

Research Article

Prevalence of Malaria among Neonates Presenting with Fever in Port Harcourt, Nigeria

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Abstract

Malaria remains one of the most significant disease burdens in Africa especially in children and pregnant women. Malaria in the newborn once considered rare has now been reported as a common phenomenon. Diagnosis of malaria in the neonatal period is usually delayed as the clinical features of malaria are non-specific, variable and similar to those of sepsis. The aim of the study was to determine the prevalence of malaria in neonates who present with fever. This was a 12 month prospective study carried out amongst neonates presenting with fever in the neonatal unit of the Braithwaite Memorial Specialist Hospital in Port Harcourt, Nigeria. Blood film for malaria parasite and complete blood counts were done for each recruited patient before the commencement of medications.

One Hundred and Three (13.2%) of 782 neonates admitted into the neonatal unit were studied. Forty five (43.7%) had positive malaria parasite giving a prevalence of malaria in febrile neonates as 43.7%. Twenty one (46.7%) were males and 24 (53.3%) were females with a M:F ratio of 1.1:1. Thirty six (80.0%) of the neonates with positive malaria parasite were aged 0-7 days while nine (20%) were between 8-28 days. Common clinical features of malaria in neonates presenting with fever were poor suck (24.4%) and jaundice (15.6%). Thirty eight (84.4%) neonates were discharged home while one (2.2%) died.

Malaria is not uncommon in the neonatal period. Poor suck and jaundice are the commonest clinical features of malaria in the neonatal period apart from fever.

Keywords: Clinical features; Malaria; Neonates; Port harcourt; Prevalence

Introduction

Malaria is a disease of global importance and the third leading cause of death in children under 5 years, after pneumonia and diarrheal diseases [1]. It is a major health problem and one of the leading

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causes of preventable deaths in Nigeria. Globally, 300 - 600 million cases are seen annually and an estimated 2.2 billion people are at risk of this infection [2]. A million annual deaths have been estimated to occur as a result of malaria of which about 80% are seen in infants and young African children [3].

In Africa, malaria has led to a huge epidemiologic burden thus further crippling the economic development in the region [4]. In Nigeria, it is responsible for 60% of outpatient visits to health facilities, 30% of childhood deaths, 25% of deaths in children under one year and 11% of maternal deaths [4]. The financial loss in Nigeria due to malaria annually is estimated to be about 132 billion naira (440million US dollars) in form of treatment cost, prevention and loss of man-hours [4].

Malaria in the neonatal period was considered rare in the past especially in endemic areas [5]. This was attributed to various protective mechanisms such as; the milk diet of the infant being deficient of P-amino-benzoic acid [6], hematologic factors such as an aging red cell population, the presence of erythrocyte foetal haemoglobin [7] and selective biting of mosquitoes among different age groups [8]. Transplacentally acquired antibodies have also been observed to play a role [8,9]. Recent studies however have shown that malaria can occur in the newborn period as these protections may not be complete [10-12].

Making a diagnosis of malaria in the neonatal period could be delayed as the clinical features of malaria are non-specific, variable and similar to those of neonatal sepsis [13]. Fever however is almost uniformly present in neonates with malaria, although the classic paroxysmal pattern described for malaria beyond the neonatal period is usually absent [5]. Sick neonates are thus almost always screened and managed empirically for sepsis alone. Blood film for malaria parasite is rarely done even in the face of poor response to treatment or deteriorating clinical condition [13].

This study was therefore carried out to determine the prevalence of malaria among neonates presenting with fever, associated clinical features and outcome of febrile neonates with positive malaria parasitemia.

Materials and Methods

It was a prospective study carried out over a 12 month period from 1st June 2013 to 30th May 2014 in the neonatal unit of the Braithwaite Memorial Specialist Hospital (BMSH), Port Harcourt in Nigeria. Informed consent was obtained from parents or authorized care givers in the absence of the parents. All neonates aged 0 - 28 days admitted into the neonatal unit with documented fever on admission or during the period of admission were recruited into the study. Axillary temperature $\geq 37.5^{\circ}\text{C}$ was documented as fever. Neonates transfused prior to the onset of fever were excluded from the study.

Detailed clinical history including age, sex, birth weight, gestational age, place of birth, mode of delivery, place of residence, age at onset of fever, other symptoms as well as maternal use of intermittent prophylactic anti malarial and the use of insecticide treated nets during the period of pregnancy were obtained.

Babies delivered in BMSH or any of the Rivers State Primary health centres were nursed in the inborn section of the SCBU whereas all babies delivered in other health facilities were nursed in the out born section.

Gestational age was calculated using the first day of the last menstrual period or ultrasound scan result done early in the pregnancy. A neonate was said to have an unknown gestational age if the gestational age could not be calculated by either method.

Half a milliliter of venous blood was obtained from each neonate recruited and sent to the microbiology laboratory for the preparation of thick and thin blood smears. Prepared slides were air dried thereafter stained with Giemsa [14] within 24 hours of collection of blood sample. Each film was examined microscopically at a magnification of X100 under oil immersion. The presence of asexual forms of malaria parasite (trophozoites or ring forms) was said to be positive for malaria parasite. Asexual malaria parasites were counted concomitantly with the leucocytes in each field and the parasite count recorded as the ratio of asexual forms per 200 leucocytes in each field. A slide is said to be negative if after examining a minimum of 200 leucocytes no malaria parasite was found [15]. For the purpose of this study, a neonate with fever was said to have congenital malaria if there was presence of malaria parasites in the peripheral blood film in the first seven days of life while acquired neonatal malaria was defined as the presence of malaria parasites in the peripheral blood film within 8-28 days of life [5]. Full blood count was also done for each recruited neonate to exclude probable sepsis.

All the patients studied were empirically commenced on treatment for neonatal sepsis with intravenous Cephalosporin (ceftazidime) and gentamicin. Patients with positive malaria parasite were in addition commenced on antimalarial (syrup Quinine).

Results were collated with the aid of questionnaires designed for the study. Data was analyzed with the aid of SPSS version 20.0 statistical software and Epi info version 7.0. The level of significance was set at 95% confidence level.

Results

A total of 782 neonates, 450 (57.5%) males and 332 (42.5%) females were admitted into the neonatal unit during the period of study. Of these, 103 (13.2%) who had fever were recruited into the study.

Table 1 shows the general characteristics of the neonates studied. Fifty five (53.4%) were males while 48 (46.6%) were females with a M:F ratio of 1.1:1. Eighty two (79.6%) neonates were aged 0 to 7 days while 21 (20.4%) were 8-28 days of age. Fifty nine (57.3%) were delivered via spontaneous vaginal delivery, 43 (41.7%) by caesarean section and one (1.0%) by instrumental delivery. Sixty six (64.1%) were term neonates (37-41 weeks), 20 (19.4%) were preterm, 3 (2.9%) were post term while 14 (13.6%) had unknown gestation. Fifty nine (57.3%) were inborn while 44 (42.7%) were out born neonates. The mean birth weight of neonates studied was 3.06 ± 0.85 kg while the mean gestational age was 38.16weeks (28-42weeks). Ninety five (92.2%) mothers of infants recruited had antenatal care while 8 (7.8%) did not receive antenatal care. Ninety four (91.3%) mothers of recruited infants used Intermittent Preventive Therapy (ITP) and 36 (35.0%) used Insecticide Treated Nets (ITN). Eighty two (79.6%) mothers lived in urban areas.

| Characteristics | No. of Neonates (n = 103) | |
|--------------------------------------|---------------------------|---------|
| | Number | Percent |
| Sex: | | |
| Male | 55 | 53.4 |
| Female | 48 | 46.6 |
| Age of Onset of Fever (Days): | | |
| 0-7 | 82 | 79.6 |
| 8-28 | 21 | 20.4 |
| Mode of Delivery: | | |
| Spontaneous vertex delivery | 59 | 57.3 |
| Caesarean section | 43 | 41.7 |
| Instrumental delivery | 1 | 1.0 |
| Place of Birth: | | |
| Inborn | 59 | 57.3 |
| Out born | 44 | 42.7 |
| Birth Weight (kg): | | |
| < 2.5 | 21 | 20.4 |
| ≥ 2.5 | 79 | 76.7 |
| Unknown | 3 | 2.9 |
| Gestational Age (Weeks): | | |
| Preterm < 37 | 20 | 19.4 |
| Term 37-41 | 66 | 64.1 |
| Post term ≥ 42 | 3 | 2.9 |
| Unknown | 14 | 13.6 |
| Use of ITP: | | |
| Yes | 94 | 91.3 |
| No | 9 | 8.7 |
| Use of ITN: | | |
| Yes | 36 | 35.0 |
| No | 67 | 65.0 |
| Place of Residence: | | |
| Urban | 82 | 79.6 |
| Rural | 21 | 20.4 |

Table 1: Characteristics of the Study Population.

ITP = Intermittent Preventive Therapy, ITN = Insecticide Treated Net

Characteristics of Neonates with Positive Malaria Parasite

The characteristics of neonates with positive malaria parasites on blood film are summarized in table 2. Of 103 neonates recruited, 45 (43.7%) had positive blood smears for malaria parasite. Twenty one (46.7%) were males and 24 (53.3%) were females with a M:F ratio of 1:1.1. The prevalence of malaria in febrile neonates was therefore 43.7%. Thirty six (80.0%) of the neonates with positive malaria parasite were aged 0-7 days while 9 (20.0%) were aged 8-28 days. Thus 80.0% had congenital malaria with a prevalence of 4.6% while 20.0% had acquired neonatal malaria with a prevalence of 1.2%. *Plasmodium falciparum* was the only specie of malaria parasite identified in the present study. Twenty five (55.6%) neonates were delivered by spontaneous vaginal delivery, 19 (42.2%) by caesarean section and 1 (2.2%) instrumentally. About half of the neonates with positive malaria parasite were inborn (51.1%). Majority of these neonates were of term gestation (62.2%) while the least were post term (4.4%). Thirty three (73.3%) had normal birth weights. Three quarters of mothers whose infants had positive malaria parasite live in urban areas. The mean birth weight of babies with positive malaria parasite was 3.017 ± 0.75 kg (2.930 ± 0.82 kg for congenital malaria and 3.017 ± 0.75 kg for acquired neonatal malaria) while the mean gestational age was 38.30 ± 2.68 weeks.

Clinical Features of Malaria in Neonates with Positive Malaria Parasite

Table 3 shows clinical features of neonates with malaria parasitemia. Poor suck (24.4%) and jaundice (15.6%) were the commonest clinical features of febrile neonates with positive malaria parasite.

| Characteristics | No. of Neonates Number | n = 45 Percent | χ ² | p value |
|--------------------------------------|------------------------|----------------|----------------|---------|
| Sex: | | | | |
| Male | 21 | 46.7 | 1.45 | 0.23 |
| Female | 24 | 53.3 | | |
| Age at Onset of Fever (days): | | | | |
| 0-7 | 39 | 80 | 2.79 | 0.09 |
| 8-28 | 9 | 20 | | |
| Mode of Delivery: | | | | |
| Spontaneous vertex delivery | 25 | 55.6 | 1.28* | 0.74 |
| Caesarean section | 19 | 42.2 | | |
| Instrumental delivery | 1 | 2.2 | | |
| Place of Delivery: | | | | |
| Inborn | 23 | 51.1 | 1.24 | 0.27 |
| Outborn | 22 | 48.9 | | |
| Gestational Age (Weeks): | | | | |
| Preterm < 37 | 7 | 15.6 | 1.15 | 0.56 |
| Term 37-41 | 28 | 62.2 | | |
| Post term ≥ 42 | 2 | 4.4 | | |
| Unknown | 8 | 17.8 | | |
| Birth Weight (Kg): | | | | |
| < 2.5 | 10 | 22.2 | 4.34* | 0.34 |
| ≥ 2.5 | 33 | 73.3 | | |
| Unknown | 2 | 4.4 | | |
| Place of Residence: | | | | |
| Urban | 34 | 75.6 | 0.81 | 0.37 |
| Rural | 11 | 24.4 | | |

Table 2: Characteristics of Neonates with Positive Malaria Parasite.

*Fischer's exact test

| Clinical Features | Positive Malaria Parasite (n = 45) No (%) | Negative Malaria Parasite (n = 58) No (%) | χ ² | p value |
|-------------------|---|---|----------------|---------|
| Poor Suck | 11 (24.4) | 22 (37.9) | 2.12 | 0.15 |
| Jaundice | 7 (15.6) | 14 (24.1) | 1.15 | 0.28 |
| Irritability | 3 (6.7) | 8 (13.8) | 1.35 | 0.25 |
| Vomiting | 3 (6.7) | 9 (15.5) | 1.93 | 0.17 |
| Lethargy | 2 (4.4) | 6 (10.3) | 1.23 | 0.27 |

Table 3: Clinical Features of Neonates with Positive Malaria Parasite.

Use of Intermittent Preventive Therapy (ITP)

Of 94 neonates whose mothers had ITP, 38 (40.4%) had positive malaria parasite. However, of the 9 neonates whose mothers did not take ITP, 7 (77.8%) had positive malaria parasite ($\chi^2 = 4.65, p = 0.031$).

Use of Insecticide Treated Nets (ITN)

Of 36 mothers who used ITN, 20 (55.6%) had positive malaria parasite while 16 (44.4%) had negative malaria parasite ($\chi^2 = 3.17, p = 0.075$).

Pattern of White Blood Cell Count

Of 45 neonates with positive malaria parasite, 5 (11.1%) had leukocytosis with white blood cell count $\geq 20 \times 10^9/L$ while 40 (88.9%) had white blood cell counts within normal limits.

Outcome of Neonates with Positive Malaria Parasite

Of 45 neonates with positive malaria parasite, 38 (84.4%) were discharged home while one (2.2%) died. This is shown in table 4.

Discussion

The prevalence of malaria in febrile neonates of 43.7% in the present study is comparable with the 46.7%, 38.5% and 35.7% in Ile-Ife

| Outcome | Positive Malaria Parasite (n = 45) No (%) | Negative Malaria Parasite (n = 58) No (%) | χ ² | p value |
|------------|---|---|----------------|---------|
| Died | 1 (25.0) | 3 (75.0) | 0.59 | 0.44 |
| Discharged | 38 (43.2) | 50 (56.8) | 0.06 | 0.80 |
| DAMA | 6 (54.5) | 5 (45.5) | 0.59 | 0.44 |

Table 4: Outcome of Neonates with Positive Malaria Parasite.

DAMA - Discharged Against Medical Advice

[16] and Port Harcourt [11,17] Nigeria respectively. It is however lower than the 13.6%, 13%, 8.25% and 4.0% observed in Lagos [18] Nigeria, Gambia [19], Kaduna [20] and Calabar [15] in Nigeria respectively. All studies in Port Harcourt have revealed high prevalences as compared to most other cities in Nigeria. This could be attributed to the high rainfall in this region and the possibility of more breeding areas for mosquitoes. The expertise of the laboratory staff could also account for the differences in the prevalence rates observed in the different centres.

Congenital malaria was observed to be commoner than acquired neonatal malaria in the present study. This was also observed in other centres in Nigeria [15, 2-21]. The increase in the frequency of congenital malaria could be due to the growing trend of resistance of *P. falciparum* to anti malarial drugs resulting in increased parasitaemia, increased virulence of the parasite and reduced transmission of antibody from mother to child [2,4,5]. In contrast, acquired neonatal malaria was observed more in the Gambia [19]. The reason for this could not be ascertained.

Plasmodium Sp falciparum was the only specie documented in the present study as observed by other researchers in Nigeria [18,20,21] and the Gambia [19]. This is however contrary to the study in Pakistan [22] which documented *P. vivax* as the commonest specie in neonates with acquired neonatal malaria. This difference could be attributed to the difference in the geographic distribution.

The female preponderance in the present study was also observed in Abuja, Nigeria [23]. This was however contrary to some other studies which documented male preponderance [19,21].

Malaria was observed more in neonates delivered by spontaneous vaginal delivery as also documented in the Gambia [19]. This is not surprising as infection could also occur at the time of vaginal delivery [12].

A greater proportion of mothers of neonates with positive malaria parasite in the present study live in urban areas as also observed in other parts of Nigeria [18,23] and Pakistan [22]. This could be due to the poor hygienic conditions usually observed in the urban areas as compared to the rural areas [21].

All neonates recruited in the present study had fever. It is however interesting to know that previous studies have documented fever as the commonest clinical feature in neonates with positive malaria parasite [19-21,23]. The other clinical features observed in febrile neonates with positive malaria parasite in the present study were poor suck and jaundice. Poor suck was also observed to be the second commonest clinical feature in neonates with positive malaria parasite in the Gambia [19] and Sokoto [21], in Nigeria while jaundice ranked second in some other parts of Nigeria [15,18,23]. In contrast, irritability, fast breathing and hepatomegaly were common in other studies [15,19,21,23] which were not documented in the present study. This

variation in the clinical features is not surprising as these features are non-specific and variable [5].

It is also worthy of note that in the present study, 11.1% of neonates with positive malaria parasite had possible probable neonatal sepsis with white blood cell counts $>20 \times 10^9/L$. Similar studies of co-infection of neonates with malaria and septicaemia was observed in Nigeria [15,23] and Pakistan [22]. It is pertinent to note that majority of neonates with positive malaria parasite in the present study had normal white blood cell count. This could imply the possibility of malaria in febrile neonates with normal white blood cell count.

There was a significantly Lower prevalence of malaria in neonates whose mothers took intermittent preventive therapy as compared with those who did not take ITP. This was however contrary to the study in Abuja [23], Nigeria where about a third of neonates whose mothers took ITP had positive malaria parasite.

The present study showed that the use of Insecticide Treated Nets (ITN) was very low (35.0%). This could be due to reduced awareness of its importance, how to hang them, how it is being used and maintained properly. It could also be due to the common reason that sleeping under the net was too hot and uncomfortable [24]. The observation in the present study that more than half of the neonates whose mothers used insecticide treated nets had positive malaria parasite was also the case in Myanmar [25]. This could be due to poor adherence to the instructions as to the correct use of ITN [25]. It could also be attributed to the fact that the anopheles mosquitoes also bite in the early hours of the morning as well as early evening when the mother is not necessarily under the ITN [25].

The outcome of malaria in the neonatal period has been observed to be good as only one (2.2%) neonate died. A study in Sokoto [21] showed that 3.8% of neonates who had positive malaria parasites and positive blood culture died while none died among neonates who had malaria parasite alone. No mortality was also observed in neonates with malaria in Calabar [15]. Although the present study did not ascertain if the neonate who died had other co-morbidities, the white blood cell count was however within normal limits.

Conclusion

Malaria is not uncommon in the neonatal period so a high index of suspicion is important to reduce morbidity and mortality. The commonest clinical features of malaria in neonates presenting with fever are poor suck and jaundice. The use of intermittent preventive therapy, by payment women significantly reduces the incidence of malaria in the neonatal period. There is also need for continuing health education on the importance of the use of ITN.

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