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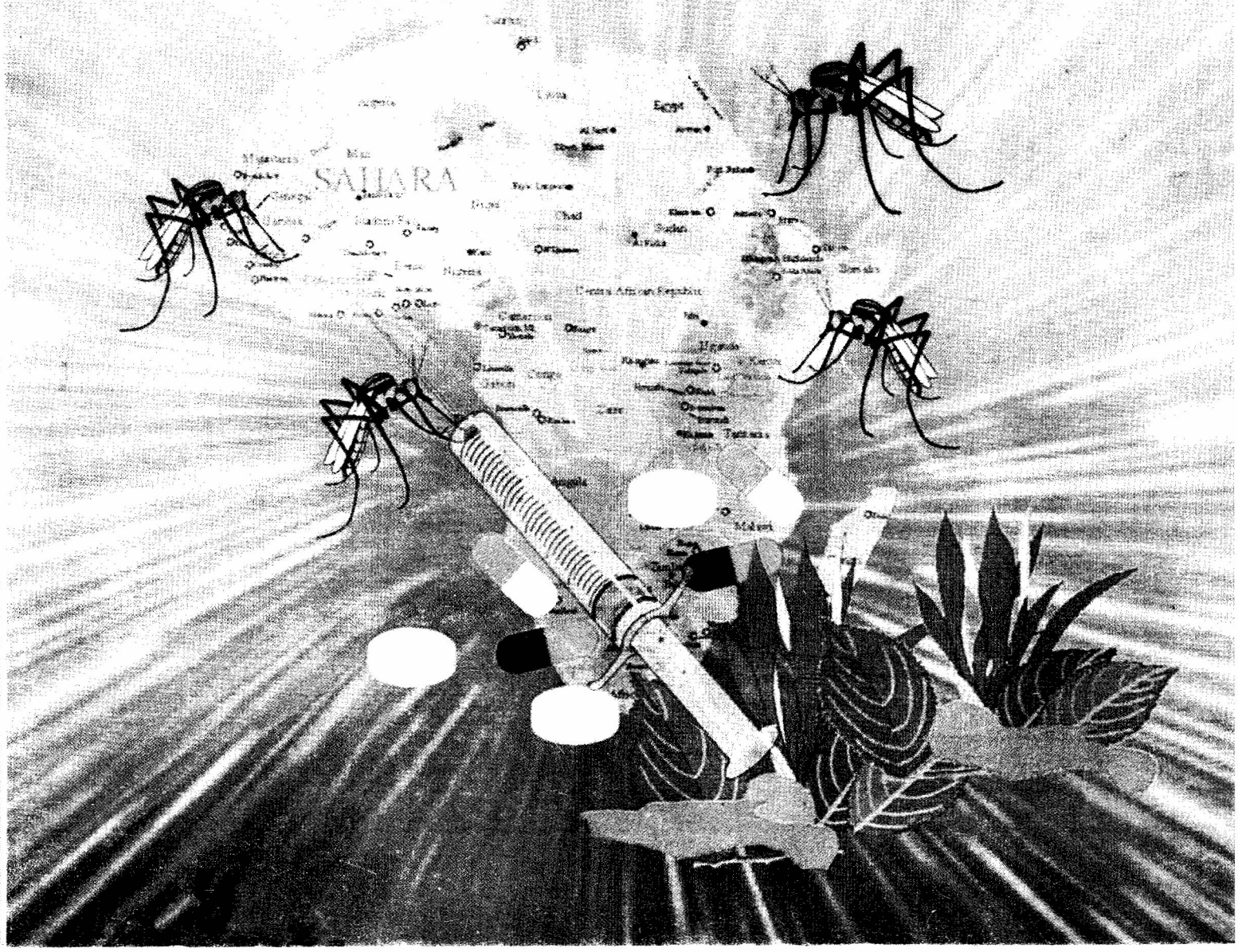

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NEONATAL MALARIA IN AN URBAN AREA OF NIGERIA.

INTRODUCTION

Neonatal Malaria is clinical malaria occurring within the first twenty-eight days of life. It includes congenital malaria, mosquito-borne malaria and post-blood transfusion malaria[1]. Congenital malaria occurs when plasmodium parasites in infected red blood cells cross the placenta into fetal circulation. The precise mechanism through which this occurs is unknown and believed to be through breaches in the placenta[2]. In malaria endemic areas parasitaemia is frequent and often associated with heavy placental infection, present in up to 47% of primigravidae as revealed by a study in the Gambia[3]. However, neonatal malaria is considered rare and largely asymptomatic or mild but could be severe and fatal when undiagnosed. In immigrants to endemic areas, it is often severe and can result in perinatal death[4].

The familiar epidemiology of malaria in endemic areas essentially is that, infants are born without malaria or demonstrate parasitaemia. They remain malaria-free for the first three to six months of life before their first attack. Malaria is relatively more frequent in children particularly in the first five years of life and most severe in children less than two. The incidence reduces with age as immunity is developed. Adults generally have high immunity to malaria[5]. During pregnancy, this immunity is altered and malaria is common. Pregnant women are 4 – 12 times more prone to malaria[6]. In the majority of cases, malaria in pregnancy is asymptomatic or mild but infrequently leads to severe anaemia and low birth weight babies. These complications are more common in primigravidae than in multigravidae.

The prevalence of cord parasitaemia vary with different geographical sites (<1% to 25). It is found to be higher in HIV positive women[7]. Neonatal malaria is observed to be rare even when cord parasitaemia has been found to be relatively high. This is believed largely to be due to malariostatic factors in the neonates like the presence of haemoglobin F in red blood cells (RBC), the reduction of erythroblastosis and relative ageing of RBC, deficiency of para-amino benzoic acid in breastfed infants and acquisition of maternal immunity[2]. Neonates thus remain malaria-free, despite heavy infested malarial placentae.

Several studies in malaria endemic areas have demonstrated that the passive transfer of IgG antibodies from mother to foetus probably suppress and often eliminate parasites from foetal circulation and is the major factor responsible for the remarkable difference between placental infection and neonatal malaria in endemic areas[9,10]. IgM does not cross the placenta. Few studies have revealed some evidence of malaria specific IgM produced by the foetus.

In recent years, paediatricians in Nigeria and other parts of Africa have observed an increase in the number of cases of neonatal malaria seen in clinical practice. Literature publications of studies in West Africa between the late 70s and mid 90s, reveal that infection rate of congenital malaria ranges between 8 – 24%[10,11,12]. A few studies have revealed evidence of malaria specific IgM produced by the foetus[13]. Is there a changing epidemiology of neonatal malaria? What is the impact of this changing epidemiology of malaria in the newborn on infant mortality and morbidity?

A study of neonatal malaria would be of public health significance as low birth weight and still-birth which are established consequences of malaria in pregnancy are preventable. Other associated risk factors and complications leading to increase morbidity and mortality of infants may be elicited. Measures already taken to reduce the incidence of malaria in pregnancy such as chemoprophylaxis would have to be enhanced while an appraisal of newer options may become necessary.

METHODS

The hospital medical records of all neonatal admissions to Massey Street Children Hospital in Lagos between Jan. and Dec. 1998 were checked. These comprise of infants one month of life or less. A total of 1182 admissions took place in that year. One thousand and four casenotes (about eighty-five percent of the admission) were retrieved and examined. The remaining 178 (15%) were missing. Information obtained from the register revealed that the age range and mean age of patients with missing casenote was similar to those used in the study. The most common admitting diagnosis was similar as well.

Cases of neonatal malaria were defined for the purpose of this study, as those ill babies with a presumptive diagnosis of malaria, from whom positive result were obtained from blood smear for malaria parasite with subsequent response to anti-malarial therapy. A total of 141 records were found with the results of a blood slide examination 91 were case of neonatal malaria as earlier defined. There were 50 cases of non-malaria cases. As microscopic blood smear for MP smear is not a routine investigation in all neonates admitted into hospital but only ordered on the basis of suspicion of malaria, the MP negative cases were considered not truly representative

of all non-malaria cases in the study population. In view of this, another 50 casenotes of neonates in which malaria was not suspected and anti-malarial therapy was not administered were randomly selected as controls along with the 50 neonates with negative blood smear for MP giving a comparable number of 100 controls to 91 cases (fig. 1).

Information from the casenotes of all 91 cases and 100 controls was extracted, using a standard questionnaire prepared for the study (appendix 1). Available data on maternal characteristics (age, education, antenatal clinic attendance, malaria chemoprophylaxis) and neonatal clinical features (symptoms and signs, temperature profile, weight profiles, drug intake, duration of admission) were collected from the casenotes for assessment of the effect of potential risk factors for congenital malaria using case control analysis. Data processing and analysis was done using EPI-INFO 6.1 Software. Statistical significance of difference in proportion and means was tested using z test and t test as appropriate.

Association between neonatal malaria and potential risk factors was assessed by odds ratios and their statistical significance was tested by chi square test.

RESULTS

Prevalence of neonatal malaria among the admissions was 9.1% (91/1004).

Sex

The sex ratio was 4:1.

Age

The age range in the study population was from 1 to 30 days with a mean of 7.7 days. For cases, the mean age was 8.7 days and 6.8 days for controls.

There was no difference in the weight of babies presenting with malaria compared with those of other ill but non-malaria babies in the control group. Generally, haemoglobin levels were lower among cases. Mean haemoglobin of the study population was found to be 12.0mg/dl with a range of 2.9 to 20.0mg/dl. Among cases and controls, the mean was found to be 11.3mg/dl and 12.7mg/dl respectively. Table I summarises the range, mean and median values of age, weight and haemoglobin.

Table II summarises how the various potential risk factors associated with Neonatal Malaria (NNM). The analysis of the data revealed a significant association between sex and malaria in the neonates admitted to hospital with odds ratio of 3.3 among cases compared to the non-malaria admissions. Male neonates were more likely to have NNM. Statistically significant association was also found between neonatal malaria and haemoglobin level. The odds ratio being 3.5. This significant association persisted even when the effect of sex was taken into account. The Mantel-Haenzel weighted odds ratio was 2.8 (95% CI 1.19; 6.25). Antenatal care, hospital delivery, age and weight gave no statistically significant association with malaria among neonates who had malaria compared with those who did not have. Information was insufficient in grouping the babies into the socioeconomic status of their mothers. It was therefore not possible to consider this very important factor in neonatal malaria.

DISCUSSION

The information on history and clinical features recorded in the casenotes was incomplete with gross underreporting. The records were not detailed to answer all the questions in the questionnaire for every neonate, giving rise to insufficient information on antenatal attendance, use of prophylactic anti-malarial therapy and hospital deliveries. It was thus not possible to examine the role of these factors on malaria in the newborn. This is a problem of using routine records retrospectively for a detailed and in depth study of this nature. In a prospective study, all the relevant information would be available and answers would be provided.

In spite of these limitations, a number of useful information emerged from this study. The prevalence of NNM was found to be 9.1%. Most of the cases occurred within the first week of life as fig. 2 revealed. This implied that majority of the cases were congenital. This prevalence is similar to that obtained from previous studies in Nigeria[12,14]. An increasing prevalence has been observed especially in the last two decades. Results of literature search reveal a range of 1.6 to 16.8% of parasitaemia in cord blood and 2.8 to 23.7% in neonatal blood. It is observed that the prevalence of parasitaemia in neonatal blood has gradually increased over the years: 0.3% in the 1950s[15,16,17,18] to 23.7%[12] in the last decade.

An interesting observation was made in the level of haemoglobin obtained among cases compared to controls (fig. 3). Thirty-four percent of cases of NNM had low haemoglobin levels compared to 13% of the neonates in the control group. The population studied was for unwell babies. Despite the fact that more babies were fatally ill in the control group (with severe clinical conditions such as neonatal sepsis, neonatal tetanus and birth asphyxia), anaemia was recorded in almost three times the number of ill babies with malaria than those more severely ill babies without malaria. If almost 10% of neonatal admissions have three times more risk of anaemia as a result of malaria, by the time they are four to six months old, with depleting immunity, they would be expected to be more prone to increased malarial morbidity and mortality from anaemia. With anaemia contributing to a high number of infant morbidity and mortality, there is strong justification for a prospective study to examine the association elicited from this study. This study has revealed the following areas of knowledge gaps for further research.

(1) Population based estimates of the incidence of neonatal and congenital malaria.
(2) Risk factors for neonatal and congenital malaria.
(3) Clinical features and natural history of neonatal and congenital malaria.
(4) Immediate and long term impact of NNM.

Table I: **Predictor variables on neonatal malaria.**

Variables	Cases n = 91	Control n = 100	Odds Ratio (95% CI)
Sex			
Male	n_1 = 73	n_1=55	1.00
Female	n_2=18	n_2=45	3.3(1.6 – 6.7)
Hb group			
1(0 – 9.9mg/dl)	n_1=29	n_1=9	1.00
2(10 – 20mg/dl) Group 2	n_2=57	n_2=61	3.5(1.4 – 8.7)
ANC Attendance			
Yes	n_1=32	n_1=34	1.00
No	n_2=13	n_2=6	0.43(0.13 – 1.44)
Hospital delivery			
Yes	n_1=22	n_1=26	1.00
No	n_2=17	n_2=22	1.10(0.43 – 2.82)
Age group			
1(0 – 7 days)	n_1=54	n_1=71	1.00
2(8 – 30 days)	n_2=37	n_2=29	(0.31 – 1.14)
Weight group			
1(0 – 2.49kg)	n_1=22	n_1=22	1.00
2(2.5 – 5kg)	n_2=36	n_2=42	1.17(0.52 – 2.63)
Outcome			
1 discharged	n_1=79	n_1=79	1.00
2 Died	n_2=7	n_2=18	0.39(0.14 – 1.06)

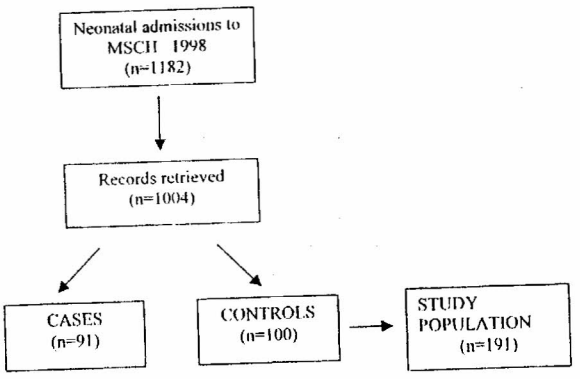

Fig. 1: **Study population.**

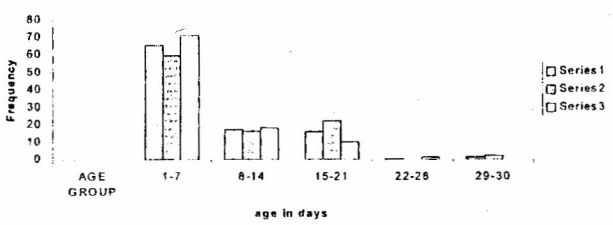

Fig. 2: **Distribution of age in weeks within the study population, among cases and controls.**

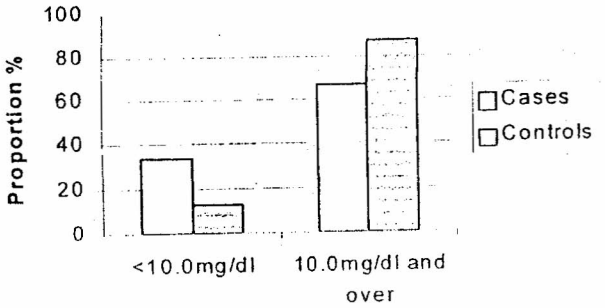

Fig. 3: **Distribution of anaemia among cases and controls.**

A number of questions remain unanswered for which further research is required.

- Would control measures of malaria in pregnancy lead to less incidence of neonatal malaria or expose the foetus and infant to less transplacentally acquired immunological response?
- Is the increasing prevalence and severity of congenital malaria as seen in urban areas, a reflection of changing epidemiology resulting from decreased malaria transmission and immunity?
- What are the roles of other possible risk factors such as the high plasmodium resistance to widely used malarial prophylaxis?
- Do other obscure risk factors such as HIV play a role in the increasing incidence of congenital malaria?

These and other identified research questions need to be addressed urgently.

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