Reducing the burden of malaria in pregnancy

Drs Paola Marchesini and Jane Crawley,
Roll Back Malaria Department, World Health Organization, Geneva

Each year, more than 30 million African women in malaria-endemic areas become pregnant and are at risk of infection with Plasmodium falciparum. Prevention of malaria in pregnancy, which can have serious consequences for both the mother and her unborn child, is a major public health challenge and a priority for the Roll Back Malaria partnership. Roll Back Malaria recommends a three-pronged approach for reducing the burden of malaria among pregnant women, namely effective case management of malaria infections, use of insecticide-treated nets (ITNs) and, in areas of stable transmission, Intermittent Preventive Treatment (IPT).

Impact of malaria in pregnancy in different epidemiological settings

The symptoms and complications of malaria in pregnancy vary according to transmission intensity and the level of acquired immunity. Although these are presented as discrete epidemiological entities, the reality is usually more of a continuum, with a range of transmission intensity, acquired immunity, and clinical presentation occurring within the same country.

Areas of low or epidemic (unstable) transmission

Pregnant women living in areas of low or unstable malaria transmission have little or no immunity to malaria, and are at a 2 to 3-fold higher risk of developing severe disease as a result of malaria infection than are non-pregnant adults living in the same area. In these areas, maternal death may result directly from the complications of severe malaria (hypoglycaemia, cerebral malaria, and pulmonary oedema being particular problems), or indirectly from malaria-related severe anaemia. Malaria in pregnancy can also result in stillbirth, spontaneous abortion, low birth weight (birth weight < 2.5 kg), and neonatal death.

Areas of high or moderate (stable) transmission

Most pregnant women in malaria-endemic regions of Africa live in areas of relatively stable transmission. In these settings, the deleterious impact of malaria is particularly apparent in first and second pregnancies. Although parasite prevalence and density are higher among pregnant women compared to non-pregnant women, infection with P. falciparum is usually asymptomatic. Partial clinical immunity acquired during years of exposure to the malaria parasite prior to pregnancy does not prevent infection, but does reduce the risk of severe disease. Clinical malaria is not, therefore, a prominent feature of infection during pregnancy, and the major detrimental effects of infection are low birth weight (LBW) and maternal anaemia. In areas of stable transmission, it is estimated that malaria during pregnancy causes up to 10 000 maternal deaths each year, mainly as a result of severe anaemia, and accounts for approximately 8–14% of LBW, and 3–8% of infant mortality. 1

Malaria and HIV

HIV infection impairs a pregnant woman’s ability to control P. falciparum infection. Women with HIV infection are more likely to have symptomatic malaria infections and to have an increased risk of an adverse birth outcome due to malaria. In the presence of HIV infection, placental malaria appears to be independent of the number of pregnancies, so that the risk of placental malaria is similar in HIV-infected multigravidae and HIV-negative primagravidae.

Prevention and management of malaria during pregnancy

Areas of low or epidemic (unstable) transmission

In areas of low or unstable transmission, control of malaria during pregnancy is achieved primarily by prompt and effective treatment of acute episodes of malaria, since IPT will be relatively ineffective in such settings. Since malaria in a non-immune pregnant woman can rapidly progress to severe disease, any pregnant woman with symptomatic malaria must receive urgent treatment with an effective antimalarial drug plus appropriate supportive treatment. Use of ITNs will decrease exposure to infective mosquito bites and would therefore be expected to provide protection from symptomatic infection.

Areas of high or moderate (stable) transmission

ITNs and IPT (see below) are the key components of the preventive package for pregnant women living in areas of stable transmission. P. falciparum parasites may be present in the placenta and contribute to maternal anaemia even in the absence of documented peripheral parasitaemia. Any pregnant woman with severe anaemia from a malaria-endemic area must therefore be treated presumptively with an effective antimalarial drug, whether or not peripheral parasitaemia is present, and whether or not she has a history of fever. In addition, all women in malarious areas (regardless of endemicity) should receive iron and folic acid supplementation as part of routine antenatal care.
ITNs
In a large randomised trial recently conducted in an area of intense perennial malaria transmission in western Kenya, use of ITNs by pregnant women was associated with a 38% reduction in the incidence of malaria parasitaemia, 47% reduction in malarial anaemia (Hb <8 g/dl plus parasitaemia), and 28% reduction in the prevalence of LBW. (See July 2003 issue of Mera).

IPT
IPT replaces the previous policy of weekly chloroquine chemoprophylaxis in pregnancy, which was limited by poor compliance and increasing resistance of *P. falciparum* to chloroquine. IPT involves the administration of a curative treatment dose of an effective antimalarial drug at predefined intervals during pregnancy, beginning after quickening (the time at which foetal movements are first felt by the mother) in the second trimester.

All women should receive at least 2 doses of IPT in the second and third trimesters of pregnancy, ideally under direct observation at the time of routinely scheduled antenatal clinic visits. IPT ensures that the placenta is cleared of parasites at the time of rapid foetal growth (see Figure 1). Maximum benefit is derived from 2–3 doses of IPT, although even a single dose is beneficial.

![Figure 2: IPT dosing schedule](image)

All women should receive at least 2 doses of IPT after quickening. *IPT may also be given at the 4th visit, if she has not received the requisite number of doses.*

Studies in Kenya and Malawi have shown that IPT with sulphadoxine-pyrimethamine (SP) significantly reduces the prevalence of maternal anaemia and placental parasitaemia, and the incidence of LBW. SP has a good safety profile in pregnancy, while the single-dose regimen allows the health worker to directly observe treatment. In several studies, no evidence of an increase in serious cutaneous side-effects or neonatal jaundice was found when SP was delivered in the second and third trimester of pregnancy. SP remains an excellent option for IPT in areas of Africa where malaria transmission is stable and resistance to SP is low. Since, however, resistance to SP is increasing throughout Africa, there is an urgent need to evaluate the efficacy, effectiveness, and safety of other antimalarial drug options. A WHO meeting to review the pre-clinical (animal) and limited human data on the use of artemisinins in pregnancy concluded that these drugs have a good safety profile, particularly in the second and third trimesters of pregnancy and during lactation, and the use of artemisinin-based combination therapy for IPT must now be evaluated.

The need for programming partnerships for malaria control during pregnancy
In two thirds of African countries recently undergoing a Demographic and Health survey, more than 70% of women attended antenatal clinic (ANC) at least once during pregnancy. Roll Back Malaria has targeted the ANC for the accelerated programme implementation of malaria control during pregnancy in those areas with stable malaria transmission and high ANC attendance. In areas with low ANC coverage, emphasis is placed on the development and strengthening of community-based programmes.

Summary
Three evidence-based strategies (IPT, ITNs, and effective case management) exist for the control of malaria in pregnancy, but the widespread implementation of effective programmes remains a considerable challenge. Many women in Africa, particularly those living in remote areas, have limited access to medical care and effective malaria control tools such as ITNs. Delivery of cost-effective malaria prevention to pregnant women will require strengthened antenatal care, integration of malaria control with other health programmes targeted at pregnant women and infants, increased community awareness, and considerable financial investment. The prize for achieving this will be safer pregnancies and a reduction in infants deaths. Prevention of malaria during pregnancy remains one of the most important and achievable goals of the Roll Back Malaria partnership.

References