The epidemiology of malaria in endemic areas generally is that, infants are born without malaria or demonstrable 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 those less than two. The incidence reduces with age as immunity is developed. Adults have high immunity to malaria.

Adults in malaria endemic areas, have high levels of specific IgG, IgM and IgA. The immunology of malaria is complex. Immunoglobulin levels parallel the infection pattern. They act by limiting the RBC either by agglutination of merozoites or neutralization of surface ligand for RBC receptors and by inhibiting the sequestration of P. falciparium infected erythrocytes and force parasites to face the lymphocytes. Several studies in malaria endemic areas, have demonstrated that the passive transfer of IgG antibodies from mother to fetus probably suppress and often eliminates parasites from foetal circulation and is the major factor responsible for the remarkable difference between placental infection and neonatal malaria in endemic areas (William H.I.O., et al 1970). Maternal IgM does not cross the placental.

The increasing prevalence of neonatal malaria raises a number of questions on associated risk factors involved. A number of host and parasite biological factors and how they relate to the pathological processes of malaria have been reviewed extensively. (Greenwood et al 1991 Marsh, 1992 and White & Ho 1992). These include genetic, immunological and nutritional characteristics in the host and the virulence of the parasite. The picture is however incomplete without considering socioeconomic and enviromental factors. Greenwood has illustrated how various epidemiological situations can occur even in areas of holoendemic malaria as a result of socioeconomic influence (Greenwood 1989). It is beyond the scope of this paper to review all of these biological and socio-economic factors of malaria. A brief mention will be made of some specific risk factors associated with neonatal malaria in relation to the objective of this study.

Risk Factors for Neonatal Malaria In An Urban Area of Nigeria

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SUMMARY

This study examines the prevalence and risk factors of congenital and neonatal malaria using the analysis of hospital records and literature reviews. Admission records of 91/1004 neonates into an urban hospital in Lagos were examined for possible risk factors compared to a selected control group of 100 babies from the same population.

The analysis revealed a male preponderance for neonatal malaria. It also showed a strong association between malaria and anaemia. There was no association between factors such as parity, socio-economic status, ante-natal care, place of delivery and neonatal malaria mainly due to incompleteness of data on these variables. This was a prominent limitation of this study as other risk factors elucidated in literature search could not be assessed.The main clinical findings of neonatal malaria were fever, respiratory and neurological manifestations.

The prevalence rate of 9.1% obtained, was in keeping with that found in recent literature. Generally, the review of literature revealed an apparent rise in prevalence over the last few decades and identified some areas of knowledge gaps which include, the need to ascertain the true population prevalence, identification of possible obscure risk factors, clear understanding of the clinical features and natural history of congenital malaria and immediate and long term impact of control measures especially as it relates to immunity. This calls for a prospective epidemiological research into the issues that have been raised.

TABLE OF CONTENTS.

CHAPTER 1: INTRODUCTION

The term neonatal malaria describes malaria within the first month of life and includes congenital malaria, mosquito-borne or acquired malaria and transfusion malaria occurring within the same period of life. It is a term that was seldom seen in medical literature but more often encountered now as the prevalence of malaria in the first month of life increases. (Ibhanesebhor SE, 1995; Thapa BR, 1987; Sodeinde O,1985). Congenital malaria as a known consequence of malaria in pregnancy, has received little attention as the other adverse effects of perinatal morbidity and mortality. It had been considered a rare disease worldwide. (Covell G, 1950; McGregor IA 1986). Recent publications from endemic areas have however challenged that assertion.(Nyirjesy P et al. 1993; Larkin GL, 1991; Fischer PR, 1995). In a recent survey undertaken in different sites in sub-Saharan Africa, the overall prevalence of neonatal parasitaemia was 7% (Reinhardt MC, 1978;). Infection rate of congenital malaria reported in some studies in West Africa have been between 8- 24% (Akindele JA et al.,1993; Diallo S et al., 1983;). It appears that in malaria endemic areas, there is growing evidence of an increasing prevalence of congenital malaria, while the in non malarious areas congenital malaria is mainly imported.

In recent years, an increase in the incidence of congenital malaria has been observed in Nigeria (Akindele, J.A. et al 1993; Ibhanesebhor SE, 1995) and Tanzania (personal communication – Chandramohan D). The incidence of congenital malaria was 9.6% (n=425) among neonatal admissions to Massey Street Children Hospital in Lagos between January and June 1998 (unpublished). The factors associated with the high incidence of congenital malaria in this urban population are not known. Several investigators have provided epidemiological evidence that placental malaria determines low birth weight and increase the risk of death in the first year of life. (Bruce-Chwatt LJ, 1952; McGregor IA et al., 1983; Watkinson M and Ruston DI, 1983.) The beneficial effect of chemoprophylaxis has also been demonstrated. (Shulman C, 1999; McDermott JM et al., 1988). However, very little work has been done on the risk factors of neonatal malaria as a perinatal problem.

Several factors such as plasmodium falciparum resistance to chemoprophylaxis, maternal immunity, gestational age of the neonate, socio-economic characteristics of mothers, parasite strain variation or density and concomitant new infections such as HIV may be associated with the risk of congenital malaria. Understanding the role of these factors is of public health significance as the consequences of neonatal malaria such as anaemia, low birth weight or failure to thrive, and mortality of infants are preventable.

This thesis aims to explore the clinical manifestations, biological and social risk factors associated with neonatal malaria from a retrospective study of neonatal malaria cases and a randomly selected group of controls admitted to a hospital in Lagos. It also discusses the various areas of gaps in present knowledge that require further research on neonatal malaria and related issues.

The thesis is structured such that section two gives a brief overview of the present level of work and knowledge on the aetiological and epidemiological issues of malaria in the first months of life including a brief reference to possible risk factors. Section three outlines the methods used and describes how the study was undertaken. Results are presented in section four while discussions on them, limitations of the study and other related issues are dealt with in section five. Section six discusses the various knowledge gaps identified for which further studies are required.

CHAPTER 2: LITERATURE REVIEW

BACKGROUND

Congenital malaria occurs when plasmodium parasites in infected red blood cells cross the placenta into fetal circulation. It was first reported in Nigeria by Bruce-Chwatt (Bruce-Chwatt L.J., 1952). The precise mechanism through which this occurs is unknown and believed to be through breaches in the placental barrier or more frequently at the time of placenta separation during the birth process.(McGregor 1986)

During pregnancy, the immunity against malaria is altered and pregnant women are 4-12 times more prone to malaria (Brabin, 1991). The parasite sequestrates in the placenta where infection is often extremely heavy. The placenta appears to act as a privileged site for parasite replication. In acute infection, parasites are seen inside the RBCs in the intervillious spaces (Bulmer, J.N. et al 1993) whereas chronic infection is depicted by the presence of malaria pigment (haemozon) in fibrous deposition in the placenta. In the majority of cases, malaria in pregnancy is asymptomatic or mild but often leads to severe anaemia and low birth weight babies. These complications are more common in primigravidae than in multigravidae.

The incidence of cord parasitaemia vary within different geographical sites (<1% to 25) and it has been found to be higher in HIV positive women (Steketee, RW et al 1996). Neonatal malaria is observed to be rare even when cord parasitaemia has been found to be relatively high (McGregor 1984). This is believed to be largely 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. Neonates thus remain malaria-free despite a heavily infested malarial placenta (McGregor 1986). However, among immigrant to endemic areas, it is often severe and can result in still birth or perinatal death (Wickramasuriya, 1937).

POSSIBLE RISK FACTORS

Malaria infection in Pregnancy

Congenital malaria and all it's complications are consequences of malaria in pregnancy. Preventing malaria in pregnancy would result in decreased infection and morbidity in neonates. In a trial of malarial chemoproplylaxis (Steketee WR 1996) among rural Malawian pregnant women, 15% of the women placental parasitaemia and 6.7% newborn had parasitaemia. Both placental malaria and maternal peripheral blood parasitaemia were highly associated with the likehood of umbilical cord parasitemia. This study found delivery during high transmission season, male sex, maternal HIV infection, first pregnancy, intra uterine growth retardation and prematurity as risk factors associated with umbilical cord parasitemia It needs to be seen if all these factors apply to other endemic areas with their local pecularities. This study did not follow up the infants born by these pregnant women beyond the delivery period and thus unable to explore these risk factors in association with neonatal malaria.

It is important to distinguish malaria in pregnancy among non-immune and immune women. Various studies (Marshall, DE 1983; Meuris S 1993) have shown that susceptibility to infection and severity of clinical manifestations depends on the level of pre-pregnancy immunity which in turn depend on the intensity and stability of malarial transmission. In areas where malaria transmission is low or unstable or if one moves from an area of low to high endemicity, because of the lower degree of immunity, the consequences of malaria are more severe. Malaria in pregnancy is thus associated with still birth, perinatal death and cerebral malaria in areas of low endemicity. (Wickramasuriya, 1937)

In malaria endemic areas, because of a higher immunity, the effect of malaria were observed to be less severe manifesting as asymptomatic or mild peripartun infections in the baby (Logic DE 1970 and Foll CV 1968 in Reed SC et al 1996). Increasingly, more severe cases of congenital malaria are being reported in endemic areas {Lehner & Andrews CJ 1998 Akindele JA 1993;} In 1993, over a 3-month rainy season,

Ibhanesebhor found a rise in prevalence to 8% from 2% in 1990. The babies had presented with clinical symptoms that were indistinguishable from those of neonatal sepsis and some of these babies had chloroquine resistance malaria (Ibhanesebhor 1993). Other investigations have made similar observations (Fisher PR 1995; Airede AI 1991). It is no longer just the mere presence of parasiaemia as in *infection* of congenital malaria but of concern is the rising problem of morbidity and mortality associated with congenital malaria as a *disease,* that make this problem one of public health importance. The questions that arise are 'Why is congenital malaria becoming more common and severe in neonates in endemic areas?' 'What host factors, biological, social or enviromental factors are involved.'

Inherited Host Factors.

Inherited red cell abnormalities such as sickle cell disease, G6PD are thought to persist in malaria endemic areas because of the relative protection against malaria confined on those with the heterozygous form (Allison 1957 Gilles et.al 1967).

In the neonatal period, the presence of haemoglobin F in red blood cells retards the growth of the parasite. The ageing of the infant's red blood cell makes it more resistance to plasmodium invasion (Cao and Mellis 1977).

Possession of some particular classes of HLA has been shown to have ameliorating effect on malaria. No specific genetic factor in the pregnant woman has been reported to protect or predispose to attacks of malaria. Pregnancy has however been associated with depression of the immune system.

Immune Response in Pregnancy

The reasons why primigravidae are more susceptible to malaria than multigravidae is still not fully understood. Fried and Duffy have however proposed that sequestration of infected red blood cells by a distinct subpopulation of parasites which bind to chondroitin sulfate A in the placenta could explain this observation. Women, they argue have little or no immunological experience to this subpopulation of parasites prior to their first pregnancy, making them more vunerrable to infection. In subsequent

pregnancies, they are more able to mount immunological response to the parasites (Fried M and Duffy PE, 1998).

During pregnancy, the immune system is adapted to prevent foetal rejection (Sargent IL 1993) by becoming depressed with both humoral and cell-mediated immunity affected. *Humoral immunity*- It is known that the mean IgG titres progressively fall in pregnancy, this however, is a relative rather than an absolute fall because of the haemo- dilution which occurs in the second half of pregnancy and the transfer of IgG to the foetus. (McGregor IA 1984). There are contradictory reports on the level of mean malaria-specific IgG titre. Some reports have shown a reduction in malaria-specific antibody titre between pregnant and non-pregnant women, while others have found increased titres associated with peripherial or placental infections (Riley EM et al. 1989; Mvondo JL et al. 1992). Apart from those contradictions, impairment of humoral immunity does not appear to explain the increased susceptibility of the malaria observed in pregnancy. Cell mediated immunity is transiently depressed in pregnancy (Hunt JS. 1992). Many hypotheses have been propounded as reasons but none of them have been established.

Some investigators have expressed concern about the use of chemoprophylaxis during pregnancy following studies in which prolonged use of prophylactics was associated with fall in maternal levels of antibody titres (Ibeziako, PA and Williams, AI 1980). They observed both IgG and fluorescent antibody titres fell with increasing gestation among women who had been on chemoprophylaxis throughout pregnancy. Mean cord IgG in the study was lower than the mean paired maternal IgG value. This study did not however have a control group who were not on chemoprophylaxis to compare with. The effect of other confounding risk factors such as parity was also not taken into account. The investigator quoted other studies with similar results from Africa but noted that reports in Caucasians differ.

Malaria Chemoprophylaxis and drug resistance.

Regular antenatal screening has been effective in providing the opportunity for prompt diagnosis and treatment in areas of low or unstable malaria transmission. On the other hand, in malaria endemic areas, as infection rate of the placenta is high and peripheral malaria infection is often present, use of chemoprophylaxis has been advocated. Even though there is often no direct correlation between placental infection and peripheral or maternal blood parasitaemia, chemoprophylaxis in pregnancy has been found to be beneficial in reducing the incidence of low birth weight babies and peripartum anaemia.

WHO recommends the use of chloroquine prophylaxis in pregnancy in malaria-endemic areas (WHO expert committee 1986) for prevention. In the face of spreading anti-malaria drug resistance of the plasmodium (particularly to the widely used chloroquine), the rising prevalence of neonatal malaria may not be unrelated to the development of drug resistance. Previous studies in Africa, have shown that the level of disease in the community increases with the emergence of drug resistance. An increasing number of cerebral malaria cases was observed at a time when drug resistance was emerging in Kinshasha . (Greenberg et.al., 1989)

In a study among Malawian pregnant women, (Steketee 1996a)the efficacy of different regimen of chloroquine was compared with that of mefloquine by measuring the level of parasiteamia at delivery in maternal peripheral blood, placental blood and in neonatal umblical blood among other things. It was noted that compared with women on mefloquine regimen, those on chloroquine were much more likely to have peripheral parasitemia (OR=6.0,95%CI=3.7-9.9), placental parasitemia (OR=5.0,95%CI=3 3-7.6) and umblical cord parasitemia (QR=2.9, 95% CI 1.6-5.3) at the time of delivery. Use of chloroquine in a setting with chloroquine-resistant parasites was considered an important determinant of malaria infections.

In Nigeria, pyrimethamine has been in use for over thirty years as a weekly administered single-drug malarial prophylaxis in pregnancy (Fleming 1970). Over a decade ago, a high resistance level to pyrimethamine was observed (Nahlen B 1989). Sixty percent of

88 pregnant women receiving weekly pyrimethamine for four weeks were examined for malaria parasites. 67% retained parasites by Day 7 and 60% by Day 14. Other workers have confirmed the presence of high level of plasmodium resistance to pyrimethamine in Nigeria (Fleming AF, 1990).

Inspite of this finding and the current national policy adoption of WHO recommendation, (National Policy on Control of Malaria 1996-2000), pyrimethamine is still the most commonly prescribed drug for malarial prophylaxis in Nigeria. (Chikudebuelum 1997)

HIV infection in mother

HIV and malaria is an emerging problem. The current prevalence of HIV among pregnant women in Nigeria is about 5.4% and as high as 30% in some parts of Africa. (MTCT, Working Group 1995). Studies in Malawi and Kenya recently found that HIV positive women are more likely to have parasitaemia at ANC and delivery despite taking prophylaxis than HIV negative women (Steketee, RW. et al 1997b). This may be an important risk factor for neonatal malaria.

The interaction between HIV and malaria could work in either direction. Of interest, would be the question of whether placental malaria increases the risk of HIV transmission (Newell M and Peckham C 1993). Most of the children infected acquire their infection vertically from mother-to-child. The rate of mother-to-child transmission is about 25%-45% in Africa (MTCT, Working Group 1995). As at Dec 1999, as estimated 1800 children became infected each day worldwide and 1600 of them are from sub-Saharan Africa (UNAIDS website).

The risk factors of vertical transmission of HIV depends on clinical immunological status during pregnancy and the duration of the infection (Lazzarin A in Newell M and Peckham C 1993). However, presence of another sexually transmitted disease and other viral or parasitic infections such as malaria could cause immunological impairment with

greater virus load in the mother. Transfusion of maternal blood could take place via damaged placental barrier resulting from inflammation caused by malarial infection. This pausible phenomenon is to be examined in a proposal (Pittrof R, Chandramohan D and Greenhood B 1999) to assess if placental malaria increases the risk of materno-fetal transfusion by measuring the level of placental phosphate alkaline phosphate (PLAP) in fetal serum. PLAP does not cross the placenta because of it's high molecular weight unless there exists a breach in placental barrier. High fetal levels in women with placental malaria compared to those without, would suggest the occurrence of materno-fetal transfusion.

Nutritional Factor

Acute malaria causes anorexia and vomiting and could affect food intake. Evidence has been provided in studies in children that poor nutritional status is known to affect the ability to mount an adequate immunologial response (Rowland et al 1977) .There is however no clear evidence that malaria-induced depression on maternal nutritional state accounts for morbidity in the baby as there are conflicting views. Jelliffe found no difference in nutritional state of women with and without placenta malaria (Jelliffe 1967). Reinhardt (1978) made contrary observation in West Africa. A fully established fact is the effect of placental parasitaemia on reducing the birth weight of the offsprings.

Some nutritional factors have been found to affect susceptibility to malaria. Maternal iron and folic acid status may be important parameters in this regard. Byles and D'Sa (1970) noted that large infusions of iron dextran into anaemic pregnant women was associated with more frequent attacks of malaria. There are reports have that oral or parenteral iron appeared to precipitate clinical episodes in patients with pre-existing infections (Murray et al 1978). Weinberg (1978) also described how competition for growth-essential iron could develop between the host and a number of pathogens. However, iron deficiency restrict pathogen replication and also impair host immunity. McGregor has argued that considering the widespread coexistence of iron deficiency anaemia and asymptomatic malaria parasitaemia in highly endemic areas, it is surprising that only few reports have described reactivation of malaria following iron therapy.

Evidence however exist that high dose iron supplementation in children predispose them to increased susceptibility to malaria infection (McGregor, IA 1988).
This susceptibility have not been found in pregnant women if the dose is prophylactic and not curative (Menendez, C 1994). Little is known about the gross nutritional status of the pregnant mother on susceptibility to malaria. Studies in children have however supported the concept that severe malnutrition retard rather than enhance malaria (Edington 1967).

Environmental and Socio-Economic Factors

It is obvious that environmental factors are important risk factors for malaria. The continued surge of malaria in most endemic areas are related to the humid hot weather in these areas. Seasonality has also been associated with increase malarial attacks as a result of increased breeding sites for mosquitoes in the rainy season (Stekette 1996). Ecological risk factors that affect the entire population for example, irrigation, dam, stream, etc would be general and have little individual influence. However, response to environmental factors that predispose to exposure of mosquito and parasite may be influenced by the individual's economic strength, level of education, awareness and perception of risk.

Health seeking behavior would also affect morbidity and even mortality of malaria. Other dependent factors would include accessibility to health facility, family support and other support systems in the community. Social norms and practices as well as the knowledge, belief and attitudes of the women to the infection would affect utilization of health services and use of chemoprophylaxis in pregnancy. The *Ghana Health Seeking Behavoiur Project* found high dropout rates at health centres due to problems of childcare and accommodation. Family and cultural tiès were also found to influence where people go to seek care (Kendall C, et al 1999).

The socioeconomic factors that have been found to increase the prevalence of malaria in the general population would also affect the pregnant woman. In a study from Colombia, significant association was found between the attack of acute malaria and size of living household, source of water, occupation and income. (Banguero H, 1984).

Dose of Parasite

In many infectious diseases, the dose and virulence of the infectious agent determines the occurrence and severity of infection. The infecting dose has been a difficult area of study in P.falciparum infection and opinions differ.

Following observations that vector control can reduce morbidity and mortalility without reducing the prevalence of infection, Greenwood and colleagues have hypothesised that the severity of malaria depends on the size of the inoculum (Greenwood, Marsh and Snow, 1991). Lines and Armstrong have however argued that the dose of the sporozoite *is largely strain specific and only if there is strain specificity can inoculum size be important* in the development of natural immunity to malaria (Lines and Armstrong 1992).

In congenital malaria, due to the pecular barrier of the placenta to infection and the protective physiological factors in the baby, the dose of the parasite may not necessarily be an important factor. Heavy placental parasitaemia is often observed in the presence of low or no peripheral parasitaemia. (Rogerson SJ and Beeson JG, 1999).

CHAPTER 3: METHODS

LITERATURE REVIEW

Literature search was done, using various databases. These included Medline, BIDS, Popeline, Healthstar, Web of Science and Cabhealth for neonatal malaria, malaria in newborn, malaria in infancy, congenital malaria, transplacental transmission of malaria, malaria in pregnancy and other related issues to synthesize existing knowledge in these areas. Relevant ones were used for this review.

During the literature search, information on the prevalence of parasitaemia in neonatal, cord, maternal or placental blood were obtained from articles from malaria endemic areas from 1970-2000. Attention was placed on prevalence rates, time and place of study. The result of the search is presented in tabular form in the chapter on results. A few selected studies from the 50s and the 60s have been included for comparison.

CASE CONTROL STUDY

The hospital medical records of all neonatal admissions to Massey Street Children Hospital in Lagos between January and December 1998 were checked. These admissions comprise of infants aged one month of life or less. A total of 1182 took place in that year.

One thousand and four case notes (about eighty- five percent of the admission) were retrieved and examined. The remaining 15% were missing. Information obtained from the register revealed that the age range (1-30 days)and mean age (7.2days) of patients with missing case note (n=78) was similar to the of population of patient whose case-notes were found and from where the study population was derived (n=1004). The most common admitting diagnoses were similar as well. (Table 1).

It was not possible to determine how many requests of microscopic blood smear for malaria parasite (MP) based on the presumptive diagnosis of malaria were made. A total of 141 case notes were found with the results of a (MP) blood slide examination; 91 were of which were MP positives and 50 had MP negative results. The neonates with positive blood smear were defined as malaria cases for the purpose of this study. As microscopic blood smear for MP smear is not a routine investigation in neonates and

only ordered on the basis of suspicion, the MP negative cases were considered not truly representative of all non-malaria cases in the study population. In view of this, another 50 case-notes of neonates in which malaria was not suspected and antimalarial therapy was not administered were randomly selected as controls along with the 50 neonates with negative blood smear for MP.(fig I)

Fig 1 STUDY POPULATION

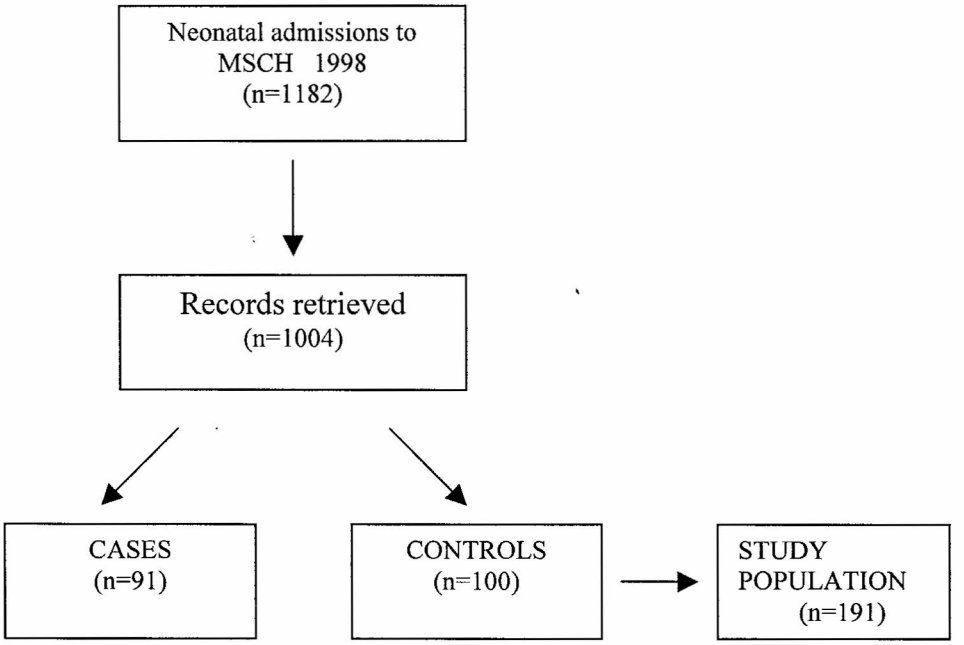


Table 1

Diagnosis of all Neonatal Admissions MSCH 1998

(n=1182)	*Retrieved Case-notes*		*Missing Case –notes*	
Disease	Number	Percentage	Number	Percentages
Neonatal Malaria	28	2.3	2	2.5
Neonatal Sepsis	274	23.1	18	23.0
Prematurity	129	10.9	8	10.2
Failure to thrive	32	2.7	2	2.6
Birth Asphyxia	152	12.9	12	15.4
Birth Trauma	5	0.4	0	0.0
Respiratory Distress Syndrone	2	0.2	0	0.0
Congenital Rubella	1	0.1	0	0.0
NeonataL Tetanus	192	16.2	11	14.2
Conjuctivitis	7	0.6	0	0.0
Haemorrhagic Disease of Newborn	10	0.8	1	1.3
Neonatal Jaundice	148	12.5	10	12.8
Obstructive Jaundice	2	0.2	0	0.0
Hypoglycaemia	2	0.2	0	0.0
Mennigitis	25	2.1	2	2.5
Bronchopneumonia/Bronchiolitis	49	4.1	4	5.2
Gastroenteritis	68	5.8	3	3.8
Others	56	4.7	5	6.4
	1182	100.00	78	100.00

Information from the case notes 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 case notes 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 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 significant was tested by chi square test.

STUDY SITE

Massey Street Children Hospital is the largest exclusive paediatric referral centre in Nigeria. It is situated in the centre of Lagos from where it attracts patients of different socio-economic and ethnic group from all over the city and its surrounding areas.
The hospital usually has about 70%-92% occupancy of its 114 beds and provides full medical services for children including immunizations, nutritional and family planning services. It is economically accessible to the majority of the populace as user fees are relatively low, consultation is free and drugs are cheap under a revolving drug-fund system. Average daily attendance is about 100-150. In the past five years, the total yearly attendance has risen from about 35 000 to 60 000 with a corresponding increase of about 3,500 to 6,000 of in-patient admission. Neonatal admissions comprise 20% of total admissions while a significantly high proportion of deaths, (40%) are due to neonatal illnesses mainly neonatal tetanus, birth asphyxia and neonatal sepsis. Though malaria in neonate is not a significant cause of death, increasingly more cases have been reported over the years. There are no accurate records of the trend in the prevalence rate of confirmed neonatal malaria cases seen in the hospital.

Transmission of malaria is stable and intense with annual rainfall (mean monthly > 10cm), relative humidity (>60%) and temperature is between 20-30^{0}C.
Plasmodium falciparium is the most commonly encountered parasite contributing about 90% of infection.
Pyrimethamine is the widely used chemoprophylaxis for malaria in pregnancy, even though the 1996 –2000 National Policy recommends the use of chloroquine in line with WHO recommendation (National Policy on Control of Malaria 1996 – 2000). Iron supplements and folic acid are prescribed routinely in antenatal clinics.
The year 1998 was chosen as the year to study because it is recent enough to give a complete and current year record and picture of the malaria problem. A full year would include both the dry and rainy seasons. The year 1998, was also the first full year of free malaria treatment implemented by the Lagos State Government.

CHAPTER 4: RESULTS

PREVALENCE RATES FROM LITERATURE REVIEW

Table 2. Prevalence of parasitaemia at delivery, in placenta, cord and neonatal blood from various studies.

Country	Investigators (ref)	3rd Trimester Pregnancy or Delivery	Prevalence (%)			Comments
			Placenta	Cord Blood	Baby	
Papua New Guinea	Lehner PJ(1988)	29.4%	Ns	14.6%	7.7%	1.Significant correlation found between anti-malarial IgG antibodies in paired maternal and cord blood. 2.Clinical malaria in 1 out of 7 cases of neonatal infection.
Nigeria (Calabar)	Ezeoke ACJ et al (1985)	8.4%	26.2%	16.8%	7.5%	No difference in mean birth weight of children from infected and uninfected mothers.
Senegal (Thies)	Diallo S et al.(1983)	15.5%	6.1%	Ns	7.8%	Figures show higher incidence of congenital malaria during the wet season.
Nigeria (Benin)	Ibhanesebhor SE; Okolo AA (1992)		45.19%			312 placentae of singleton deliveries.
Nigeria (Benin)	Ibhanesebhor (1995)				8%	
Nigeria (Jos, Bauchi & Eku).	Egwunyenga OA et al.(1996)	21.8% Bauchi 23.2% Jos 17.5% Eku				n=1905 women
Uganda	Kasumba I N (1999)	8.6%	6.7%			
Nigeria (North)	Egwunyenga OA et al.(1995)	44.5%		10.95%	2.82 %	Prevalence of infant parasitaemia confined to babies within 1st week of birth.
Zaire (Urban/rural)	Nyirjesy P(1993)	21%	33%	9%	7%	n=302; neonatal malaria increased the risk of perinatal death (RR=7.2)
Malawi	Steketee Rw etal (1996)	15.8% (283/1,790)	19.9%	7.1%	N/S	Study compared the efficacy of different doses of chloroquine to mefloquine as chemoprophylaxis.
Nigeria (Ibadan)	Akindele JA Sowunmi A(1993)				23.7 %	Weekly pyrimethamine not effective in preventing infection in 21.4% of cases.

Country	Investigators (ref)	Prevalence (%).				Comments
		3rd Trimester Preg or Delivery	Placenta	Cord Blood	Baby	
Nigeria (Lagos)	Lamikanra OT(1993)	2.97%	2.94%	1 sample	nil	101mothers and their 105 neonates studied.
Central/West Africa	Zinsou RD(1987)	12.1%	ns	1.6%	Ns	Antibody levels also used to diagnose malaria. Study also examined pathological changes in the placenta.
Nigeria (East)	Spitz AJ(1959)	Ns	23.7%	ns	0%	41.2% of babies were LBW babies from mothers with infected placenta; 27% LBW babies in mothers with non infected placenta
Nigeria (Lagos) Nigeria	Bruce-Chwatt LJ(1952) Covell (1950)	33%	23.8%	Ns	0% 0.3%	Mean birth weight of babies with non-infected placenta was 145mg higher than mean birth weight of babies from infected placenta.
Zaire	Steketee RW(1988)	25%				953 neonates and their mothers
Guinea Conakry	Sylla A et al.(1988)	32%	ns	nil	ns	
Zaire Kinshasa	Omanga U et al.(1990)	13%	ns	ns	4%	953 neonates and their mothers studied. Study focus *was on birth wt. No* significant diff. in mean birth wt. between infants from infected and non-infected placentae.
Guinea-Bissau	GarciaDomin g-uez J et al (1987)	63.3%	Ns	11.5%	Ns	
Mozambique (Maputo)	Bergstrom et al . (1993)	17.3%	ns	1.5	ns	More maternal parasitaemia in rural than in urban centre; 23% vs 19%
Zaire	Nyirjesy P(1993)	21%	33%	9%	7%	
A malaria endemic area	Balaka B. et al (2000)				7.7	Study in new born (0 – 7 days old): CMD* = 1.7% CMI** = 19%
Zambia	Larken & Thuma (1991)		63%		29%	n=65 neonates. 7 out of 19 babies had clinical malaria

*CMD = congenital malaria disease
**CMI = congenital malaria infection.
***ns = not supplied.

The table above shows the level of parasitaemia in the mothers during the last trimester of pregnancy or at delivery, and also parasitaemia in the placenta, cord blood and

neonate's blood. The countries where the studies were carried out and references are indicated. Result of literature search on the prevalence revealed a wide range in levels of parasitaemia from various places; mother's blood (2.97%-63.3%), placenta (2.94%-63%), cord (1.6%-16.8%) and infant's blood (0-29%). While most studies examined neonatal parasitaemia at birth, some considered only neonates in the first week of life (Egwunyenga OA et al 1995) and others followed-up babies to one month of life (Akindele JA 1993). More prevalence studies with relatively higher rates of neonatal parasitaemia were reported in the last two- three decades are than in the preceding years.

Case control Study

One thousand one hundred and eighty-two unwell neonates were admitted into Massey Street Children Hospital in 1998. Six hundred and seventy were males and 512 females. There were a total of 441 deaths, with the overall mortality of 37.3% off all neonatal admissions.

One thousand and four case notes (about eighty- five percent of the admission) were retrieved and examined. The remaining 15% were missing. There were 91 cases of confirmed malaria and 100 controls. Information obtained from the case records of the 191 babies revealed the following:

Prevalence

Prevalence of neonatal malaria among the admissions was 9.1% (91/1004) (95% C I 7.4,11.1).

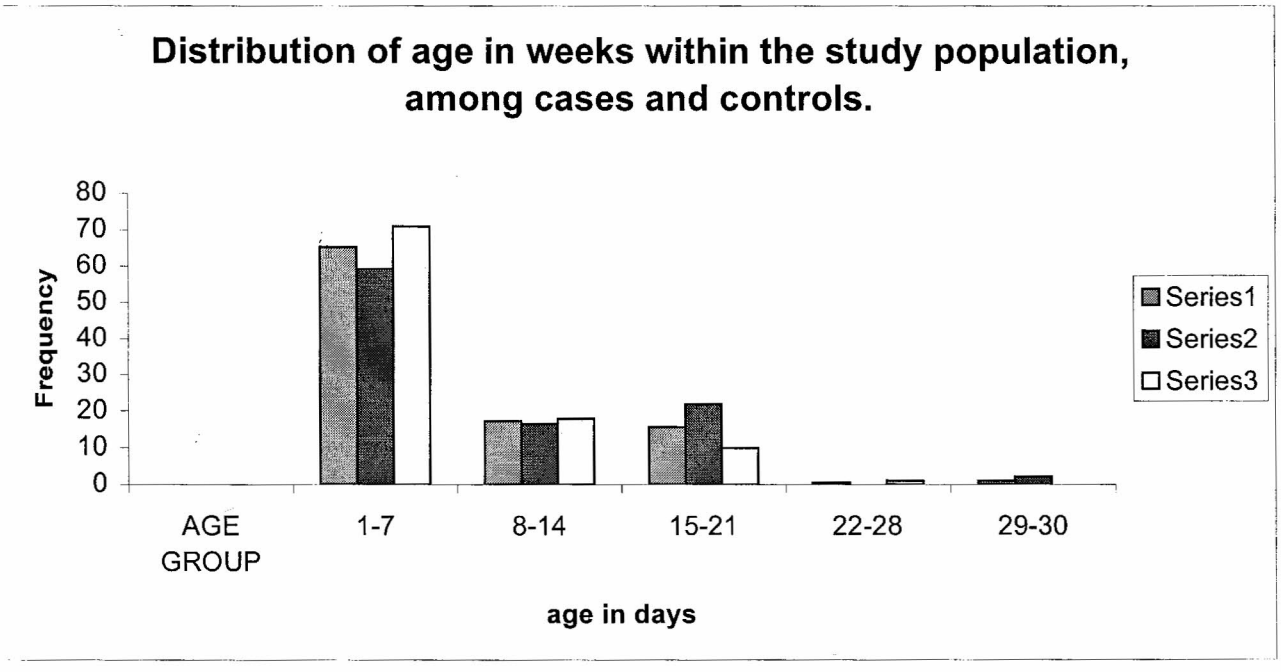
Sex

The male to female ratio in the study population of 191 babies was 2:1. Among cases (n=91) the sex ratio was 4:1 and among controls (n=100) 1.2 : 1.

Age

The age range in the study population was from 1 to 30 days with a mean of 7.7days. For cases, the mean age was 8.7 days and 6.8 days for controls. Sixty-three point five percent of the study population were seven days old or less. Fig 1 shows the age distribution in weeks for the study population, cases and controls (series 1,2 & 3 respectively).

Fig 1



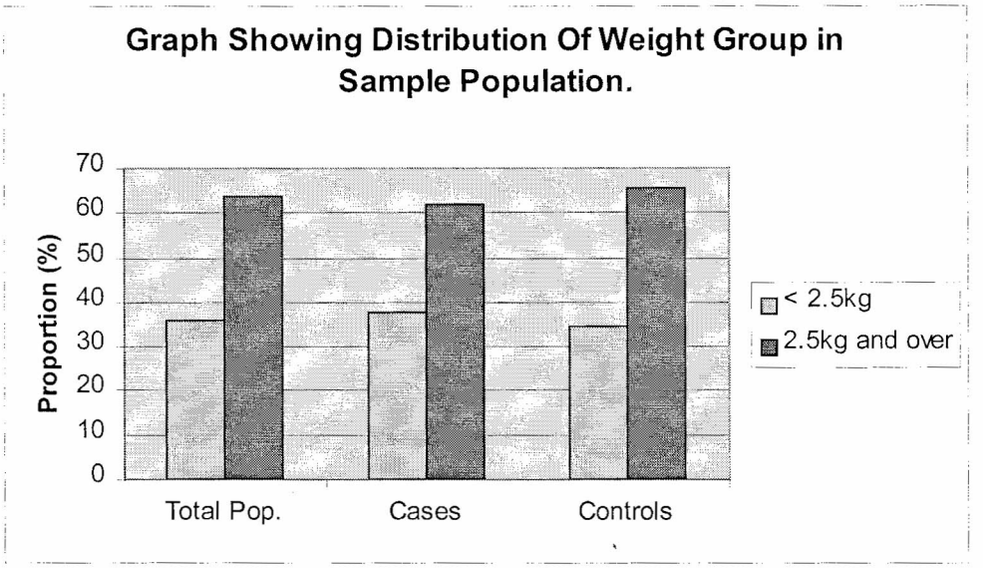


Fig 2

The weight range in the study population was from 1.0kg to 4.8kg. 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. In all the three groups: the study population cases and controls, the mean weight was 2.7kg (Fig 2).

Haemoglobin level

Generally, haemoglobin levels were lower among cases. Mean heamoglobin of the study population was 12.0mg/dl (range 2.9 to 20.0mg/dl). Among cases and controls, the mean was 11.3mg/dl and12.7mg/dl respectively. This gives a difference in mean of 1.4mg/dl and a 95% CI (0.35,2.45) suggesting that at 5% level of significance, the mean haemoglobin levels of cases and control were statistically different.

Fig 3 below compares the haemoglobin level below and above 10.0mg/dl among the cases and controls. There was a higher proportion of neonates among malaria cases with anaemia (haemoglobin, <10.0mg/dl) 33.7% compared to 12.9% in the control group. The difference between the two proportions was 20.8% (95%CI 20.66, 20.93), suggesting that the difference between babies with anaemia among cases compared to those in the control group is statistically significant.

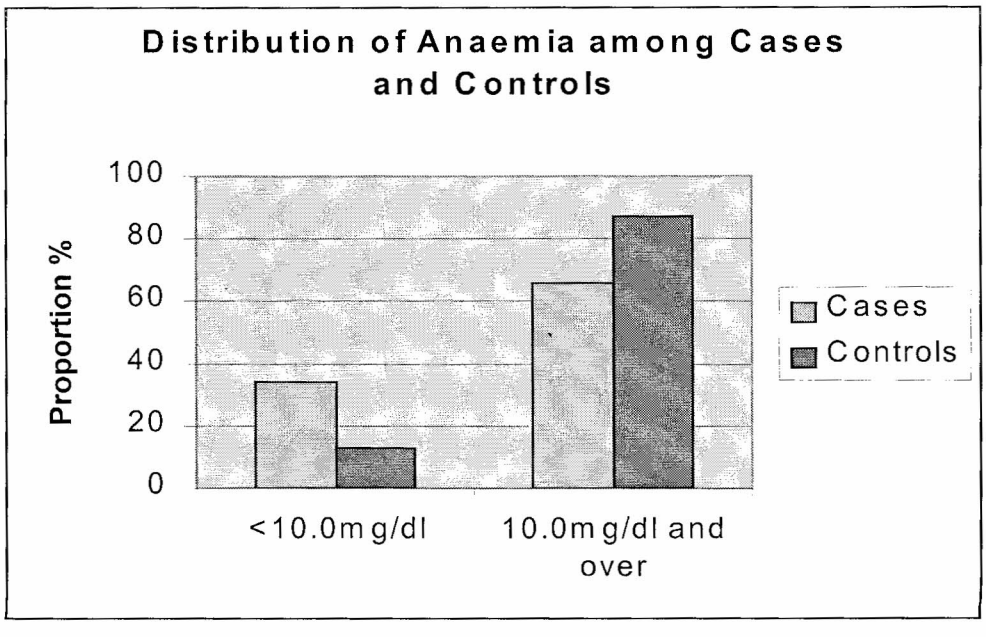


Fig 3

Other Variables

Antenatal attendance were 85% (34/40) and 71% (32/45) in the among controls and neonates with malaria.

Forty-one point two percent of the neonates in the study population were delivered by primiparous women. Records of parity were only available in only 9% of the study population on the parity. This variable was thus not analysed any further. The proportion

of neonates delivered in hospital were similar in all groups being 55.2% (48/87), 54.2% (26/48) and 56.4% (22/39) in the study population, control and cases respectively. Transfusion was required in 6.8%(13/191) of the patients in the entire study population. Babies requiring blood transfusion were found to be 61.5% among cases and 38.5% among controls. The population of cases requiring blood transfusion was 8.8% compared to those in the control group 5%. The difference in these two proportions was 33%; and (95% CI -0.037, 0.103) suggesting lack of significance.

Two case of transfusional malaria (blood transfusion being the source of parasites) were encountered.

Mortality among the controls was18% (18/25) and 7.7% (7/25) among cases of neonatal malaria. 95% CI of the difference in proportion was 0.009 to 0.197, suggesting that mortality was significantly higher in the non malaria ill babies than those with malaria. More babies died of all other causes of neonatal morbidity than from malaria.
Most of the deaths were in babies with neonatal tetanus; 3/7 deaths among cases and 7/18 in controls resulting in a total of 40% of the deaths. Twenty percent of deaths occurred in babies with sepsis and 16% in those with birth asphyxia. No autopsy results were available to ascertain the exact cause of death.

The association of various potential risk factors with neonatal malaria.

The analysis of the data revealed various associations summarised in table 3 below. There was a significant association between sex and malaria in neonates admitted to hospital with odd ratio of 3.3 among cases compared to the other non-malaria admissions. Statistically significant association was also found between malaria and haemoglobin level which persisted even when the effect of sex was taken into account. The Mantel- Haenzel weighted odds ratio was 2.8 (95% CI 1.19, 6.52).
The test for interaction was not significant p >0.521. This suggests that haemoglobin and sex act independently on malaria.

Table 3. Effect of Predictor Variables on Neonatal Malaria

Variables	Cases n=91	Control n= 100	Odds Ratio (95% CI)
Sex			
Male	73	55	1.00
Female	18	45	3.3(1.6- 6.7)
Hb group			
1 (0-9.9mg/dl)	29	9	1.00
2 (10-20mg/dl) Group 2	57	61	3.5(1.4-8.7)
ANC Attendance			
Yes	٥٢	٣٤	١.٠٠
No	13	6	0.43 (0.13-1.44)
Hospital Delivery			
Yes	22	26	1.00
No	17	22	1.10 (0.43-2.82)
Age Group			
1(0-7 days)	54	71	1.00
2(8-30 days)	37	29	(0.31-1.14)
Weight Group			
1(0-2.49kg)	22	22	1.00
2(2.5-5kg)	36	42	1.17 (0.52-2.63)
Outcome			
1 Discharged	84	82	1.00
2 Died	7	18	0.39 (0.14-1.06)

ANC attendance, hospital delivery, age (grouped as below or above one week of life) and weight (in two groups of below and above 2.5kg) gave no significant association with malaria in infants less than one month old when cases and controls were compared. Information was lacking in grouping the babies into various social classes of their mothers, it was therefore not possible to consider the association between socio-economic status and malaria in newborn babies.

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The clinical characteristics of malaria among cases.

Malaria alone was the final diagnosis in 26 of the 91 cases (28.6%). The other babies with malaria had it in conjunction with other illnesses. Table 4 shows the breakdown of the diagnosis occurring in association with malaria. The most commonly associated illness with malaria were sepsis and birth asphyxia.

Congenital malaria occurred in 59.3% (54/ 91) of the cases of neonatal malaria. These were babies who were less than 7 days old at the time of diagnosis. Plasmodium falciparum malaria species were identified as the parasite in all cases. Parasite density was generally low. Malaria parasites were reported as *heavy*, indicated as +++ (>20 parasite/field), *moderate* ++ (2-19 parasites/field) and *low* + (one parasite/field) (Etiene L 1980). There were no babies with heavy parasitaemia, 17.6% has moderate parsitaemia and 82.4% had low parasitaemia.

Of the 44 (36.1%) babies that weighed below 2.5kg (low birth weight), 8 were premature babies while 1 baby was small for gestational age. The true prevalence of babies presenting with weight less than 2.5kg (excluding preterms) was 18.3% in the study population.

Table 4 The Diagnosis Of Cases.

Malaria alone	26
Malaria with	
Neonatal Tetanus	8
Neonatal Sepsis	15
Neonatal Jaundice	7
Haemolytic Disease of the Newborn	2
Post tranfusion malaria	2
Birth Asphyxia	12
Prematurity	8
Bronchopneumonia	3
Bilirubin Encephalopathy (Kernicterus)	3
Others	5
Total:	**91**

Table 5: Presenting clinical features among cases of neonatal malaria.

FEATURE	N	%
Fever	63/68	92.6
Difficulty in breathing	28/30	93.3
Inability to feed	13/24	35.1
Pallor	27/39	69.2
Hepatomegaly	12/18	66.7
Jaundice	22/33	66.72
Lethargy	13/13	100
Irritability	10/10	100
Splenomegaly	4/11	36.4
Vomiting	7/14	50
Seizure (myoclonic jerks)	22/23	95.7
Apnoea	6/7	85.7
Abdominal distension	4/5	80
Abnormal cry	9/10	90
Yellow eyes	21/27	77.8
Anaemia	29/86	33.7

Table 5 shows the clinical characteristics of the study group. Generally, presenting symptoms were non specific with malaria indistinguishable from neonatal sepsis on clinical examination. The clinical features comprised mainly of fever, respiratory and neurologic symptoms. Other common features were poor feeding, poor weight gain and jaundice.

CHAPTER 5: DISCUSSION

The prevalence obtained in this study is similar to that obtained from previous studies in Nigeria. (Ibhanesebor 1995, Ezeoke AC 1985). An increasing prevalence has been observed especially in the last two decades. Results of studies from various malaria endemic areas reveal a range of 1.6 to 16.8% of parasitaemia in cord blood and 2.8 to 29% in neonatal blood (Table II). It is observed that prevalence have gradually increased over the years; 0.3% (Covell, 1950, Bruce-Chwatt 1952) from 1950s to 8% in the 1990s (Lehner, 1988; Diallo, S 1983; Ibhanesebor 1995).

It is however pertinent to note that the definition of congenital malaria differ between studies. While some workers refer to the detection of parasitaemia in neonatal blood as congenital malaria. (Fischer, PR.1997), other prefer to include the presence of clinical symptoms in association with parasitaemia. Some studies have confined their definition to babies less than 7 days old (Egwunyenga, 1995) with the justification that since there is no exo-erythrocytic stage, the cycle is shorter than the normal 10 –14 days. Some other studies have not taken this fact into consideration and described congenital malaria even after several weeks (Hulbert, 1992).

One conflicting result was, however, found in Nigeria in 1993. No case of congenital malaria was detected in a series of 101 pregnancies and their 105 newborn babies over a three month period.{Lamikanra, 1993 }. Relatively low prevalences of 2.97% and 2.94% were also obtained from maternal and cord blood respectively. It is probably that the women in this study differ from those of other studies in respect of their exposure to other risk factors; parity, use of prophylaxis or socio-economic factors.

The prevalence of 9.1% obtained in this study is probably an underestimation of the true prevalence because some cases of malaria positive smear would have been missed as not all admissions for the whole year were screened. Eighty-five percent of cases-notes were

retrieved. It is not known how many more cases of malaria would be among the missing 15% case-notes. Doing microscopic examination only once for malaria parasite also limits the chance of finding all parasitaemic cases. (Hulbert, 1992). Another reason to suspect that the observed prevalence is an under estimation is the fact that cord blood were not examined. In a study in Zaire higher percentages of parasitaemia were found when both cord blood and neonatal blood were considered together in the determination the prevalence of congenital malaria (Nyirjesy, 1993). Without considering cord blood some cases would have been missed especially if they were mild and do not require hospitalization. Since the population of infants studied were those of ill babies, the prevalence rate obtained in this study will relate more with symptomatic congenital malaria disease (CMD) rather than with asymptomatic congenital malaria infection (CMI) cases which is usually a higher rate.

The cases and controls were retrospectively collected from hospital admission records. This is a selective population and may have more cases of severe neonatal malaria than the normal population. However, since most neonatal malaria cases are likely to be mild, only the few severe cases would be admitted. The majority of cases would not reach the hospital or would be treated on out patient basis. This would actually lead to under estimation rather than an over estimation of the true prevalence.

Age and weight are potential confounders but were found to be similarly distributed in the study population among cases and control. The control group is therefore a reasonable representation of the total population where the cases have been drawn. The mean weight in this study (2.7kg) was lower than the mean weight of neonates in Nigeria. In a study of 3922 consecutive term, singleton, live births, mean weight in males were 3.27kg and 3.18kg in females (Fakeye and Adetoro 1989). The lower value obtained in this study could be due to ill-health in the babies studied.

Since the babies in this study were born outside the study hospital, it was not possible to determine their birth weight. Weight within then first week of life is a close approximation to birth weight as weight loss occurs in the first few days of life due to

physiological dehydration before birth weight is regained (Azubuike and Nkanginieme 1999). This process could take 7-10 days. It is however subject to individual variation. 18.3% cases of *low birth weight* (babies < 2.5kg and one week old or less who were not born preterm) would therefore only approximate to real incidence of low birth weight (LBW) babies among cases of neonatal malaria in this study. Previous studies have found frequency of LBW in associated with malaria to be between 11.1-13.2% in Nigeria (Dawodu and Laditan, 1985; Briggs unpublished, Ozuamabo and John 1989 in Brabin et al 1999).

There is no doubt about the effect of placental malaria on decreasing fetal birth weight. Early contentions have been put to rest with results of large studies which have given ample evidence (Brabin et al 1991,{McDermott, Wirima, et al. 1996). The acceptance of this fact is evident in the suggestion that birth nomogram could become a promising practicable indicator to monitor the success or failure of any intervention against malaria during pregnancy (Brabin et al 1999). As birth weight is affected by a number of factors such as eclampsia, hypertention and prematurity as well as placental malaria, this may not be an accurate scale or indicator. Incidence of congenital malaria or cord parasitaemia if accurately, easily and cheaply diagnosed may be a more sensitive indicator to use.

The male to female ratio in the control group was comparable to the overall hospital admissions (1.2: 1 versus 1.3: 1). However, odds of male babies having neonatal malaria was higher compared to female babies. (OR 3.3 95% CI 1.6 to 6.7). The odds ratio reveal the role of sex as a risk factor for neonatal malaria in this population of infants studied. Similar observation was made in a study in Malawi. An association was found between male sex and umbilical parasitaemia (OR 1.6 95% CI 1.1-2.3){Redd, Wirima, et al. 1996}. In another study in Nigeria, the male to female ratio among neonatal malaria was 1.7:1. (Ibhanesebhor, 1995). The exact reason for this increase risk in male neonate is not known. However, male neonates are known to have higher risk of infections. For example, male neonates have been observed to have higher susceptibility

to infection such as septisaemia and urinary tract infections (Thompson DJ 1966; Okolo AA 1985).

There were more babies (59%) who were less than seven days old among cases of neonatal malaria. This reveal that congenital malaria is more common than acquired malaria in this study population. Similar observation have been made by other workers. Ibhanesebhor found 75% among cases at Benin in Nigeria.

Antenatal care and hospital delivery were not significantly associated with NNM in this study. This could be due to the weakness of using routine records in the study. About 50% of patients had history of antenatal care recorded. It was not possible to determine the length of ANC undertaken and most importantly no way of ascertaining drug compliance. ANC care is a weak variable for assessing association in areas where chemoprophylaxis is not given under supervision or where there is high incidence of drug resistance to the prophylaxis being used. Hospital delivery may ensure greater chance of complete treatment of peripartum malaria in the mother and expected to affect the incidence of neonatal malaria. This study was unable to determine this assertion. It has been established that the primigravidae are more prone to malaria and the peripartum effect of malaria more seen in them and their off-spring. It was not possible to determine this fact as only 17 out of 91 cases had the information on parity of mothers.

The clinical features recorded in the case notes were incomplete with gross underreporting. The records were not detailed to answer all the questions in the questionnaire. And this is a problem and inadequacy of using routine records retrospectively for a detailed and in depth survey of this nature. In a prospective study, all the relevant information would be available and answers would be provided. The large proportion of missing values made it impossible to make accurate deductions from the findings.

There was also evidence of inaccurate records. Incidence of yellow eyes was more than that of jaundice. This is doubtful, as usually, mothers do not often notice yellow eyes

until seen on examination by attending physician. Pallor was found in 67% of neonates where as from laboratories records anaemia was 34%. This discrepancy would however be due to the rather low cut-off (10mg/dl) of haemoglobin level used for anaemia in this study. The range of normal haemoglobin levels for healthy newborn babies is 14-20mg/dl and levels less than 12mg/dl are considered abnormal (Emordi I 1999).

In this population of unwell babies, anaemia was found in 34% of cases of neonatal malaria compared to 13% among the controls. The fact that the population studied are unwell babies would mean that were the haemogloblin level obtained be a consequence of bias, it would only lead to an under-estimation and not to an over-estimation. More babies died in the control group of severe neonatal problems such as neonatal tetanus, overwhelming septisaemia, severe birth asphyxia and neonatal meningitis.

Inspite of the severe nature of their diseases cumulating in more deaths, cases of anaemia were still recorded in more than twice the number of babies with malaria than these fatally ill neonates in the control group. If almost 10% of neonates are at three times at risk of having anaemia in the first month of life, they would be more prone to malaria morbidity and mortality by the time they are four to six months old and have lost an appreciable part of the protective immunity acquired transplacentally. Population studies are required to ascertain the true incidence of anaemia resulting from malaria in the neonatal period.

This study was undertaken within the hospital comparing malaria and non-malaria cases among ill babies on hospital admission for ease of case ascertainment and access to fast, cheaply obtained information. The flaws have been pointed out. There may exist risk factors which are obscured as a result of using a population of ill children. This could include or relate to issues of access to health care facilities and cost of care. The results would however be an under-estimation and not an over-estimation of the magnitude of the problem and add to the justification for a prospective population study.

Before a proper prospective study is undertaken, it would be necessary to clearly define congenital malaria, and differentiate congenital malaria infection (asymptomatic) from congenital malaria disease (symptomatic). The issue of deciding prevalence from either cord or peripheral neonatal blood would also need to be addressed.

CHAPTER 6:CONCLUSION

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 pact

Population based estimates of neonatal and congenital malaria.

The marked variations have observed in prevalence rates could be due to the use of different sampling frames as definition of congenital and neonatal malaria differ from study to study. Another reason could be that the various pecularities of different locations such as differences in levels of endemicity, use of malarial prophylaxis and degree of plasmodium resistance. This calls for epidemiological research in different localations. True population estimates will give an indication of the magnitude of the problem and assist in allocation of scarce resources for appropriate control measures.

Risk factors for neonatal and congenital malaria.

Not much is known in this area. Since congenital malaria is a complication of malaria in pregnancy, the risk factors of malaria in pregnancy would be surrogate for congenital malaria. Much more work has been done in malaria in pregnancy. However, there are still areas of knowledge gap such as to the exact mechanism of increased susceptibility of infection by the primigravidae, why the placenta harbours so much plasmodium parasites, HIV and malaria and controversy surround the benefit of insecticide treated bednets. (Menendez, C 1995). There is also need to find an effective, cheap and safe drug for prophylaxis.

Little is known about the specific role of foetal and neonatal biological factor, such as the immune system and how haemoglobins act in preventing parasites from infecting red blood cell. Enviromental and social factors predisposing to increased incidence of neonatal malaria remain unexplored.

Clinical features and natural history of neonatal and congenital malaria

This study has revealed that neonatal malaria is often unrecognised by physicians. As it is not sought for and often exist in association with other neonatal diseases, it is often missed. The clinical features are similar to those of other neonatal conditions and the course is not well defined. A policy of including microscopic investigation for malaria parasite smear as part of the routine investigation of all sick infants requiring hospital admission in a malaria endemic area or screening of all newborn infants needs to be considered. As treatment of malaria does not preclude congenital malaria, all infants of mothers with malaria in the last trimester of pregnancy may need to be screened and treated whether they manifest clinical features or not. Decision on such policies should be evidence based on well designed randomised controlled studies.

Immediate and long term impact of congenital malaria on immunity and clinical manifestation of malaria infection.

In this study, malaria was strongly associated with anaemia. In early infancy, anaemia secondary to malaria has not been a significant clinical problem. Chronic anaemia may however predispose to increased morbidity and mortality in later infancy as maternal immunity wanes. This observation requires investigation.

The long term impact on immunity is difficult to predict and has long been a topic of debate. In recent times, the issue of long term impact of malaria control on development of immunity in early life has received some attention. Snow and colleagues (Snow 1997) found that the populations with the highest transmission intensities had the lowest risk of severe disease, while those with the lowest transmission intensities were found to have the greatest risk of disease. They proposed that *a critical determinant of life time disease risk is the ability to develop clinical immunity early in life during the period when other mechanisms operate.* They went further to conclude that in high endemic areas, transmission control measures may reduce immunity and cause a change in the clinical manifestation of the disease

In examining this finding in the context of the present work on the increasing prevalence of neonatal malaria and associated risk factors, a number of questions arise.

- Does this mean that control measures of malaria in pregnancy would lead to less exposure of the foetus and infant and less immunological response?

- Is the recent increase in prevalence and severity of congenital malaria as observed 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 or

- Do other obscure risk factors such as HIV play a role in the increasing incidence of congenital malaria?

These and other research questions identified require urgent answers.

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APPENDIX:

NEOMAL '98 QUESTIONNAIRE FORM

A. General Information:

Hospital No:…….. Weight on admission:……..
Name: …….. Sex:……
Age on admission (in days):…… Duration of admission (in days):……..

B. Essential Data:

MP Positive: …….. Negative: ……. Not done: …… Done no result: ……
Date of MP investigation: …… Age of patient (at time of investigation): ……..(in days)
Haemoglobin level: …… Age: ……

C. Mother's Record:

Parity:…….. Duration of Pregnancy: ……..
ANC Yes …….. No …….. Unknown ……
Where ANC was undertaken: ……..…… Not recorded: ……
Health facility: ……. Home: ……
TBA: …….. Others: ……
Where delivered: ……
Use of anti malarials in pregnancy: Yes: …… No: ……..

D. Symptoms:

	Yes	No	Unknown
Fever			
Cough			
Diarrhoea			
Vomiting			
Refusal of feeds			
Others			

E. Signs:

	Yes	No	Unknown
Pallor			
Jaundice			
Dyapnoe			
Tache/cardia			
Hepatomegaly			
Splenomegaly			
Oedema			
Lethargy			
Imitability			
Seizures			
Tone (n) ….. ↓…. ↑ ….			

Management

Drugs …….. (2) …….. (3) ……..
Antimalarials ……
Blood Transfusion Yes …….. No …….. Unknown ……..

G. Differential Diagnosis …… ……..
Diagnosis on discharge ……
OUTCOME: Discharged …….. Died ……

H. Results of Lab Investigation

FBC Total WBC …… Differential N ……

E .....
L .....
B .....

E & U
Semin bilimbin Total ..... Diff .....
CSF Gross picture .....Microscoping & Culture
.....
Protein .....Sugar
.....

Others .....