Annals of African Medicine
Vol. 3, No. 4; 2004: 170 – 173

NEONATAL MALARIA IN A MESOENDEMIC MALARIA AREA OF NORTHERN NIGERIA

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Abstract
Background: Though neonatal infections are most common reason for admissions in the newborn in Nigeria, Neonatal Malaria, which was thought to be uncommon, is becoming increasingly reported in areas of malaria hyperendemicity. These reports have described not only malaria parasitaemia in these babies, but also some symptoms attributable to malaria. There are no known documented clinical studies in areas of malaria mesoendemicity, which also have high prevalence of neonatal infections.
Method: As a preliminary investigation to document the incidence of neonatal malaria in a mesoendemic area, as well as identify possible risk factors for its occurrence, a prospective study was carried out in the special care baby unit of ABU Teaching Hospital, Kaduna Nigeria, over a one year period (December 2001- November 2002). As part of the investigations for evaluation of sick neonates admitted into the unit, thick and thin blood films stained with Giemsa stain were examined for malaria parasite using standard techniques. Specie identification and quantification were carried out.
Results: Of the 206 children tested, there was positive malaria parasitaemia in 17 (8.25%). Only P. falciparum malaria was identified. There were no mixed infections. Parasite density varied between 1,000 –20,000 asexual forms/μL. Analysis revealed a strong association between neonatal malaria and maternal genital infections (OR 4.51, p= 0.006). There is some association between neonatal malaria and both primigravidity (OR 3.01, p=0.035) and maternal fever developed within 2 weeks to parturition (OR 2.78, p=0.04). Fever was the most strongly associated clinical feature (OR 8.12, p=0.0002) at presentation.
Conclusion: The study has confirmed the presence of neonatal malaria in this environment. There is need for detailed characterization of the aetiological agents of maternal genital infections with which neonatal malaria is strongly associated and investigate the placenta integrity in relation to such infections. Fever in the neonate should be taken as a strong pointer to the possibility of neonatal malaria.

Key words: Malaria, neonatal, mesoendemic

Introduction

Neonatal infections are the commonest reason for admissions into most special care baby units in Nigeria.[1] They also account for 20-25% of neonatal mortality.[2 - 4] Important among the causes are Staphylococcus aureus, Klebsiella species and Escherichia coli.[5] Neonatal malaria has been thought to be rare in malaria endemic areas from earlier studies,[6, 7] but more recent reports especially from the areas of malaria hyperendemicity [8, 9] are suggesting evidence to the contrary. Bacterial and viral infections are known to co-exist with malaria in older children and in whom clinical presentations are also similar.

The high prevalence of neonatal infections in our environment, coupled with reports of neonatal malaria in hyperendemic zones and the possibility of these two conditions co-existing in any one baby, prompted the need to investigate the current status of neonatal malaria in the mesoendemic malaria area.

Method

The study was carried out in an area of malaria mesoendemicity and designed as a preliminary investigation to document the incidence of neonatal malaria as well as identify possible risk factors for its occurrence. A prospective study was carried out in the special care baby unit (SCBU) of ABU Teaching Hospital, Kaduna, over a one-year period (December 2001- November 2002). Questionnaires were administered to document possible risk factors in the mothers for the occurrence of neonatal malaria and describe clinical features in the babies. Only full term babies were studied as the unit had no facility for care of preterm babies at that time. As part of the investigations for evaluation of sick neonates admitted into the unit, thick and thin blood films were made for malaria parasite identification and quantification. The films were fixed and stained using 4% Giemsa stain for thirty minutes. The stain was washed off in tap

water and the dried slides examined under X100 magnification with oil immersion lens. Parasite density was determined counting parasites against 400 leucocytes in a thick film and multiplying by 6000 (the average white blood cell count /μL). Blood samples were sent for microscopy and culture. Complete blood count was also done. The data was analyzed using Epi info "version 6" software. Incidence of malaria parasitaemia was determined. Odds' ratio and intervals for 95% confidence were obtained as estimate of relative risk of identified factors and possible associations. Statistical significance was assessed using Chi square and P value <0.05 was considered significant.

Results

A total of 206 full term sick neonates who were admitted into the SCBU were screened for malaria parasitaemia. There were males and females with a male: female ratio of 1:1.2. There was positive malaria parasitaemia in 17 (8.25%) of the children. Parasite density varied between 1,000 –20,000 asexual forms/μL. Only P. falciparum malaria was identified. There were no mixed infections. These 17 neonates were born between the months of May and September, within which are the months for peak malaria transmission in the area as shown in Figure 1. All the children presented at the first week of life. Their age and sex distribution is as shown in Table1. There were 4 neonates (23%) presenting in the first 24 hours of life, the youngest being at 3 hours of age. The overall male: female ratio was 1.1:1.

Maternal factors

The gravidity of the mothers as compared to the age at which their babies presented is illustrated in figure 2 below. Six of the babies (35%) were born to primigravidarous women. Odds ratio is 3.01 with 95% CI of 0.9 – 9.74. P value 0.035(significant). Of these, three presented within the first 24 hours of life. There was history of fever in last 2 weeks of pregnancy in seven of the mothers (Odds ratio 2.78, 95% CI of 0.88 - 8.62 and P value 0.04 {significant}).There was also history of maternal genital infection during pregnancy warranting treatment in 5 of the mothers, which was highly significant. (Odds' ratio 4.51 with CI of 1.20 – 16.27, p value 0.006. However, there was inadequate information about the aetiology and sensitivity patterns of such infection. Five women had history of premature rupture of membranes > 48 hours before delivery. (Odds' ratio 0.66, 95% CI of 0.19 - 2.14, p value 0.45 (Not significant)

Table 1: Age and sex distribution of neonates with positive malaria parasitaemia

Age at presentation (days)	Sex		Total
	Male	Female	
Day 1	1	3	4
Day 2	2	1	3
Day 3	1	0	1
Day 4	0	1	1
Day 5	3	2	5
Day 6	2	1	3
Total	9	8	17

Figure 1: Month of delivery of neonates with malaria parasitaemia

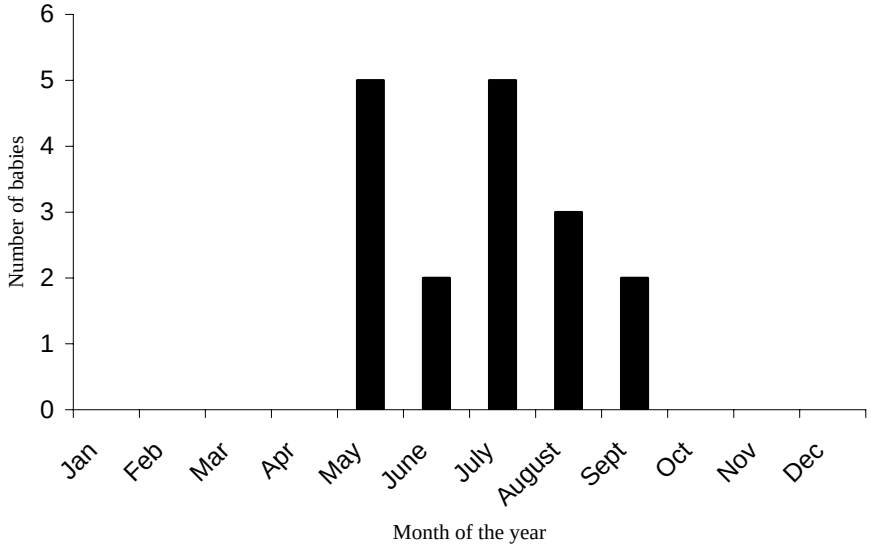

Figure 2: Gravidity of mothers and age of neonates at presentation

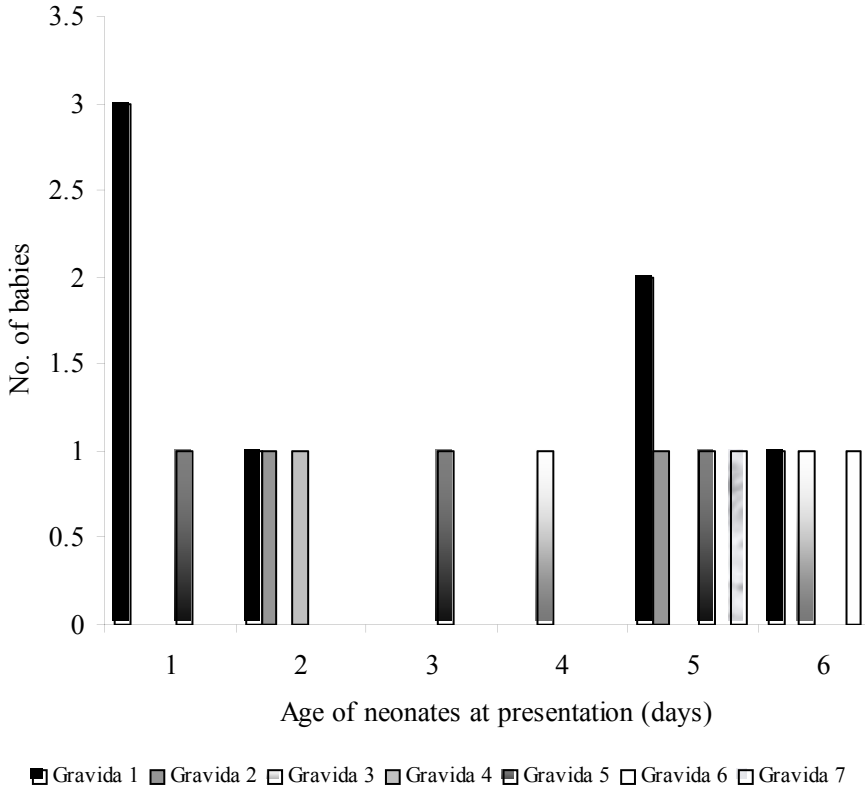

Table 2: Risk factors for malaria infection in 206 sick neonates at Ahmadu Bello University Teaching Hospital, Kaduna

Risk factor	Malaria parasites		Odds ratio	95% confidence interval	Chi square	p value
	Positive (n = 17)	Negative (n = 189)				
Maternal						
Gravidity 1	6	29				
Gravidity 2+	11	160	3.01	0.9 – 9.74	4.40	0.035 (SIGN)
Maternal genital infection						
Positive	5	16				
Negative	12	173	4.51	1.20 – 16.27	7.47	0.006 (SIGN)
Maternal fever within 2 wks of delivery						
Present	7	38				
Absent	10	151	2.78	0.88 – 8.62	4.06	0.04 (SIGN)
Premature rupture of membranes						
Present	5	73				
Absent	12	116	0.66	0.19 – 2.14	0.56	0.45 (NS)
Mode of delivery						
Vaginal	15	141				
Instrumental	-	4				
Abdominal	2	44	-	-	1.67	0.43 (NS)
Baby						
Fever at presentation						
Yes	14	69				
No	3	120	8.12	2.08 – 36.95	13.63	0.0002 (SIGN)
Jaundice at presentation						
Yes	7	90				
No	10	99		0.25 – 2.31	0.26	0.61 (SIGN)
Blood culture						
Positive	6	20				
Negative	11	46		0.16		0.69 (NS)

SIGN = significant; NS = not significant

Mode of delivery and outcome

In 15 of the children, delivery was by spontaneous vertex delivery. These babies were "apparently normal" at birth. The other 2 deliveries were by Caesarean Section (C/S). One of them (delivered by emergency C/S) had malaria parasitaemia by 3 hours of life. This baby also had had severe birth asphyxia. The other baby was a product of an elective C/Section and presented at 5th day of life. The type of delivery was not statistically significant (p value 0.43). The major clinical symptoms were fever (14) and jaundice (7). Only fever was significantly related (p value 0.0002). Others included convulsions (2), excessive crying (2), and difficulty in breathing and poor suckling.

Out of these 17 children with malaria parasitaemia, positive blood cultures were obtained in 6 of them (Table 2) with Staphylococcus and Klebsiella being the predominant organisms cultured. This was not statistically significant chi square 0.16, p value 0.69)

The neonates were all treated with Chloroquine given as an initial subcutaneous dose (5mg/kg body weight) and followed by daily oral doses of Chloroquine (10mg/kg body weight) in the next two days. There was 100% fever clearance by end of second days' dose and 100% parasite clearance at the end of therapy.

Discussion

This preliminary investigation into the occurrence of neonatal malaria in a mesoendemic malarious region has shown an incidence of 8.25%. This is quite significant for a condition thought to be rare. In Tanzania, a region of malaria hyperendemicity prevalence of up to 16.7% have been obtained in cross sectional surveys, [8] while in similar endemic areas of South Western Nigeria, prevalence of 23.7% have been reported. [10] As in most studies, P. falciparum with low parasite density rates of less than 20,000/μL were also encountered. There was a clustering of cases during periods of rainy season when there is the peak of maximal transmission. During periods of such maximal transmission it has been documented that there are higher parasite rates as evidenced by the greatest mortality from falciparum malaria in children aged less than five years and in older children higher rates of asymptomatic malaria parasitaemia. [11] This might suggest that incidence of congenital malaria could be related to high parasite rates in the mothers at this season. Earlier work showed that the placenta should be an effective barrier to malaria parasites, however, many more recent reports among which is that of Egwunyenga et al[12] have shown evidence of transplacental passage of P. falciparum, confirmed by detection of falciparum specific IgM antibodies in the blood of newborns.

What factors might contribute to this breach of the placental barrier such that neonates as early as in the first few hours of life would be parasitized? Primigravidarous women are known to be predisposed to heavier placental parasitization in malaria endemic areas, and they have constituted 35% of the mothers of neonates found in this study. With a highly significant history of maternal genital infections, there might be an effect on placental integrity as an effective barrier against transplacental transmission of malaria. Already, in HIV infected mothers, recent findings show that co-infection with placental malaria and HIV during pregnancy significantly increases the risk of HIV transmission from mother to newborn.[13] HIV alone or together with other genital infections may also breach this placental barrier to increase risk for neonatal (?congenital) malaria. The youngest parasitized baby who was detected at 3 hours of age was delivered by surgery. The role of the mode of delivery on this early incidence was not significant.

The commonest symptoms in these neonates were fever, jaundice and convulsions. These are the similar to symptoms of neonatal sepsis and have been also documented by workers in Benin. [14] In this study however, fever was most significantly related to neonatal malaria.

This preliminary study has documented occurrence of neonatal malaria in an area of malaria mesoendmicity. There is need for further detailed research to investigate the placenta integrity in relation to the maternal genital infections especially HIV coinfection. This would be accomplished by a further study on congenital malaria.

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