Congenital malaria: an overview

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Abstract: Congenital malaria is a public health concern globally. This report reviews publications on congenital malaria in the last two decades (1990-2010) with the view to establishing the current global epidemiological trends and the public health implications. A Medline Entrez-PubMed search was performed and published studies on congenital malaria in the last two decades (1990–2010) were identified. A combination of key words “congenital malaria” were used for the search which yielded 180 publications as of December 2010. Of the 180 publications, 93 were within the period 1990 to 2010. Bibliographies of all publications selected were checked for additional relevant references and were obtained and included in the review. The critical issues identified and discussed include the (i) current global trends of congenital malaria; (ii) controversies associated with the frequency of occurrence of congenital malaria; (iii) mechanism and clinical features; (iv) role of maternal HIV infection (v) effects of congenital malaria on infants; (vi) diagnostic challenges; and (vii) treatment considerations. Operational research into various aspects of congenital malaria is essentially lacking as many unresolved issues requiring urgent scientific investigation abound. Public health policy on malaria control should integrate guidelines on congenital malaria management and control.

Keywords: Plasmodium; malaria, congenital; diagnosis, treatment, pregnancy

Introduction

Malaria continues to remain the most severe and complex health challenge facing the vast majority of the countries in tropical and sub-tropical regions of the world. It is one of the most predominant infectious diseases associated with underdevelopment, poverty and ignorance (Worrall et al., 2005). Malaria is still a major contributor to high rate of the global infectious disease-related mortality and morbidity particularly in Africa, South-East Asia, Eastern Mediterranean Regions and parts of South America (WHO 2008). In the World Malaria Report (WMR) of 2009 the World Health Organization (WHO) estimated that 243 million cases of malaria occurred worldwide in 2008, and majority of the cases (85%) occurred in the African Region, followed by the South-East Asia (10%) and Eastern Mediterranean Regions (4%) (WHO 2009). According to the WMR, malaria accounted for an estimated 863,000 deaths in 2008, of which 89% were in the African Region, followed by the Eastern Mediterranean (6%) and the South-East Asia Regions (5%) (WHO, 2009).

Plasmodium falciparum is considered as more dangerous than the other three species (P. vivax, P. malariae and P. ovale) of the human malaria parasites because it is responsible for virtually all the severe malaria cases and deaths (WHO, 1997; 2000a). The sub-Saharan Africa remains the region with the highest burden of malaria accounting for nearly 90% of global malaria deaths because P. falciparum is the predominant species and the most effective malaria vector - the mosquito Anopheles gambiae - is the most widespread in the region and the most
difficult to control (WHO, 1992). However, increasing number of reports has indicated that *P. vivax* is also associated with significant malaria disease especially in parts of Asia and South America (Nimir et al., 2006; Guerra et al., 2010).

In areas of high malaria endemicity most of the malaria-associated morbidity and mortality are recorded in young children (Uneke, 2009a; Snow et al., 2004). Available evidence indicates that pregnant women are also highly vulnerable to malaria in these endemic areas (Uneke, 2007a; Tagbor et al., 2008; Schantz-Dunn & Nour, 2009; Davis et al., 2010). However, the impact of the malaria burden is much more devastating among children particularly in sub-Saharan African region. Almost all of the malaria deaths in sub-Saharan Africa occur in children below five years of age and this translates to the child mortality of nearly 1 million each year (DFID, 2004; Hopkins et al., 2007; WHO, 2008). Indeed, a child dies of malaria every 30 seconds, a death toll of about 3000 children every day in the sub region alone (WHO, 2003, 2008). Reports from studies and reviews within the last few years are of the consensus that malaria causes at least 20% of all deaths in children under 5 years of age in sub-Saharan Africa (Rowe et al., 2006; Gyapong & Garshong, 2007; Hopkins et al., 2007; Sharp et al., 2007). However, it is pertinent to state that many of the reports presenting data on the burden of malaria among young children appear not to focus on infant specifically (Larru et al., 2009). This is presumably because it is thought that infants under the age of six months are relatively protected against clinical malaria as a result of maternal antibodies transfer and the presence of foetal haemoglobin (Snow et al., 1998; Klein Klouwenberg et al., 2005; Duah et al., 2010). However, findings from a number of hospital-and community-based studies within sub-Saharan Africa suggest that the burden of malaria during the six first months of life may be substantial (Afolabi et al., 2001; Nweneka & Eneh 2004; Larru et al., 2009). Thus the burden of malaria among young children might be higher than what is generally estimated.

The high burden of childhood malaria in endemic regions of the world has been associated with malaria during pregnancy (Murphy & Breman 2001). In sub-Saharan Africa for instance, malaria affects an estimated 24 million pregnant women (Steketee et al., 2001) and each year between 75,000 and 200,000 infant deaths are attributed to malaria infection in pregnancy globally (Steketee et al., 2001; WHO, 2003). Pregnant women residing in malaria endemic areas often experience a high frequency and density of parasitemia, resulting to high rates of maternal morbidity including fever and severe anaemia, with abortion and stillbirth, and with high rates of placental parasitisation (Brabin 1983; Steketee et al., 2001). Severe parasitization of the placenta by malaria parasites particularly *P. falciparum* and *P. vivax* which is known as placental malaria can result in transplacental transmission of the parasite to the foetus and consequently to congenital malaria (Brabin, 1983; Menendez & Mayor 2007; Uneke, 2007b).

Congenital malaria resulting from the transplacental transmission of malaria parasites particularly *P. falciparum* from mother to foetus, is well described by some early reports (Schwetz & Peel 1934; Covell, 1950; Reinhrdt et al., 1978). However the precise definition of congenital malaria is still a subject that is not devoid of controversy debatable, but symptoms usually occur 10 to 30 days postpartum (Behrman et al., 2004). The disease can be observed in a day-old baby or be delayed for weeks or months (Hashemzadeh & Heydarian, 2005). In 80% of the cases of congenital malaria, the most common clinical features include fever, anaemia, and
spleenomegaly (Remington & Klein, 1995). Some reports indicate that other signs and symptoms which could manifest are hepatomegaly, jaundice, regurgitation, loose stools, and poor feeding, and occasionally, drowsiness, restlessness, and cyanosis (Remington & Klein 1995; Hashemzadeh & Heydarian 2005).

In recent times there has been renewed public health concern about the increase in the burden of congenitally acquired infectious diseases including malaria (McGovern et al., 2007). The global drive towards making motherhood safer, improving perinatal outcome and enhancing neonatal health has made congenital malaria an important public health issue (Halin, 2002; van Geertruyden et al., 2004; Bhutta et al., 2005). The purpose of this paper was to review some current epidemiological developments in congenital malaria and to highlight the public health implications with respect to the management of congenital malaria, public health policy guidelines and operational research needs. In this review, congenital malaria was defined as the presence of asexual stages of malaria parasites in cord blood smear at delivery or peripheral blood smear of the baby in the first 7 days of life, irrespective of clinical symptoms.

To achieve the objective of this paper, a Medline Entrez-PubMed search was performed and reported studies on congenital malaria in the last two decades (1990–2010) were identified. A combination of key words “congenital malaria” were used for the search which yielded 180 publications as of December 2010. Of the 180 publications, 93 where within the period 1990 to 2010. The 93 publications were then selected for the review. Bibliographies of all publications selected were checked for additional relevant references and were obtained and included in the review. Particular attention was paid to articles providing information on the prevalence of congenital malaria, the clinical significance, role of maternal HIV infection, diagnosis and treatment considerations, and policies on prevention and control.

**Congenital malaria: rare or frequent event**

For a long time the frequency of the occurrence of congenital malaria remained a subject of controversy with many reports before the 1970s describing it as an extremely rare event (Covell, 1950; Bruce-Chwatt, 1952; Logic & McGregor, 1970). Some other reports in the 1980s however noted that the low reported incidence of congenital malaria particularly in Africa was surprising since malaria occurs more commonly in pregnancy (McGregor, 1983; Lehner & Andrews, 1988). More recently, findings from a number of studies from sub-Saharan Africa have described congenital malaria as a rare event largely because the prevalence of malaria parasite in cord blood or neonatal blood was very low and few newborns developed clinical disease during the first few weeks of life (Lamikanra 1993; Djibo & Cenac, 2000; Adachi et al., 2000; Sule-Odu et al., 2002). These studies had speculated that the effectiveness of the placenta to restrain the malaria parasite passage to the foetus and the remarkable capacity of the foetus to resist infection as demonstrated by Miller & Telford (1997) was responsible for the rarity of congenital malaria. It was further argued that the resistance to congenital malaria is enhanced by physical barrier of the placenta to infected red cells, the passive transfer of maternal antibodies, and the poor environment afforded by foetal erythrocytes for plasmodial replication, due to their foetal haemoglobin composition and low free-oxygen tension (Miller &
Telford, 1996). Moreover, because neonates in Africa rarely present with clinical disease, congenital malaria was assumed to be of little clinical importance in areas of high malaria endemicity (Steketee et al., 1996a).

Interestingly however, evidence from most of the cross-sectional studies conducted in parts of sub-Saharan Africa on congenital malaria within the last two decades (1990-2010) clearly indicates that congenital malaria is not as uncommon as previously thought. In fact, congenital malaria prevalence in majority of the cross-sectional studies within the last five years (2005-2010) ranged from 10.8% to as high as 54.2% (Table 1). In most of these recent reports there was a strong association between placental malaria and umbilical cord parasitaemia which was suggested to be responsible for the congenital malaria (Uneke, 2007a, b, c). Until recently, it was unclear if the presence of malaria parasites in umbilical cord blood was an indication of infection acquired antenatally or a result of contamination with infected maternal blood at delivery. In a 2006 report however, Malhotra et al. (2006) demonstrated from their study in Kenya that malaria parasites identified in cord blood were acquired antenatally by transplacental transmission of infected erythrocytes and that primigravid and secundigravid women with placental malaria were at increased risk for congenital infection. This finding therefore confirmed earlier reports which had noted that the rate of transplacental transmission of malaria in endemic region was high and suggested that the placental barrier is not very effective when infected with malaria parasites (Redd et al., 1996; Brabin et al., 2004).

Table 1: Prevalence of congenital malaria as reported by various studies in malaria endemic areas of sub-Saharan Africa from 1990-2010.

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Study location</th>
<th>Prevalence of congenital malaria (%)</th>
<th>Year of publication</th>
<th>Study authors/reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional</td>
<td>Lagos, Nigeria</td>
<td>13.6</td>
<td>2010</td>
<td>Lesi et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Western Kenya</td>
<td>10.8</td>
<td>2009</td>
<td>Perrault et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Muheza, Tanzania</td>
<td>19.1</td>
<td>2008</td>
<td>Mwangokia et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Calabar, Nigeria</td>
<td>13</td>
<td>2008</td>
<td>Ekanem et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Sagamu, Nigeria</td>
<td>10.9</td>
<td>2008</td>
<td>Sotimehin et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Ibadan, Nigeria</td>
<td>5.1</td>
<td>2007</td>
<td>Falade et al.</td>
</tr>
<tr>
<td>Retrospective</td>
<td>Sagamu, Nigeria</td>
<td>17.4</td>
<td>2006</td>
<td>Runsewe-Abiodun et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Lagos, Nigeria</td>
<td>15.3</td>
<td>2006</td>
<td>Mukhtar et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Ile-Ife, Nigeria</td>
<td>54.2</td>
<td>2005</td>
<td>Obajunwa et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Southern Cameroon</td>
<td>7.8</td>
<td>2005</td>
<td>Akum et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Sagamu, Nigeria</td>
<td>0.7</td>
<td>2002</td>
<td>Sule-Odu et al.</td>
</tr>
<tr>
<td>Prospective survey</td>
<td>Niamey, Niger</td>
<td>13.3</td>
<td>2000</td>
<td>Djibo &amp; Cenac</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Dar-es Salaam, Tanzania</td>
<td>0.33</td>
<td>2000</td>
<td>Adachi et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Ibadan, Nigeria</td>
<td>15.0</td>
<td>2000</td>
<td>Olowu et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Ibadan, Nigeria</td>
<td>2.6</td>
<td>1997</td>
<td>Achidi &amp; Salimonu</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Jos, Nigeria</td>
<td>2.82</td>
<td>1997</td>
<td>Egwunyenga et al.</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>Various sites in SSA</td>
<td>23.0</td>
<td>1997</td>
<td>Fischer</td>
</tr>
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</table>
It is thus not very unlikely that early reports which indicated that congenital malaria was a rare event in endemic areas may have underestimated the prevalence of the disease since transplacental transmission of malaria parasites was not an uncommon event even in semi-immune women who usually have high levels of anti-malaria acquired immunity (Menendez & Mayor, 2007). It is pertinent to add that there exist a number of factors which to a large extent influence the estimation of congenital malaria. Menendez and Mayor (2007) described these factors as (i) differences in the definition of congenital malaria; (ii) levels of maternal immunity; (iii) the type of blood sample examined (peripheral blood of neonates or cord blood); (iv) the expertise in blood-smear examinations; (v) the method of parasite detection (Giemsa staining or polymerase chain reaction (PCR); or even (vi) a reflection of true environmental differences. The lack of consideration of these factors could give rise to congenital malaria underestimation. For instance Perrault et al. (2009) found 0% of cord blood infection by microscopy and 10.8% of cord blood infection by PCR in the same population. These differences are the major limitations in the comparison of studies on congenital malaria and so the interpretation should be done cautiously. Despite finding that 13.3% of neonates examined had malaria parasite Djibo & Cenac (2000) indicated they found no cases of congenital malaria with clinical signs in their study. Furthermore four studies from various parts of Nigeria which examined both umbilical cord blood and neonatal blood for malaria parasites observed that the frequency and density of parasitaemia were consistently higher in cord blood than the neonatal blood (Lamikanra, 1993; Egwunyenga et al., 1995; Obiajunwa et al., 2005; Mukhtar et al., 2006). Therefore a proper estimation of congenital malaria must take these influencing factors into consideration to avoid underestimation of the prevalence of the disease. The stark reality however, is that congenital malaria is no longer a rare event.

Mechanisms and clinical features of congenital malaria

In spite of the increase in the number of recent reports indicating that congenital malaria frequently occurs, the mechanism of transplacental passage of the malaria parasite from mother to foetus is still obscure. It has been postulated that the possible mechanisms include direct penetration through chorionic villi, premature separation of the placenta, and the possible physiologic transfusion of maternal red blood cells to the foetal circulation in utero or at the time of delivery (De Silva et al., 1982; Menendez & Mayor, 2007; Reynolds et al., 2007). A number of previous studies have identified many other factors that directly influence the occurrence of
congenital malaria. These factors include: (i) pre-existing level of malaria immunity in the pregnant woman (Hviid, 2004; Bir et al., 2006; Rogerson et al., 2007); (ii) occurrence of severe malaria during pregnancy (Lagerberg, 2008; Coll et al., 2008); (iii) absence of immunity especially pregnant women travelling to endemic areas (Coll et al., 2008); (iv) placental malaria especially among primigravid and secundigravid women (Uneke, 2007c; 2008); and (v) maternal human immunodeficiency virus (HIV) infection (Uneke, 2007c; Perrault et al., 2009).

The onset of symptoms in congenital malaria typically occurs at 10-30 days postpartum (Behrman et al., 2004), which is the estimated half-life of maternal immunoglobulin G in the infant (Reynolds et al., 2007). The most common clinical features in 80% of cases are fever, anaemia, and splenomegaly (Remington & Klein, 1995) and these features can be observed in a day-old baby or in some cases be delayed for several weeks or even months (Hashemzadeh & Heydarian, 2005). Other signs and symptoms include hepatomegaly, jaundice, regurgitation, loose stools, and poor feeding, and occasionally, drowsiness, restlessness, and cyanosis can also be seen (Hashemzadeh & Heydarian 2005; Remington & Klein 1995; Ibhanesebhor, 1995). The delay in the onset of the disease has been attributed to factors that may protect the infant initially, particularly infants born to mothers residing in endemic areas. These factors include foetal haemoglobin, abnormal haemoglobins that are resistant to malarial infection, the secretion of lymphocytes or macrophage-derived toxic substances across the placenta to foetal circulation, and partial malaria chemotherapy during pregnancy (Reynolds et al., 2007).

Effect of maternal HIV infection on congenital malaria

The human immunodeficiency virus (HIV) infection has been described as a major factor that is contributing to worsen the burden of malaria in most endemic areas particularly in sub-Saharan Africa (Abu-Raddad et al., 2006). Evidence abound indicating that HIV infection interacts negatively with malaria, with each disease driving the progression and transmission of the other (Whitworth et al., 2000; French et al., 2001; Patnaik et al., 2005). Some studies have demonstrated that HIV increases the risk of clinical and severe malaria, while malaria increases HIV replication in vitro and in vivo (Xiao et al., 1998; Whitworth et al., 2000; French et al., 2001; Patnaik et al., 2005; Kamya et al., 2006). Both HIV infection and malaria are known to critically intersect in pregnancy and have serious consequences in pregnant women, their foetuses and their infants (Ticconi et al., 2003; ter Kuile et al., 2004). It is estimated that approximately 1 million pregnancies per year are complicated by co-infection with malaria and HIV in sub-Saharan Africa (WHO, 2004). However, whether the dual infection with malaria and HIV in pregnancy increases the risk of congenital malaria is yet to be unequivocally established, as studies examining these relationships are few and have inconsistent findings and a wide range of unanswered questions (ter Kuile et al., 2004; Perrault et al., 2009; Uneke, 2009b).

Nevertheless, in a recent report from Western Kenya, Perrault et al. (2009) demonstrated that malaria and HIV co-infection in pregnancy increased placental parasite density and the rate of antenatal malaria transmission. The authors found that HIV serostatus was strongly correlated with cord blood infection, suggesting that HIV may impact congenital malaria primarily by allowing for higher parasite densities in the placenta (Perrault et al., 2009).
finding was consistent with an earlier report by Steketee et al. (1996b) who showed via a multivariate analysis that HIV infection was an important determinant of umbilical cord parasitaemia and added that HIV potentiates malaria infection in the umbilical blood of newborns especially in multigravidas. In addition, findings from another early study noted that HIV infection was associated with umbilical cord parasitaemia in univariate analysis and was probably acting as surrogate marker for maternal malaria infection (Reed et al., 1996). Reports from the 12th World AIDS Conference in Geneva also provided additional information from various researchers indicating that the presence of HIV may reduce a pregnant woman’s ability to control the perinatal transmission of malaria (Anderson, 1998).

On the contrary, reports from Kisumu, Kenya (van Eijk et al., 2002) and rural Malawi (Verhoeff et al., 1998), did not observe any consistent effect of maternal HIV on congenital malaria. Although it has been demonstrated that maternal HIV infection induces pathological changes in the placenta that potentially could interfere with the materno-fetal transfer of antibodies, the mechanism of this process and whether a decreased transfer of antibodies to some malaria antigens has an impact on increased susceptibility to congenital malaria is not known (WHO, 2005). Clearly more research is required to properly elucidate this interaction between malaria and HIV with respect to congenital malaria.

**Effects congenital malaria on infants**

There is a dearth of studies on the effects of congenital malaria on infants. The few available studies providing information on the burden of malaria in early infancy, especially the neonatal period reported a wide range of results that were inconclusive and contradictory (Runsewe-Abiodun et al., 2006; Ekanem et al., 2008; Mwaniki et al., 2010). The direct burden of neonatal malaria infection in terms of prevalence and outcome is therefore not well described in malaria endemic areas. Available evidence however indicates that some newborns in endemic areas who are parasitaemic at birth, the parasites spontaneously clear without the newborn ever becoming ill (Lesko et al., 2007). The protective effect of the maternal antibodies passed to the newborn and also the protective role of the foetal haemoglobin in slowing the rate of parasite development are thought to be responsible for the parasite clearance (Sutherland et al., 2007; Moormann, 2009). In malaria endemic areas parasite clearance rates ranging from 87% to 100% have been documented (Obajunwa et al., 2005; Mukhtar et al., 2006).

Congenital malaria in some newborns particularly those whose mothers are non-residents of malarious areas, could be life threatening. The presence of malaria parasites in cord blood or in the asymptomatic newborn may be related to an increased risk of anaemia in infancy (Remington & Klein, 1995; Ndyomugyeniy & Magnussen, 2000; Hashemzadeh & Heydarian, 2005). There is sufficient evidence indicating that malaria causes anaemia through haemolysis and increased splenic clearance of infected and uninfected red blood cells and cytokine-induced dyserythropoiesis (Menendez et al., 2000; Nagel, 2002; Ekvall, 2003). If untreated this could result in life-threatening anaemia, metabolic acidosis and, death (Ekvall et al., 2001; Crawley, 2004). In a comprehensive review on congenital malaria, Menendez & Mayor (2007) noted that newborn exposure to blood-stage malaria antigens may have profound long-
term effects during infancy and childhood by priming the immune responses of the foetus, by inducing immune tolerance, which could result in a reduced (priming) or increased (immune tolerance) susceptibility to malaria in the infant and child. This is however subject to further investigation and confirmation.

**Diagnosis of congenital malaria and the challenges**

The diagnosis of malaria in most developing countries particularly in sub-Saharan Africa has been described as very challenging (Uneke 2008b). Early and accurate diagnosis and appropriate case management are essential to addressing congenital malaria, and have been advocated consistently by the World Health Organization as one of the main interventions of the Global Malaria Control Strategy (WHO, 2000). Hence prompt and accurate diagnosis cannot be overstated because the congenital malaria caused by *P. falciparum* that is not diagnosed and promptly treated is potentially rapidly lethal, especially in babies born to non-immune women (Menendez & Mayor, 2007).

A lot of diagnostic challenges are however, encountered when performing the diagnosis of malaria among the vulnerable groups like pregnant women and neonates in endemic areas such as sub-Saharan Africa (Uneke, 2008b). It is pertinent to state that most cases of congenital malaria are misdiagnosed initially because of the lack of specific symptoms and a general lack of awareness of this uncommon disease (Reynolds et al., 2008). Because malaria is endemic in this region, it is often difficult to diagnose, and thus report, "classic" congenital malaria (Uneke, 2007b). One of the major factors constituting diagnostic problems is that it is much more difficult to differentiate congenital malaria from those acquired from mosquitoes following delivery (Balatbat et al., 1995). Thus, the proponents of the rarity of congenital malaria have argued that the majority of the cases of malaria noticed in newborn infants in Africa were probably transmitted by mosquitoes (Uneke, 2007b). In fact, it was suggested that several diagnostic problems may also have been responsible for the increasing incidence of congenital malaria (Romand et al., 1994), in addition to the fact that the frequency of congenital malaria also depends on factors such as perinatal clearance of occult parasitemia, maternal immunity, and coexisting infections (Miller & Telford, 1997).

The diagnosis of malaria is established by the microscopic identification of organisms on Giemsa-stained smears of peripheral thick or thin blood smears. The Giemsa-stained smears diagnostic technique is widely used in most malarious areas for the diagnosis of congenital malaria. This technique is considered fraught by many pitfalls including: artifacts often mistaken for parasites; Maurer’s clefts often confused with Schuffner's dots, causing *P. falciparum* to be diagnosed as *Plasmodium vivax*; Babesia and Bartonella infections often mistaken for malaria; young gametocytes of *P. falciparum* often mistaken for *P. vivax* (WHO, 2000). In addition to this, there is a high chance of not finding the parasite by the microscopic method in babies that are having congenital malaria. Stauffer & Fischer (2003), had reported that a single smear without parasites is not sufficient to rule out malaria.

In Gaziantep, Turkey for instance, researchers studying congenital malaria were able to find malaria parasites only in repeat blood smears (Başpınar et al., 2006), and in India,
Congenital malaria was detected accidentally in cases investigated because they were essentially asymptomatic (Kothare et al., 1987). Findings from a recent study in Western Kenya indicated that the prevalence of placental and cord blood infections were 17.2% and 0% by microscopy, and 33.1% and 10.8% by polymerase chain reaction (Perrault et al., 2009). These findings suggest that the diagnosis of malaria in neonates using the microscopic technique is frequently missed and previous estimates of congenital malaria prevalence may be under-representative because of the limited sensitivity of light microscopy used in the majority of studies (Perrault et al., 2009). There is evidence proving that congenital malaria is usually mistaken for sepsis or infections in the TORCHS syndrome (toxoplasmosis, rubella, cytomegalovirus, herpes, and syphilis) (Hulbert, 1992). Therefore for the purpose of performing accurate diagnosis of congenital malaria, a good index of suspicion, a careful physical examination and repeated peripheral blood smears are therefore needed (Perrault et al., 2009). Sometimes, parasitemia cannot be shown on blood smear, and plasmodial antigen detection or polymerase chain reaction of the blood may be necessary (Perrault et al., 2009).

### Treatment of congenital malaria

There are very few recent studies that have provided information and data on appropriate and effective treatment of congenital malaria. However, there are no clearly established protocols for the clinical management of congenital or neonatal malaria. Menendez & Mayor (2007) noted in their review that in order to establish treatment recommendations it would be useful to distinguish between babies born to non-immune women, in which case congenital falciparum malaria, whether symptomatic or not, should be treated with quinine (10 mg/kg orally every 8 h, or same dosage in intravenous infusion until oral administration is possible). However there have been reports of high level of chloroquine resistance in the treatment of malaria by a number of studies. In Pakistan, chloroquine resistance of 26.66% was recorded among babies born with congenital malaria and this resulted in a mortality rate of 16.66% (Khichi et al., 2005).

In Nigeria a cure rate of 89.1% was recorded in the treatment of babies with symptomatic congenital malaria with oral chloroquine but the treatment failures subsequently received oral sulfadoxine-pyrimethamine with good outcome (Orogade et al., 2008). In another recent study by Harrington & Duffy (2008), quinine plus clindamycin was reported as being effective in the treatment of *P. falciparum* congenital malaria, and chloroquine for the treatment of other malaria parasites, such as *P. vivax*. The authors added that severe cases of congenital malaria should be managed with intravenous quinine or with intravenous artesunate, which has recently been approved for investigational use in some countries including the United States. The same authors have advised that primaquine is not required for infants with congenital *P. vivax* or *P. ovale*, but should be offered to their mothers after excluding G6PD deficiency (Harrington & Duffy, 2008). In a very recent study in India, it was reported that a baby with congenital malaria failed to respond to chloroquine treatment but responded well when oral artesunate was used (Avabratha et al., 2010).

The rising incidence of resistance to chloroquine which has been the drug of choice in malaria treatment necessitates investigation on the efficacy of other antimalarials for the
treatment of congenital malaria. There are very few studies reporting the use of drugs such as quinine, artesunate and mefloquine in neonates and the studies with use of oral artesunate is even scanty (Patel & Belsare, 2002; Ming, 2008). These drugs have been used effectively in older children and could be hence adapted for neonates to treat congenital malaria. In China, a study comparing the efficacy of artesunate versus quinine in the treatment of congenital malaria observed that the total effective rates of the artesunate treatment group and the quinine group were 92.31% and 83.33% and the clearance rates of Plasmodium were 92.31% and 78.57%, respectively (Patel & Belsare, 2002). The study therefore demonstrated that efficacy of artesunate over quinine and noted that it can be used as drug of first choice for treatment of congenital malaria. More studies are however required to further elucidate the potency of artesunate in the treatment of congenital malaria.

Conclusion

A very vital lesson derived from this review of the reports on congenital malaria is that the disease is no longer an uncommon occurrence. Congenital malaria has now assumed a public health concern both in malaria endemic and semi-endemic areas. As countries all over the world and international aid agencies such as WHO intensify efforts towards the control of malaria it is important that such efforts do not neglect congenital malaria control. There is clearly a lack well established guidelines for the definition, diagnosis and treatment of congenital malaria. Operational research into various aspects of congenital malaria is also essentially lacking as many unresolved issues requiring urgent scientific investigation abound. Public health policy on malaria control should also take into cognizance the importance of integrating guidelines on congenital malaria management and control.

References


