A review of the current state of malaria among pregnant women in Papua New Guinea

IVO MUELLER¹, STEPHEN ROGERSON², GLEN D.L. MOLA³ and JOHN C. REEDER¹

Papua New Guinea Institute of Medical Research, Goroka, Department of Medicine, Royal Melbourne Hospital, University of Melbourne, Australia and School of Medicine and Health Sciences, University of Papua New Guinea, Port Moresby

SUMMARY

Besides young children, pregnant women are at high risk of malaria in highly endemic countries. This paper reviews evidence from studies conducted in Papua New Guinea (PNG) in the last 20 years on the burden and prevention of malaria in pregnancy and highlights gaps in our knowledge of malaria in pregnancy in PNG. Overall, primigravidae were found to be at higher risk than multigravidae, with up to 40% of primigravidae but only 10-25% of multigravidae infected with Plasmodium falciparum at delivery. Such infections were found to be associated with a 128-145 g decrease in birthweight. Mean birthweights reported between 1980 and 2003 range from 2.58 to 2.72 kg in primigravidae and 2.84 to 3.09 kg in multigravidae, with 21% to 48% and 9% to 19% of babies born to primigravidae and multigravidae, respectively, of low birthweight (<2500 g). The negative impact of malaria in pregnancy is compounded by relatively low rates of antenatal coverage. The current PNG national treatment policy which prescribes a treatment course of first-line antimalarial treatment (currently chloroquine and sulphadoxine-pyrimethamine) at first antenatal clinic contact, followed by weekly chloroquine prophylaxis and iron and folate supplementation, may no longer be effective given the high levels of resistance to chloroquine in PNG and poor compliance. In order to reduce the burden of malaria in pregnancy in PNG, alternative methods of control such as insecticide-treated nets and intermittent preventive treatment in pregnancy (IPTp), as well as improved modes of delivery of maternal health interventions, are urgently needed.

Introduction

Malaria in Papua New Guinea (PNG) is the leading cause of outpatient attendances nationally, the third commonest cause of hospital admission and the second commonest cause of death, and causes the greatest burden of lost disability-adjusted life-years (DALYs) at 4894/100,000 per year. Accordingly, malaria is a top priority of the national health response. As in highly endemic areas elsewhere in the world, in PNG both prevalence of malaria infection and incidence of morbidity are highest in young children (1,2) and pregnant women (3). Maternal deaths (to which malaria in pregnancy contributes significantly) are the fifth leading cause of lost DALYs. With a maternal mortality ratio of 370/100,000 childbirth is still among the highest mortality risks for women of childbearing age in PNG.

Malaria in pregnancy and maternal health

Precise estimates of the burden of malaria in pregnancy are not available, but regional patterns of birthweight indicate that alongside maternal nutrition and socioeconomic factors malaria is a major causative factor for the high prevalence of low birthweight (LBW) in lowland and coastal parts of PNG (4). In Madang and Maprik, where most in-depth studies on malaria in pregnancy have been

¹ Papua New Guinea Institute of Medical Research, PO Box 60, Goroka, Eastern Highlands Province 441, Papua New Guinea
² Department of Medicine, Royal Melbourne Hospital, University of Melbourne, Parkville, Victoria 3052, Australia
³ School of Medicine and Health Sciences, University of Papua New Guinea, PO Box 5623, Boroko, National Capital District 111, Papua New Guinea
done, mean birthweights reported between 1980 and 2003 range from 2.58 to 2.72 kg in primigravidae (PG) and 2.84 to 3.09 kg in multigravidae (MG), with 21% to 48% and 9% to 19% of babies born to PG and MG, respectively, of low birthweight (<2500 g) (3,5-9). Comparative studies between malaria-endemic coastal PNG and the malaria-free highlands suggest that malaria in pregnancy is responsible for up to 11% of anaemia and 40% of low birthweight in coastal areas (6).

In the only published study looking at the history of infections during pregnancy, Brabin et al. (3) found that the prevalence of malaria infections at first antenatal clinic (ANC) visit in primigravidae peaked at 9-16 weeks of gestation (55%). No similar trend was observed for multigravidae. Despite receiving chloroquine prophylaxis at all ANC visits, the average prevalence of infections at any ANC visit was 34% in PG, 30% in secundigravidae (SG) and 19% in MG. Several published studies looked at prevalence of malaria infection at delivery. Infection rates were significantly higher in primigravidae, reaching over 40% both in peripheral and placental blood in some studies (Table 1).

Placental pathology was not investigated in early studies, but a recent study in Madang found that 42% of women delivering at Alexishafen Health Centre showed evidence of active, chronic or past chronic malaria infection on placental histology (10).

In a pooled sample that contained roughly equal numbers of PG, SG and MG, Allen et al. (9) found that peripheral and placental infection at delivery were associated with a 128 g and 145 g decrease in birthweight respectively. Other PNG studies lacked sufficiently large sample sizes to find significant differences in birthweight in relation to malaria infection status.

Anaemia is a very common feature in pregnant women in many parts of lowland

<table>
<thead>
<tr>
<th></th>
<th>PG</th>
<th>SG</th>
<th>SG and MG</th>
<th>MG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peripheral</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Madang, 1986-1987</td>
<td>44%</td>
<td>26%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Madang, 1994-1996</td>
<td>25%</td>
<td>20%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Madang, 2002-2003</td>
<td>26%</td>
<td>11%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td><strong>Placental</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maprik, 1986-1988</td>
<td>41%</td>
<td>23%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Madang, 1994-1996</td>
<td>34%</td>
<td>26%</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Madang, 2002-2003</td>
<td>24%</td>
<td>13%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td><strong>Placental histology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Madang, 2002-2003</td>
<td>63%</td>
<td>50%</td>
<td>33%</td>
<td></td>
</tr>
</tbody>
</table>

PG = primigravidae
SG = secundigravidae
MG = multigravidae
PNG. In 1986-1988, 89% of women delivering at the major referral hospital in Madang had a haemoglobin level (Hb) of <11 g/dl and 19% of PG and 17% of MG had severe anaemia, i.e., Hb <7 g/dl (6). Haemoglobin values measured at first booking at a rural health centre in Madang were significantly lower in both PG (8.6 g/dl) and MG (8.7 g/dl) than in non-pregnancy controls (10.4 and 10.2 g/dl respectively), despite similar levels of iron deficiency, with a tendency for haemoglobin levels to decrease with increasing length of gestation and to be lower in PG with concurrent malaria infection (−0.7 g/dl, p = 0.15) (5). How far these drops are directly related to malaria or simply due to physiological dilution in pregnancy, most of which will have occurred in PNG women prior to booking, is unclear. However, the fact that malaria control interventions such as intermittent preventive treatment in pregnancy (IPTp) result in significantly increased haemoglobin levels (11), underlines the importance of malaria as a cause of anaemia in pregnancy. Up to 40% of women showed signs of iron deficiency. With chloroquine (CQ) prophylaxis and treatment for severe anaemia, Hb in these women recovered to 9.6 g/dl in PG and 9.3 g/dl in MG at delivery with no significant difference between women positive and negative for malaria. Perhaps related to increasing coverage of iron/folate supplementation following their introduction into the national treatment guidelines in 1985, haemoglobin values during pregnancy and at delivery have been higher in recent studies (9), and the proportion of women severely anaemic (Hb <7 g/dl) at delivery decreased to 13% in 2002-2003 (10).

Anaemia (Hb <8 g/dl) was significantly associated with a decrease in birthweight in PG (−281 g) but not in MG (−84 g) (5). However, in-depth studies showed that anaemia is mainly linked to an increased risk of preterm delivery rather than a decrease in birthweight in term infants (9).

Although non-falciparum malaria is common in PNG, little is known about its effect on pregnant mothers and their babies. In a study in the mid-1980s the prevalence of P. vivax was lower in pregnant mothers attending ANC (3) (and under CQ prophylaxis) than in the postnatal period, but this is likely to be more a reflection of the high effectiveness of CQ prophylaxis against non-falciparum malaria than of reduced risk in pregnancy. However, further in-depth studies are needed to assess the contribution of non-falciparum malaria to malarial disease in pregnancy in PNG.

There have been only a few studies on congenital malaria, but the limited data indicate that transplacental transfer of P. falciparum parasites is common. In a small study in Madang umbilical cord infection was found in 7 of 15 children (47%) born to women with parasitaemia at time of delivery (12); 4 of these children also had detectable peripheral parasitaemia. Little is known about transplacental transfer of other malaria species, although at least one case of a symptomatic P. vivax infection acquired in utero has been described (13).

Very little is known about the problem of malaria in non-immune women living in areas of low endemicity such as the highlands. The overall burden of malaria in pregnancy is likely to be low as indicated by the substantially higher haemoglobin levels and lower rates of LBW in highland areas (6). However, due to low immune status acquired infections are more likely to be severe and mortality rates in pregnant mothers with severe malaria can be as high as 50% (14).

The detrimental effects of malaria in pregnancy are compounded by low rates of antenatal coverage and supervised deliveries. Nationally, only 33% of women receive any antenatal care during their pregnancy and 44% of deliveries are supervised; however, there are large regional variations. Antenatal coverage can drop below 50% and the proportion of supervised deliveries falls to as low as 10-15% in some rural districts of the country (15).

Two factors contribute to this low antenatal coverage and low rate of supervised deliveries: limited access to health care and strong customary beliefs surrounding childbirth. While the number of women delivering at provincial hospitals has greatly increased over the past two decades, rates of supervised deliveries in rural areas have been decreasing due to a range of factors. In many rural parts of PNG, women will have to walk for several hours through often difficult terrain to reach the nearest health centre. With a decline in mobile ANC clinic coverage, access to both ANC and delivery services is therefore severely limited. Unless a delivery plan for supervised birth is worked
out with the woman and her husband during the ANC period, many women will not be able to reach the health centre once labour has started, regardless of complications. Staffing levels and morale are other important obstacles to good clinical care. Women often state that they do not deliver at the health centres because they do not want to be attended to by male nurses, or because they are not sure if the health centre will be open or they will be able to find a nurse if they arrive after hours.

In addition, childbirth is still the focus of many customary beliefs and restrictions in some PNG cultures. Childbirth, like menstruation, is often believed to have a ‘polluting’ influence, in particular on men, and assistance to women in labour is often limited. In some places women in labour will go to the bush and deliver their babies completely unattended. There may also be strong beliefs associated with the disposal of placentas that inhibit women from delivering at a health facility.

Policy, prevention and treatment

Both malaria and safe motherhood have been identified as priority areas in the 2001-2010 PNG National Health Plan (15). The plan calls for a reduction of maternal mortality to 260/100,000 and LBW to <10%, while at the same time aiming to increase ANC coverage to 90% and the proportion of supervised deliveries to 70%. The goals for maternal mortality and LBW will not be reached without effective control of the detrimental effects of malaria in pregnancy.

Given the problems with access to adequate health care and the reluctance of mothers to deliver at health centres, preventive interventions have to be the main approach to improving the health of pregnant mothers and their babies.

The current PNG national treatment policy prescribes a treatment course of first-line antimalarial treatment (currently chloroquine and sulphadoxine-pyrimethamine (SP)) at first ANC contact followed by weekly chloroquine prophylaxis and iron and folate supplementation. However, the usefulness of chloroquine prophylaxis is questionable, given the high levels of resistance to chloroquine (16) in PNG and well-known problems of compliance. Even in the mid-1980s and 1990s chloroquine prophylaxis had little effect on malaria infection rates at delivery (5,9,17) although it was associated with increased haemoglobin levels (5,9) and decreased risk of preterm delivery (9). Thus, in the absence of information regarding alternative approaches, the policy is continuing today.

The use of insecticide-treated bed nets (ITNs) during pregnancy is also advised as part of the national guidelines, but to date no special bed net distribution for pregnant mothers is in place. In many areas ITNs can be bought from health centres but supplies are unreliable and prices often a deterrent. This situation is expected to change in the near future, as PNG has secured a grant from the Global Fund for AIDS, Tuberculosis and Malaria that will allow the provision of long-lasting ITNs to all people living in malarious areas in PNG. Monitoring the impact of this program on adverse pregnancy outcomes will be an important part of assessing its effectiveness.

Current treatment guidelines for malaria in pregnancy indicate the use of CQ and SP for uncomplicated disease, oral quinine with SP for treatment failure, and parenteral quinine for severe malaria in pregnancy. The clinical efficacy of CQ plus SP against P. falciparum is still high (93%) (18); however, the high levels of parasitological failure (up to 15%) indicate that these drugs will reach the end of their life span sooner rather than later. Although not yet part of the official treatment guidelines for pregnancy malaria, artesunate and IM artemether are second-line treatments for malaria in non-pregnant people, and are regularly used to treat women in their third trimester admitted to hospital with a presumptive diagnosis of malaria.

Future research needs

The high levels of morbidity and mortality indicate that the current policies for prevention and treatment of malaria in pregnancy are inadequate and new or improved approaches are needed. Research into new options for the prevention of malaria in pregnancy such as intermittent preventive treatment (IPTp), the better integration of ITNs and/or new and improved forms of prophylaxis is of high priority. In the medium term, new drugs for the treatment of malaria in pregnancy will be needed.
The above interventions will, however, only be successful if they can fit into local circumstances, customs and beliefs. Operational research studies into modes of delivery of maternal health interventions, in particular on ways of increasing coverage of ANC and supervised deliveries, as well as a better understanding of women’s perceptions of their own health, are thus needed if the high levels of maternal mortality, severe maternal anaemia and low birthweight are to be reduced.

The special epidemiology of malaria, and the genetic and cultural diversity, as well as imminent changes to malaria control policies, make PNG an ideal location to conduct in-depth studies into different aspects of malaria in pregnancy. Of particular interest are the aetiology and pathology of non-falciparum malaria in pregnancy or the effect of PNG-specific host genetic protective traits such as Southeast Asian ovalocytosis, alpha-thalassaemia or Gerbich blood group negativity on the risk and effects of malaria in pregnancy.

Building on earlier work the PNG Institute of Medical Research is committed to tackling the challenges posed by the high levels of malaria and maternal mortality in the country and thereby contributing to a better and healthier future for all PNG women.

REFERENCES