry cotton wool ball for about five minutes. The films were Giemsa-stained and microscopically examined under oil immersion with x 600 magnification. A minimum of 200 high power fields were examined in each thick and thin films by counting asexual forms relative to leucocytes in thick blood films: 500 asexual forms of *P. falciparum* or the number of such parasites corresponding to leucocytes were counted, whichever occurred first. From this figure, the parasite density was calculated by using Trape's formula [15]:

Parasite/micromillilitre = $\frac{\text{No. of Parasite}}{\text{No. of leucocytes}}$ x 8,000

Differences between means were compared using the Student's "t" test and differences between proportions were compared using the Chi squared (x^2) test; p values of < 0.05 were taken as being significant.

Results

There were a total of 104 mother-baby pairs: 77 pairs from Adeoyo Maternity Hospital (AMH) and 27 pairs from the University College Hospital (UCH), the corresponding number of babies were 79 and 28 (3 pairs of twins). Gestational ages ranged between 32 and 43 with a mean of 38.6 weeks in AMH, whilst it was 33 and 42 with a mean of 37.7 weeks at UCH. The birthweights of babies at AMH ranged from 1.3 to 4.3 kg with a mean value of 2.86 kg whilst the corresponding figures for UCH were 2.1 to 3.9 kg and 3.01 kg, respectively. Male: female ratios were 1:1.05and 1:1.55, respectively.

Parasitaemia was present in 29% of the mothers at AMH and in 15% of the UCH mothers, whilst neonatal parasitaemia was detected in 14% of AMH and 7% of the UCH groups (Table 1). The parasite densities in the mother baby pairs are as depicted in Table 1, showing the higher densities in mothers from AMH and the comparatively low neonatal parasite densities. Regarding pyrimethamine usage in pregnancy and the effect on the neonate, 36% of the parasitaemic babies were delivered at the AMH, to mothers who had received pyrimethamine in pregnancy whilst 64% of the parasitaemic babies were delivered to mothers who did not receive malarial prophylaxis. Fifty - three per cent of the non-parasitaemic AMH babies were delivered to mothers who received pyrimethamine in pregnancy whilst the mothers of the 47% non-parasitaemic babies did not receive pyrimethamine (x^2 =1.03; $P < 0.5$); Table 2. Both parasitaemic babies delivered in UCH were delivered to mothers who received pyrimethamine during pregnancy; 69% of the non-parasitaemic babies were delivered by mothers who received pyrimethamine while 31% of the non-parasitaemic babies were delivered to mothers who did not receive pyrimethamine in pregnancy (x^2 = 0.86; $P < 0.5$) Table 2. Overall, the UCH mothers' usage of pyrimethamine in pregnancy was more than that of the AMH group. Analysis of the effect of maternal pyrimethamine prophylaxis on birth-weight showed that of the AMH–delivered babies, the birth-weights of those babies whose mothers received pyrimethamine ranged between 1.8 and 4.3 kg (mean of 2.90 kg), while those of the babies whose mothers did not receive any pyrimethamine ranged between 1.3 and 3.8 kg with a mean of 2.81 kg (t = 0.75 $P < 0.5$) (Table 2). The corresponding figures in the UCH–delivered babies were 2.1–3.9 kg, with a mean of 2.93kg, and 2.65–3.65kg, with a mean of 3.07 kg; (t = 0.64; $P < 0.5$), respectively (Table 2). Pyrimethamine usage did not appear to have a significant effect upon birth-weight at either hospital just as maternal pyrimethamine treatment did not have a significant effect upon infant parasitaemia (Table 2).

Discussion

The present study confirms the fact that congenital malaria is not uncommon in Ibadan as had previously been noted. A combined 12.5% incidence rate of parasitaemia in newborns aged less than 48 hours is remarkable. This may be indicative of a breakdown in the mechanical barrier provided by the placentae in those mother-baby pairs, since this barrier has been adduced as one of the major factors for the rarity of congenital malaria. The barrier is believed to prevent the transfer of malaria parasites from the mother to the fetus and this placental function is maintained in most pregnancies, even when the placenta itself is densely parasitised. Subsequently, as highlighted in the present study, the densities of maternal parasitaemia in malarial endemic areas is often higher compared to neonatal parasitaemia. Additionally, the very low geometric mean parasite densities of 0-143 observed in AMH babies as compared to the high maternal densities (0-43,956) could be explained on the basis of the poor ability of fetal haemoglobin to support parasite growth as well as the presence of maternal antimalarial IgG in these babies [16].

Table 1: Positive parasitaemia in mother-baby pair

Parameters	UCH n=27	Adeoyo n=77
Positive Parasitaemia		
+Mothers	4(15%)	22(29%)
**Babies	2(7%)	11(14%)
Parasite densities/micromillilitre:		
Mothers	0-61	0-43,956
Babies	0-61	0-143

***Combined incidence of neonatal parasitaemia = 12.5%*

Table 2: Relationship between maternal prophylaxis, neonatal parasitaemia and birthweights

		UCH Neonatal Parasitaemia+		Adeoyo Neonatal Parasitaemia*	
		Yes	No	Yes	No
Pyrimethamine Prophylaxis					
Yes		2(100)	18(69)	4(36)	36(53)
No		0(0)	8(31)	7(64)	32(47)
Total		2(100)	26(100)	11(100)	68(100)
		Birthweight (kg)		Birthweight (kg)	
Yes	Range	2.1-3.9		1.8-4.31	
	Mean	**2.93		++2.90	
No	Range	2.65 – 3.65		1.3 – 3.8	
	Mean	**3.07		++2.81	

+X^2 = 1.03; p <0.5, ++t = 0.75; p<0.5
*X^2 = 0.86; p <0.5 **t = 0.64;p<0.5*
Figures in parentheses represent percentages.

The common practice for pregnant mothers in endemic areas to use malarial prophylactic drugs especially pyrimethamine must be reviewed. Over 71% of the mothers from the University College Hospital (UCH), and 50.6% of those from Adeoyo Maternity Hospital (AMH) had used pyrimethamine regularly during the course of the index pregnancy. This study has shown that the incidence of parasitaemia was not significantly different between mothers who had taken pyrimethamine and those who had not; in fact the mothers of the two babies with parasitaemia in UCH had regular pyrimethamine prophylaxis in pregnancy. This may be seen as confirming the earlier documentation of the non-efficacy of pyrimethamine prophylaxis by demonstrating both *in vitro* and *in vivo* resistance of *P. falciparum* to the drug [12]. This finding indicates the need to search for more effective prophylactic agents. Lastly, pyrimethamine

prophylaxis had no significant influence on the mean birth-weights, though at AMH, babies whose mothers had pyrimethamine prophylaxis had slightly higher (though not significant) mean birth-weights than those whose mothers did not receive prophylaxis.

In conclusion, there is a need for health workers to be more aware of the danger of misdiagnosis posed by congenital malaria in our environment as it can mimic many neonatal conditions, e.g., cardiovascular disease, infection of the gastro-intestinal tract and septicaemia to mention a few. We need to search for it, especially in cases of unexplained pyrexia in the newborn and carry out meticulous blood film examinations for these parasites. As it seems that pyrimethamine is not as effective as previously thought, health workers may need to prescribe for the pregnant woman a combination of agents such as maloprin: dapsone (100 mg) and pyrimethamine (12.5 mg). Studies from the Gambia have shown the efficacy of this drug combination [17,18]. Oral proguanil 200 mg daily is also an effective prophylactic drug and obstetricians need to veer away from the routine practice of prescribing pyrimethamine as prophylaxis in pregnancy.

Regarding the possible effect of the socio-economic status on the prevalence of congenital malaria, the AMH mothers were more densely infected than the UCH mothers. This may be related to the lack of protection against mosquito bites and subsequent acquisition of malaria, the lack of maintenance of a clean environment seen in the low socio-economic areas where stagnation of water may be the norm. Coupled with these may be the ignorance about preventive measures against the acquisition of malaria and the lack of funds to purchase these drugs even in those who know. A lot of work needs to be done to educate these women about malaria and the deleterious effects on the mothers and their babies.

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