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Original Research Article

Asymptomatic congenital malaria among neonates of mothers attending antenatal clinic in University of Medical Sciences Teaching Hospital, Akure

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ABSTRACT

Background: Congenital malaria can be a serious cause of morbidity and mortality in the neonates if not detected. Clinical features of congenital malaria are non-specific and could be confused with other forms of infections in the newborn. The study sets out to document presence of asymptomatic congenital malaria among neonates of mothers attending antenatal clinic in University of Medical Sciences Teaching Hospital, Akure.
Methods: Mother-baby pairs were recruited into the study from the maternity section of the hospital, blood samples were taken from maternal peripheral blood, placental maternal side, cord blood and peripheral blood of the newborn babies and analyzed for presence of malaria parasite by microscopy methods. Data analyses were done using Statistical Package for the Social Sciences (SPSS) version 24.0
Results: Eighty-six (79.6%) of the babies were positive for malaria parasites, 59 (54.6%) of them were male children and 49(45.4%) were female. Fifty mothers (58.1%) had peripheral or placental parasitaemia. Babies of mothers who used long lasting insecticide treated nets (LLIN) and intermittent preventive therapy IPT-SP were significantly less infected while babies of first- and second-time mothers were significantly more infected. Majority of the babies 77/86 (89.5%) however had low intensity parasitaemia.
Conclusions: Congenital malaria is no more a rare disease especially in endemic regions, prevention of mother-to-child transmission should be aggressively pursued.

Keywords: Asymptomatic, Akure, Congenital malaria, UNIMEDTH

INTRODUCTION

Congenital malaria is the infection of a newborn baby with malaria parasites directly from the mother before or during delivery.[1] Congenital malaria was previously thought to be rare but recent reports suggest otherwise with increasing number of cases.

Many of the malaria cases present like other neonatal conditions since routine malaria parasite checks are often not done and when done, the diagnosis of congenital malaria is made difficult by the low density parasitaemia in the cord blood and the peripheral blood samples of the newborn babies.[2] Globally, an estimated 125 million pregnant women reside in countries of the world where they are at risk of being infected with malaria annually; leading to Malaria-In-Pregnancy.[3]

Malaria-in-pregnancy is an important preventable cause of adverse neonatal outcomes such as abortion, still birth, low birth weight babies, preterm birth, intrauterine growth restriction and congenital malaria.[4] While congenital malaria has a prevalence variation in sub-Saharan Africa that range from 0 to 54% due to variation in definition of

congenital malaria, maternal immunity and the various types of the diagnostic methods used, the prevalence ranges from 2% to 7% in Nigeria at different times and some other Nigerian studies have also reported higher prevalence rates ranging from 5.1% to 46.7%.[2,5] The aim of this study therefore was to investigate the prevalence of congenital malaria in UNIMEDTH Akure using both cord blood and neonatal peripheral blood film for malaria parasite in babies delivered to mothers with placental malaria parasitaemia.

METHODS

Study design

The study was a prospective and cross-sectional survey from April to November, 2024 to investigate prevalence of congenital malaria among infants of mothers who attended the antenatal clinics and delivered in the University of Medical Sciences Teaching Hospital, Akure.

Study place

The study was conducted in the Maternity section and the neonatal unit of the University of Medical Sciences Teaching Hospital, (UNIMEDTH) Akure. UNIMEDTH is a tertiary centre in Ondo State which provides highly specialist care in areas of medicine, surgery, pediatrics, obstetrics and gynaecological services.

The obstetric unit has 60 bed capacity which receives referred cases from private and other lower public hospitals in Akure and neighboring towns while the neonatal unit is a level III NICU which has a capacity for 20 admissions and receives babies from the labour ward and the operating theatre of the hospital.

Study population

The study population included consenting consecutive pregnant women in the third trimester, who attended ANC in the hospital, had their delivery in the centre and their corresponding newborn babies.

Ethical approval and informed consent

Ethical approval was sought from the Research and Ethics committee of the Ondo State Ministry of Health, UNIMEDTH and informed consent was obtained from the pregnant mothers after the advantages of the research had been explained to them.

Blood sample collection

Blood samples were collected from maternal peripheral blood, placental maternal side, cord blood and peripheral blood of the newborn babies. These were kept in the EDTA bottles to prevent clotting and immediately sent to the laboratory for thick and thin blood smears for microscopy method to screen for malaria parasite.

Parasite intensity

Thick and thin blood films were smeared on the same slide side by side, read by a trained laboratory scientist to see where 4 to 8 white blood cells (WBC) could be viewed.[6] The number of malaria parasites counted in each high-power field was multiplied by a constant (8,000) then divided by 200. Parasitaemia intensity was expressed as the number of asexual forms of *P. falciparum* per microlitre of blood.

Parasite count × 8,000) / 200 = Parasites per microliter of blood

Inclusion criteria

All consecutive mother-baby pair in the maternity and newborn sections of the hospital.

Exclusion criteria

Non consenting mothers were excluded.

Data analysis

The data obtained in the study was subjected to statistical analysis using Microsoft Excel and the Statistical Package for the Social Sciences (SPSS) version 24.0 statistical software for Windows (IBM, Armonk, N.Y., United States).

Prevalence was calculated using the formula.

Prevalence = (Numbers of Positive Samples)/(Total Number Examined) ×100. Data were also subjected to Carls Pearson's Chi-Square to test the significant difference at $p<0.05$.

RESULTS

A total of 108 mother-baby pairs were recruited. The results showed that 77 (71.3%) of the neonates were within one hour of life, 21 (19.4%) were 2 hours old, 7 (6.5%) were 3 hours old, 1 (0.9%) was 8 hours old while 2 neonates (1.9%) were 12 hours old (Table 1). Table 1 further showed that 59 (54.6%) of the neonates were male children and 49 (45.4%) were female. Forty-two neonates (38.9%) were in the first birth order, 34 (31.5%) were in the second birth order, 17 (15.7%) were in the third birth order, 10 (9.3%) were of the fourth birth order and 5 (4.6%) were in the≥5th birth order. Birth order indicates the position of the baby in the family; birth order 1=first child, birth order 2=second child etc. None of the babies had APGAR score less than 3, three babies (2.8%) had APGAR score of 4-5, three (2.8%) had APGAR score of 6 and 102 babies (94.4%) had APGAR score 7 or higher.

Table 1 further showed that 86 (79.6%) of the babies were positive for malaria parasites; the prevalence of malaria therefore was 79.6% while 22 (20.4%) were negative for malaria parasite. Ninety-nine (91.7%) were Christians,

while parents of 6 (5.6%) practice Islam and 3 (2.8%) practice other religions. Ninety (83.3%) of the babies were of the Yoruba extraction, 2 (1.9%) were Hausa, 9 (8.3%) were of the Igbo extraction and 7 (6.5%) were from other tribes. None of the babies died. Table 2 showed the mean gestational age, weight, length and occipitofrontal Circumference (±SD) of the neonates.

Table 3 showed the factors associated with congenital malaria. Of the 86 babies who were positive for malaria, 64 (74.4%) were born by mothers who were para 1-2 (parity indicates number of babies carried to term by the mothers), 21 (24.4%) were born by mothers who were Para 3-4 while only one (1.2%) was born by a mother who was Para 5. The babies of the first- and second-time mothers (Para 1-2) were significantly more infected than others ($\chi2$=7.8, p=0.02). All the mothers had antenatal care. Thirty-three (38.4%) of the babies whose mothers used long lasting insecticide treated nets (LLIN) were positive for malaria parasite while 53 (61.1%) of the babies whose mothers did not use long lasting insecticide treated nets were positive; the babies whose mothers did not use LLIN were therefore significantly more infected ($\chi2$=4.22, p=0.04). Forty-nine (57.0%) of the babies whose mothers used indoor residual spray (IRS) were positive for malaria parasite while 37 (43.0%) of the babies whose mothers did not use IRS were positive, the babies whose mothers use IRS were slightly more infected but the difference was not significant ($\chi2$= 3.53, p=0.06). Nine (10.5%) of the babies whose mothers used intermittent preventive therapy with (IPT) with sulphadoxine/pyrimethamine (SP) were infected with malaria parasites while 77 (89.5%) of the babies whose mothers did not use IPT/SP were infected; the babies whose mothers did not use IPT/SP were significantly more infected ($\chi2$= 4.71, p=0.03).

Furthermore, Table 3 showed that of the 86 babies who were infected with malaria parasite, 50 (58.1%) of their mothers had peripheral blood parasitaemia or placental parasitaemia while 36 (41.9%) mothers did not have peripheral or placental parasitaemia. The babies whose mothers had peripheral or placental parasitaemia were significantly more infected with P. falciparum ($\chi2$=10.6, p=0.001). Majority of the babies 77/86 (89.5%) however had low intensity parasitaemia while 9 (10.5%) had medium intensity parasitaemia and none of the babies had high intensity parasitaemia. ($\chi2$=18.42, p=0.0001).

Table 1: Socio-demographic characteristics of the neonates.

Variables		Total	%
Age (in hours)	1	77	71.3
	2	21	19.4
	3	7	6.5
	8	1	0.9
	12	2	1.9
Gender	Male	59	54.6
	Female	49	45.4
Birth order	1	42	38.9
	2	34	31.5
	3	17	15.7
	4	10	9.3
	≥5	5	4.6
APGAR score	≤ 3	0	0
	4-5	3	2.8
	6	3	2.8
	≥ 7	102	94.4
Malaria parasite	Positive	86	79.6
	Negative	22	20.4
Religion	Christian	99	91.7
	Muslim	6	5.6
	Others	3	2.8
Tribe	Yoruba	90	83.3
	Hausa	2	1.9
	Igbo	9	8.3
	Others	7	6.5
Outcomes	Alive	108	100
	Dead	0 (0)	0 (0)

Birth order: indicates the position of the baby in the family, Birth order 1=first child, birth order 2=second child etc, Others: other tribes (Benue, Ebira, Efik, Urhobo), Others: other religions (traditional religions).

Table 2: Mean age, gestational age, weight, length and OFC of neonates (±SD).

Mean temperature (±SD)	**36.7°C±0.42**
Mean birth weight (Kg) (±SD)	2.48±0.58
Mean length (cm) (±SD)	45.0±2.03
Mean OFC (cm) (±SD)	34.6±1.97
Mean Gestational age (weeks) (±SD)	36.0±2.0

OFC: occipitofrontal circumference.

Table 3: Factors associated with congenital malaria.

Characteristics	MP positive n=86 (%)	MP Negative n=22 (%)	Total (%) n=108 (%)	$\chi 2$	P value
Mothers' parity					
P1-2	64.0 (74.4)	17.0 (77.3)	81.0 (75.0)	7.82	0.02
P3-4	21.0 (24.4)	1.0 (4.5)	22.0 (20.4)		
p≥ 5	1.0 (1.2)	4.0 (18.2)	5.0 (4.6)		
Maternal antenatal					
Yes	86.0(79.6)	22.0 (20.4)	108 (100)	6.64	0.001
No	0.0	0.0			
Maternal use of LLIN					
Yes	33.0 (38.4)	19 (86.4)	52.0 (48.2)	4.22	0.04
No	53.0 (61.6)	3.0 (13.6)	56.0 (51.8)		
Maternal use of IRS					
Yes	49.0 (57.0)	12.0 (54.5)	61.0 (56.5)	3.53	0.06
No	37.0 (43.0)	10.0 (45.4)	47.0 (43.5)		
Maternal use of IPT in pregnancy					
Yes	9.0 (10.5)	20.0 (90.9)	29.0 (26.9)	4.71	0.03
No	77.0 (89.5)	2.0 (9.1)	79.0 (73.1)		
Maternal malaria parasitaemia					
Yes	50.0 (58.1)	12.0 (54.5)	86 (79.6)	10.60	0.001
No	36.0 (41.9)	10.0 (45.5)	22 (20.4)		
Placental parasitaemia					
Yes	50.0 (58.1)	12.0 (54.5)	86.0 (79.6)	10.6	0.001
No	36.0 (41.9)	10.0 (45.5)	22.0 (20.4)		
Cord blood parasitaemia					
Yes	86 (79.6)	0.0 (0.0)	86.0 (79.6)	6.64	0.01
No	0.0 (0.0)	22.0 (20.4)	22.0 (20.4)		
Mean parasite intensity (±SD)					
Low intensity parasitaemia (<1,000 parasites/ ul)	77.0 (89.5)	-	86.0 (79.6)	18.42	0.0001
Medium intensity parasitaemia (1,000 -9,999 parasites/ul)	9.0 (10.5)	-			
High intensity parasitaemia (≥10,000 parasites/ul)	0.0 (0.0)	-			

NB:, LLIN: long lasting insecticide treated nets, IPT: Intermittent preventive therapy, IRS: Indoor residual spray of insecticide, MP: malaria positive, SD: standard deviation, ul: microlitre.

DISCUSSION

All the study participant were neonates within 24 hours of life. The mean gestational age of the babies was 36.0±2.0 weeks, mean birth weight was 2.48±0.58 kg, mean length was 45.0±2.03 cm and mean occipitofrontal Circumference (±SD) of the neonates was 34.6±1.97 cm while all the babies had normal temperature with the mean temperature being 36.7°C±0.42. Fifty-nine (54.6%) of the neonates in the present study were male children and 49 (45.4%) were female, therefore the M:F ratio was 1.2:1. Most earlier studies also reported male preponderance but the study from Jos reported an equal number in male and female affectation.[7]

Prevalence of congenital malaria

The current study revealed that the prevalence of congenital malaria was 79.6%. This is higher than the 5.1% reported in an earlier large (1,875 samples) multi-centre study from Oyo, Kwara and Kaduna States in Nigeria where the prevalence would have varied among

the centres.[8] Our study was a smaller (108 samples) mother-baby pair compared to theirs. The prevalence in the present study was also higher than prevalence of 17.4% from Sagamu, 46.7% in Ile-Ife, 28.6% in Abuja, 5.3% in Jos, 13.6% in Lagos, 60.2% earlier reported from Akure and 58.5% in another centre in Jos, 7 but lower than the prevalence of 96.3% in Sokoto.[7,9-15]

Elsewhere, in more advanced countries, prevalence was 14.5% in Papau New Guinea, 1.9% in an Asian Indian population and only 108 cases seen from year 1915 to 2011 across eastern, central, southern regions of China, as well as in the low-lying region of southwest China.[16-18] Though majority of the studies adopted similar methodology in diagnosing the infection, the local endemicity of the disease, geographical location, rate of use of preventive measures, method of control of the disease, effective public health measures, robust infrastructure and unconducive climatic condition for malaria transmission could have accounted for the varied prevalence seen across the regions. Moreover, congenital malaria is largely asymptomatic, parasites can clear spontaneously and may not warrant treatment, which was the situation in the large multi-centre study where there was spontaneous clearance of parasitaemia in 62.1% of neonates before day 2 of life.[8]

Factors associated with congenital malaria

In the current study, all mothers had antenatal care and had one form of malaria preventive measure or the other. The babies of the first- and second-time mothers (Para 1-2) were significantly more infected than others. This is consistent with previous reports, these mothers are particularly more susceptible to placental malaria parasitaemia, because they lack immunity to the placental-binding parasite form, which is acquired over successive pregnancies through repeated exposure.[19,20] Women who have not been pregnant before, lack immunity to the placenta-specific form of the parasite, which binds to chondroitin sulfate A (CSA) on the placenta.[20] Studies have shown that infected red blood cells that bind to CSA are rare in non-pregnant adults and so the placenta may select for this specific parasite phenotype, thereby increasing the risk for the first-time mothers.[21] In the present study, the babies whose mothers had peripheral or placental parasitaemia were significantly more infected with *P. falciparum*. Placental inflammation and malaria parasitaemia coupled with low immunity in the mothers are reported risk factors for cord blood malaria parasitaemia and they are strongly associated with congenital malaria, majority of the babies 77/86 (89.5%) in the current study however, had low intensity parasitaemia and none of the babies had high intensity parasitaemia.[22]

In the current study, 9 (10.5%) of the babies whose mothers used intermittent preventive therapy with sulphadoxine/pyrimethamine (IPT-SP) were infected with malaria parasites while 77 (89.5%) of the babies whose mothers did not use IPT-SP were infected; the babies whose mothers did not use IPT-SP were therefore significantly more infected with malaria parasites. Previous studies in literature have demonstrated IPT-SP to be a strong protective factor against placental and congenital malaria.[23,24] Using the long-lasting insecticide-treated nets (LLIN) is also an important strategy in the prevention of malaria and by extension, congenital malaria.[23,24] In the present study, babies whose mothers did not use LLIN were significantly more infected with malaria parasites, however, there was no significant difference between babies whose mothers used indoor residual spray (IRS) and those whose mothers did not.

CONCLUSION

Congenital malaria is no more a rare disease especially in endemic regions. The need to aggressively prevent the infection in the pregnant mothers and promptly treat index cases will be beneficial to neonates who are at risk of the disease.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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