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CLINICAL PRESENTATION OF CONGENITAL MALARIA AT THE LAGOS UNIVERSITY TEACHING HOSPITAL

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ABSTRACT

Background: Congenital malaria has been increasingly documented in endemic regions. It is important to recognize those clinical features that are due to congenital malaria, which if undetected, might worsen the morbidity of the newborn. The aim of this study was to document the clinical presentation of neonates with congenital malaria born at the Lagos University Teaching Hospital and followed up for 28 days.

Methods: A total of 100 consecutive mothers and their newborns were recruited between August and October 2002 (during the rainy season) from the labour ward and followed up from birth to 28 days of age. Blood films from the placentae and babies were stained with Giemsa stain within 24 hours of collection. All parasitaemic babies that became symptomatic were screened for sepsis using acute phase responses and cultures. All data were entered into a prepared proforma. Symptoms were attributed to malaria when sepsis screening was negative.

Results: Congenital malaria was documented in 13.6% of babies at delivery. Jaundice, irritability and poor feeding were most common symptoms associated with congenital malaria. Irritability and poor feeding had positive predictive values (PPV) of 100% on Day 14.

Conclusion: Babies who present with poor feeding and irritability on Day 14 of life should be screened for malaria in addition to the routine investigations for neonatal sepsis.

Key Words: Clinical Features, Congenital Malaria, Lagos. *(Accepted 12 March 2009)*

INTRODUCTION

Malaria continues to be a serious public health problem in the world, especially in tropical countries. Congenital malaria is one of the three recognized types of neonatal malaria, the others being acquired and transfusional.[1,2] Congenital malaria occurs when malaria parasites cross the placenta either during pregnancy or at the time of delivery, and is diagnosed when asexual forms of the parasite are seen on the blood smear of the baby within the first week of life.[2, 3] Congenitally acquired malaria was first described in 1876 with an incidence of 0.18-0.3%.[4] It is said to occur more commonly in babies born to non-immune mothers with malaria.[5] However, recently there have been increasing reports in both the indigenous population of malaria endemic regions and in the non-endemic areas.[6-9] The current incidence is now put at 8 - 15.3%.[7,10-14] However, an unusually high incidence of 46.7% was documented among newborns in Ile-Ife, a city in the rain forest region of South-West Nigeria.[15]

The clinical presentation of malaria in the neonate is non-specific and very similar to that of neonatal bacterial infections.[12] Neonatal sepsis is a very common problem in our environment. With the changing pattern of congenital malaria, it is important to determine the clinical features that may be more specific to identify babies with congenital malaria as against with neonatal sepsis. Failure to recognize the symptoms that are due to congenital malaria might worsen the prognosis for survival in the infected baby. This study was undertaken to document the clinical features of congenital malaria among babies born in an endemic region and followed up for 28 days. It is hoped that this will improve early diagnosis and assist the clinician in instituting appropriate intervention among babies with congenital malaria.

SUBJECTS AND METHODS

A total of 100 consecutive mothers and their newborns were recruited from the labour ward and followed up from birth to 28 days of age after obtaining an informed consent. Prior ethical clearance was obtained from the hospital's ethics committee. Refusal of consent from the mother and birth before arrival were exclusion criteria. The study was conducted over a three-month period between August and October 2002 (during the rainy season) was part of a larger study of congenital malaria among the newborn at the Lagos University Teaching Hospital. Some data from this study had been earlier published.[14]

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Patient Handling Protocol: One ml of blood was taken from the mother, cord and placentae. From each baby 0.5ml of venous blood was obtained from the dorsum of the hand within 1 hour of delivery and thick and thin blood smears were prepared immediately. All slides were labelled according to standard technique[16] and were air-dried. Slides were then placed horizontally in a slide holder in a covered container and protected from insects and dust. Blood films from mothers, placentae, cords and babies were stained with Giemsa stain by a WHO certified microscopist within 24 hours of collection. Each film was examined at a magnification of x100 under oil immersion and the presence of trophozoites or ring forms (asexual forms) on the film was taken as laboratory evidence of malaria. Asexual malaria parasites were counted concomitantly with white blood cells in each field, and parasite counts were recorded as the ratio of asexual forms per 200 white blood cells in each field. A minimum of 200 fields was examined before a slide was declared negative. Parasite counts were done using standard methods.[16] The babies were followed up on days 3, 7, 14 and 28 at which physical examination of each infant was conducted. All parasitaemic babies that became symptomatic were screened for sepsis using acute phase responses and cultures. All data were entered into a prepared proforma. Symptoms were attributed to malaria when sepsis screening was negative. The criteria for anti-malaria treatment were the presence of asexual malaria parasitaemia on blood film and the development of symptoms or persistence of asexual parasitaemia at the point of discharge from follow up. All babies with symptomatic congenital malaria were treated with oral chloroquine base (10mg/kg on day 1, 10mg/kg on day 2 and 5mg/kg on day 3). This was the standard treatment at the time of the study. Babies with persistent parasitaemia at the time of discharge from follow up who did not become symptomatic were similarly treated.

Data Analysis

The data was entered, validated and analyzed using Epi info version 6.04 software package.[17] Clinical features of babies with positive malaria parasites were compared with those with negative smears on days 3, 7, 14 and 28. Continuous variables were expressed as means and standard deviations if they were normally distributed and as median and range if skewed. Means were tested by Students **t** test or ANOVA while the appropriate non-parametric test was applied to skewed data. Results were presented in the form of Tables and Figures. Where the numbers were small, Fishers exact test was used. A p-value<0.05 was taken as statistically significant.

RESULTS

One hundred mothers and their placentae as well as 104 babies and their cord blood were studied. Ninety-six mothers gave birth to singleton babies while 4 mothers had a set of twins each. A total of 14 (13.6%) babies had positive asexual parasitaemia. Tables 1 shows the symptomatology of the babies at follow up and demonstrates that the commonest symptoms were jaundice, hepatomegaly, poor feeding and irritability. Most of the babies were asymptomatic. Table 2 shows the association between jaundice and malaria parasitaemia. Jaundice was significantly associated with malaria parasitaemia between Day 7 (p=0.04) and Day 14 only (p=0.002). Table 3 shows that the association between irritability and malaria parasitaemia is most significant on Day 14 (p=0.0004). Table 4 also demonstrates a significant association between poor feeding and malaria parasitaemia on Day 14 (p=0.0004). There was no significant association between hepatomegaly and malaria parasitaemia among the babies studied (Table 5). Similarly there was no association between fever and malaria parasitaemia (not shown).

Table 1: Symptomatology among Babies at Follow Up.

Symptom/ Sign	Day 3 n=103(%)	Day 7 n=90(%)	Day 14 n=81(%)	Day 28 n =81(%)
Jaundice	29 (27.9)	25 (27.8)	9 (11.0)	1 (1.2)
Hepatomegaly	8 (7.7)	8 (8.8)	7 (8.5)	2 (2.4)
Poor feeding	6 (5.8)	1 (1.1)	3 (3.7)	0
Irritability	5 (4.8)	1 (1.1)	3 (3.7)	1 (1.2)
Hypothermia	3 (2.9)	0	0	0
Pyrexia	1 (1.0)	2 (2.2)	3 (3.7)	0
Pallor	1 (1.0)	1 (1.1)	0	0
Convulsion	1 (1.0)	0	0	0
Cyanosis	1 (1.0)	0	0	0

Table 2: Jaundice Related to Parasitaemia in Babies.

Day	Jaundice	Positive MP	Negative MP	PPV	NPV	P Value
	+	4	25	13.8	91.9	0.26
	–	6	68			
7	+	5	20	20.0	95.4	0.04
	–	3	62			
14	+	4	5	44.4	95.8	0.002
	–	3	69			
28	+	0	1	0.0	98.8	0.98
	–	1	79			

PPV = Positive Predictive Value
NPV = Negative Predictive Value

Table 3: **Irritability Related to Parasitaemia in Babies.**

Day	Irritability	Positive MP	Negative MP	PPV	NPV	P value
3	+	0	5	0.0	89.8	0.58
	_	10	88			
7	+	0	1	0.0	91.0	0.14
	_	8	81			
14	+	3	0	100.0	94.9	0.0004
	_	4	74			
28	+	0	1	0.0	98.8	0.98
	_	1	79			

PPV = Positive Predictive Value
NPV = Negative Predictive Value

Table 4: **Poor Feeding Related to Parasitaemia in Babies.**

Day	Poor feeding	Positive MP	Negative MP	PPV	NPV	P value
3	+	2	3	40.0	91.8	0.17
	_	8	90			
7	+	0	1	0.0	91.0	0.14
	_	8	81			
14	+	3	0	100.0	94.9	0.0004
	_	4	74			
28	+	0	0	0.0	98.8	-
	_	1	80			

PPV = Positive Predictive Value
NPV = Negative Predictive Value

Table 5: **Hepatomegaly Related to Parasitaemia in Babies.**

Day	Hepatomegaly	Positive MP	Negative MP	PPV	NPV	P value
3	+	2	5	28.6	91.7	0.13
	_	8	88			
7	+	1	6	14.3	91.6	0.49
	_	7	76			
14	+	2	4	33.3	93.3	0.08
	_	5	70			
28	+	0	2	0.0	98.7	0.97
	_	1	78			

PPV = Positive Predictive Value
NPV = Negative Predictive Value

Table 6: **Trend in Mean Weights, Haemoglobin and Malaria Parasitaemia at Follow Up.**

	Day 0 n = 104	Day 3 n = 103	Day 7 n = 90	Day 14 n = 81	Day 28 n = 81	p Value
Mean Weight (SD)	3074 (511)	2962 (546)	2878 (546)	3227 (594)	3660 (645)	<0.001
Mean Haemoglobin (SD)	14.5 (1.5)	14.4 (1.2)	14.1 (1.7)	14.0 (3.2)	13.8 (7.6)	0.6
Mean Placental Parasite Count (SD)	5249 (16,569)					
Median Placental Parasite Count (Range)	846 (168-65113)					
	n = 14	*n = 10*	*n = 8*	*n = 7*	*n = 1*	
Mean Parasite Count (SD)	*377 (358)*	*390 (225)*	*327(245)*	*620(283)*	*212 (0)*	*0.2*
Median Parasite Count	*205*	*412*	*205*	*571*	*212*	

Figures in italics represent sub-set of babies with malaria parasitaemia

Table 6 and Figures 1 and 2 show the trend in mean weights and haemoglobin values in babies with and without congenital malaria. There was a similar weight pattern in both groups. The slight differences were not statistically significant (p=0.8). The mean haemoglobin values over 28 days were also similar. Sepsis screening done on all the symptomatic babies were negative.

Figure 1: **Trend in Weights in Babies With and Without Congenital Malaria.**

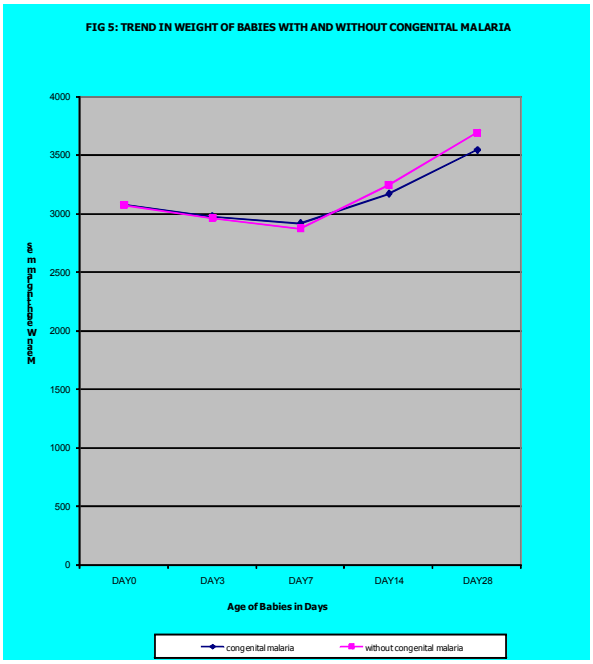
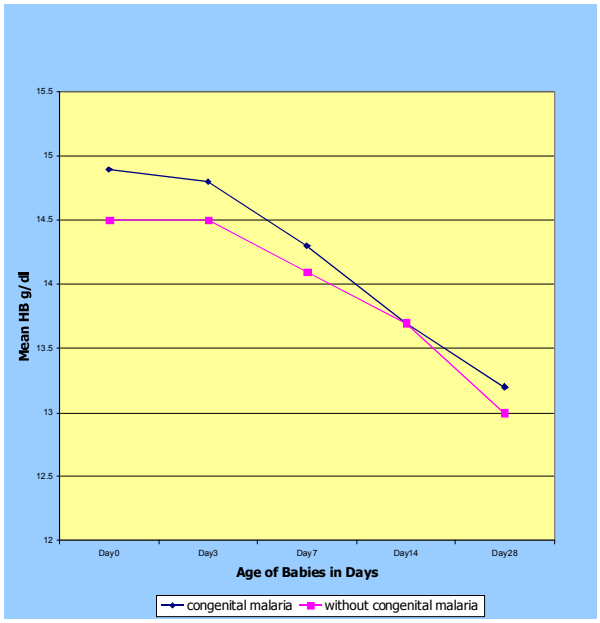


Figure 2: **Trend in Haemoglobin Values in Babies With and Without Congenital Malaria.**



DISCUSSION

The finding of 13.6% of babies born to mothers at the Lagos University Teaching Hospital has been discussed in an earlier publication of data from the larger study.[14] The findings most frequently documented in babies with congenital malaria at follow-up were jaundice, poor feeding, and irritability and these were statistically significant on Day 7 (jaundice) and Day 14 (irritability and poor feeding). Other common findings were hepatomegaly and fever but these were not associated with congenital malaria. These findings have been documented in neonates by Ibhanesebhor,[12] Thapa et al[18] and more recently by Ojukwu et al.[13] However, notable differences exist between our findings and other studies. While in two studies,[12,13] fever and respiratory distress featured high on the list of symptoms that characterised neonatal malaria, these finding were either not seen or seen in only a few babies in our study. It is possible that the study methodology might explain the observed differences. Ours was designed as a cohort study of well babies while the others have been prospective, cross-sectional studies of sick babies.

Whatever the study design, the question arises if these symptoms and signs can accurately detect those babies with congenital malaria. Our study shows that babies who are two weeks old and are irritable and feeding poorly might have congenital malaria. These findings had a 100% positive predictive value on Day 14. In other words, babies who did not have these symptoms on Day 14 did not have malaria parasites in their peripheral blood smear. It is noteworthy that these signs and symptoms can be seen in other conditions that affect the newborn such as neonatal sepsis. In the present study neonatal sepsis was not present in any of the symptomatic babies. We suggest that that clinicians and health workers caring for neonates in a malaria endemic region should consider the possibility of congenital malaria in addition to other diagnoses especially when poor feeding and irritability are observed at 14 days of life.

Anaemia was not found to be a feature of congenital malaria in the present study as there was no difference in the mean haemoglobin of those with and without congenital malaria. Ojukwu et al observed a similar finding[13] On the contrary, Ibhanesebhor[12] and Thapa et al[18] found anaemia to be one of the features of congenital malaria at birth. On follow up, we noted that babies with congenital malaria seemed to have a lower haemoglobin from Day 14 onwards although this was also not statistically significant (p=0.6). We did not come across any published studies in which serial haemoglobin values were done for babies with congenital malaria for comparison with our findings. One possible explanation for not finding a significant association between anaemia and congenital malaria could lie in the low parasite density observed in our study population. It is possible that the well documented protective effect of foetal haemoglobin might also explain our failure to find any significant adverse outcomes of congenital malaria such as anaemia among

these babies.[19] Regarding birth weight, we did not find any association between congenital malaria and low birth weight. Even at follow up, we did not observe any differences in the weight pattern among babies with congenital malaria compared with those without. Again, we believe that this expected association that has been documented by other workers,[6,10,20] might have been obscured by the small numbers of our babies who were delivered prematurely or had low birth weight and by the relatively low placental parasite density. In addition the mean placental parasite density was low in our patients. The suggestion that prematurity and low birth weight are more common with heavily parasitized placentae,[10, 21] might further explain our failure to find this association among our patients.

In conclusion, we have demonstrated that in our environment, the commonest clinical presentations of babies with congenital malaria are jaundice, poor feeding and irritability. As these can be seen in neonatal sepsis we recommend that symptomatic babies with poor feeding and irritability from Day 14 should be screened for malaria in addition to the routine investigations for neonatal sepsis. This study throws up some implications for research and practice. These include the confirmation of whether infants born to women in an endemic area, symptomatic or not, should be screened for malaria. We therefore recommend the confirmation of our findings in a larger, multi-centre study.

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