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PREVENTION AND TREATMENT OF MALARIA IN PREGNANCY IN SUB-SAHARAN AFRICA

Integrating prevention and treatment of malaria with antenatal care services is key to improved maternal and newborn outcomes in malaria-endemic areas of Africa.

The Roll Back Malaria summit in 2000 brought new urgency to efforts to eliminate malaria in sub-Saharan Africa. To date, more than half of the malaria-endemic countries have established country-specific strategic plans and guidelines for effective prevention and treatment of malaria in pregnancy (MIP).

Malaria continues to have a devastating impact, however, on the health, economic and human resources of the poorest countries in sub-Saharan Africa. The most vulnerable populations are pregnant women, their unborn babies and children under five years of age. Approximately 25 million women become pregnant in malaria-endemic areas of Africa each year (Steketee et al. 2001). Malaria is the leading cause of under-five mortality and constitutes 10% of the continent's overall disease burden (WHO 2003).

WHAT IS MALARIA?

Malaria is a parasitic infection transmitted by mosquitoes in tropical and sub-tropical areas of the world. *Plasmodium falciparum*, the most lethal species, is the type of malaria most prevalent in Africa. The level of immunity to the infection a woman has when she becomes pregnant depends on the intensity of malaria transmission where she lives.

In Africa, south of the Sahara:

60% of cases of malaria worldwide

75% of global *P. falciparum* malaria cases

80% of malaria deaths (WHO/UNICEF 2005)

In areas of epidemic or low (unstable) transmission, pregnant women will not have immunity and usually will become ill when infected. The risk of severe illness is two to three times greater for pregnant women than non-pregnant women in these areas (Luxemburger et al. 1997). The mother may die from severe malaria or from malaria-related severe anemia. The risks to the fetus include spontaneous abortion, stillbirth, premature birth and neonatal death (Menendez et al. 2000).

In areas of high and moderate (stable) transmission, pregnant women usually will not have clinical symptoms of malaria because they have developed sufficient immunity to the infection. In these areas, maternal anemia and infection of the placenta by malaria parasites can lead to impaired fetal nutrition and low birth weight.

Studies suggest that in areas of Africa with stable malaria transmission, *Plasmodium falciparum* infection in pregnancy contributes to 2–15% of maternal anemia, 8–14% of low birth weight and 3–8% of infant mortality. This translates into an estimated 400,000 cases of severe maternal anemia, a potentially fatal condition, and from 75,000 to 200,000 infant deaths annually (Steketee et al. 2001). Women in stable transmission areas have the greatest risk of developing these complications during their first and second pregnancies (Brabin 1983; Jelliffe 1968; McGregor, Wilson and Billewicz 1983; Steketee et al. 1988).

Malaria and HIV

Co-infection with HIV and malaria has compounded negative effects for the pregnant woman and her unborn baby. The prevalence and intensity of malaria infection during pregnancy are higher among HIV-infected women, and the risk to the woman and her newborn exists regardless of the number of times a woman has given birth (Verhoeff et al. 1999). A cohort study conducted in western Kenya showed that co-infection more than doubled the risk of moderate to severe anemia in all pregnant women (Ayisi 2003). This means that a considerable proportion of children born to mothers with both HIV and malaria are more likely to be born at a low birth weight and die in infancy.

HIV infection in pregnancy is also associated with reduced efficacy of malaria prophylaxis and treatment. HIV-infected pregnant women in areas with stable malaria transmission should receive either intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) or daily cotrimoxazole prophylaxis to prevent opportunistic infections if the stage of HIV infection requires such (WHO 2004b). In HIV-infected women, more than two doses of SP are needed to have the same benefit as two doses of SP in HIV-negative women. The 2004 World Health Organization (WHO) technical consultation meeting concluded that as HIV prevalence increases, so will the number of cases of MIP attributable to HIV (WHO 2004b).

WHAT CAN BE DONE

Prevention and treatment interventions for MIP do not require high technology and their provision is not limited to the hospital setting. Many interventions can occur at any point in the

household-to-hospital continuum of care (de Graft-Johnson et al. 2005). Home and community-level activities include health education and counseling about prevention of malaria and early detection and treatment of malaria in pregnant women and their newborns. At the facility level, malaria interventions should be integrated with existing services. Antenatal care is a key entry point for a broad range of preventive health services, including prevention and treatment of malaria, tuberculosis, sexually transmitted infections, HIV/AIDS and anemia, as well as tetanus toxoid immunization. Nearly 70% of women in Africa attend antenatal clinics at least once during their pregnancy, and many attend at least twice (WHO/UNICEF 2003). Thus, antenatal care is the best platform from which to implement MIP programs (WHO 2004a).

Integration of services refers not only to using antenatal care as the platform for delivering MIP prevention and control interventions, but also to developing the administrative systems required for planning, resource allocation, financial management, monitoring and evaluation, and human capacity development. Such integration should begin at the national level, with establishment of national standards and guidelines, and continue through all levels of the health care system.

Effective strategies for reducing the impact of MIP must address both the need to prevent illness in asymptomatic pregnant women and the need to manage the disease in women who are clinically ill. The WHO *Strategic Framework for Malaria Prevention and Control during Pregnancy in the African Region* recommends the use of IPTp, vector control using insecticide-treated bed nets (ITNs) and effective case management of malaria illness and anemia (WHO 2004a). These guidelines emphasize the importance of initiating preventive measures as part of antenatal, postpartum and newborn care, as well as effective case management for all clinical cases of malaria.

Intermittent Preventive Treatment in Pregnancy

The WHO recommends that all pregnant women in areas of stable transmission receive IPTp with an appropriate antimalarial as a routine part of antenatal care. Weekly chemoprophylaxis with chloroquine (CQ) is no longer recommended because of poor compliance and increasing resistance to the drug (WHO 2004a). SP is the current antimalarial drug of choice for IPTp in stable transmission areas of low SP resistance. Clinical trials have demonstrated that use of IPTp with SP is associated with reduced peripheral and placental malaria, anemia and low birth weight (Kayentao et al. 2005; Njagi et al. 2003; Parise et al. 1998; Schultz et al. 1994; Shulman et al. 1999).

The WHO recommends that pregnant women receive at least two doses of IPTp with SP (one dose comprises three tablets of SP, each containing 500 mg sulfadoxine and 25 mg pyrimethamine) at the first and second scheduled antenatal care visits after fetal movement begins (quickening). The doses of SP should be spaced at least one month apart. For women attending antenatal care late in pregnancy, even one dose may be beneficial. In areas of high HIV prevalence, pregnant women may experience the maximum benefit of IPTp when given a third dose of SP during the last scheduled antenatal care visit or when given monthly IPTp (Filler et al. 2006; Parise et al. 1998; Shulman et al. 1999). It should be noted that concomitant use of IPT along with iron and folate to prevent and treat anemia in pregnancy is acceptable only if the daily dose of folate does not exceed 0.4 mg. In countries where folate in higher doses is used, a serious drop in the efficacy of SP has been seen (Ouma et al. 2005).

Certain areas of sub-Saharan Africa have experienced increasing SP resistance. However, even in countries with moderate SP resistance (defined as treatment failure rates up to 50%), IPTp with SP is efficacious in the prevention of MIP (WHO 2005).

Vector Control

Insecticide-Treated Nets. ITNs kill and repel the mosquitoes that carry malaria, providing protection for both mothers and newborns. In areas of stable transmission, use of ITNs has been associated with lower prevalence of malaria infection and fewer premature births (D'Alessandro et al. 1996; Ter Kuile et al. 2003). Although ITNs are relatively inexpensive, their cost may be prohibitive for many of the women who need them. New, long-lasting ITNs (LLITNs) must maintain full protection through 20 washings or three years in order to be recommended by the WHO Pesticide Evaluation Scheme.

The WHO/Regional Office for Africa (AFRO) Strategic Framework recommends that pregnant women in areas of stable and unstable transmission consistently sleep under an ITN, starting as early in pregnancy as possible, and continue to do so postpartum with their newborns and children under five.

Indoor Residual Spraying (IRS). IRS with liquid insecticide, usually DDT, kills mosquitoes that come into contact with the sprayed surface and, in the case of DDT, reduces the number of mosquitoes entering indoor spaces (WHO 2005). Although IRS can achieve high coverage through house-to-house, publicly funded and managed approaches, the WHO states that IRS programs are probably better suited for areas of "focal endemicity and epidemic-prone areas." The WHO further states that IRS programs are of limited value in most rural areas with stable transmission (WHO 2004c).

Case Management for Malaria Illness

Appropriate management should be available to all women with clinical cases of malaria. In endemic areas, women with symptoms of malaria should have access to diagnosis and treatment though antenatal care services. Diagnosis of malaria infection is typically based on the presence or recent history of a fever and whether the woman lives in an area of stable or unstable transmission. Parasitological diagnosis of malaria is ideal if reliable light microscopy or rapid diagnostic tests are available. If this is not possible, the decision about whether to initiate treatment must be based on the clinical picture (WHO 2006).

A woman who has a fever (or recent history of fever) with or without symptoms such as chills, headache, body/joint pains or loss of appetite may have *simple* or uncomplicated malaria. Management of uncomplicated malaria should include administration of antimalarial drugs according to national guidelines, as well as close monitoring.

Quinine is the most effective of the drugs considered safe for women with simple malaria in the first trimester and for severe malaria throughout pregnancy (Yartey 2006). In the second and third trimesters, the newer artemisinin-based combination therapies (ACTs) that include artemisinin and its derivatives may be given according to country guidelines. However, since there is limited experience in the use of ACTs in pregnancy, it is essential that countries establish pharmaco-vigilance systems to track potential adverse events (WHO 2006).

A woman with a fever (or recent history of fever) and complications—such as unconsciousness or convulsions, rapid or difficult breathing, severe vomiting and/or dehydration, weakness/fatigue or low blood sugar—may have severe malaria. Women with severe malaria need emergency care delivered by a skilled provider. Such care may include stabilization, appropriate referral, administration of appropriate antimalarials, blood transfusion and other life-saving measures (WHO 2006, 2002).

Malarial illness in HIV-infected pregnant women who receive cotrimoxazole prophylaxis ideally should be managed with antimalarial medicines that do not contain sulfonamides or sulfones (WHO 2004b). However, as malaria is a life-threatening infection, treatment with sulfa-containing antimalarials should not be withheld in this circumstance if other options are not available.

Case management of malaria should also include diagnosis and treatment of accompanying anemia according to national guidelines.

EDUCATION AND COUNSELING

Skilled providers and community health workers can work together to provide an additional element of a preventive strategy—education and counseling about MIP.

As part of antenatal care, skilled providers give women information and counseling on the dangers of malaria, as well as the steps they can take to help protect themselves, their newborns and their children under five. These messages should address the importance of practices such as continuing antenatal care, taking iron and folate to prevent and treat anemia, receiving the next scheduled dose of IPTp, sleeping under an ITN, and covering arms and legs in the evening. As part of their birth planning, the woman and her family should also receive assistance in developing a complication readiness plan that specifies exactly what to do and where to go if danger signs of malaria arise.

These health messages can be delivered by community health workers during home visits or community events. Community interventions are needed to create the necessary enabling environment for women and newborns to sleep under ITNs because there are often social barriers to the demand for, access to and utilization of ITNs. Where LLITNs are not available, such community interventions can also help ensure that the ITNs retain insecticidal effectiveness by mobilizing the community to reapply insecticides to their nets in a timely manner.

PROGRAMMING AND POLICY SUPPORT

There are a number of global and regional efforts to develop policies and support country-level implementation for the prevention and control of MIP. The Roll Back Malaria (RBM) Partnership—founded in 1998 by the WHO, United Nations Development Programme, United Nations Children's Fund (UNICEF) and the World Bank—has two regional networks in Africa: East African RBM (EARN) and West African RBM (WARN).

The United States Agency for International Development (USAID)-funded Malaria Action Coalition (MAC) includes the Centers for Disease Control and Prevention (CDC), the Rational Pharmaceutical Management Plus Project (RPM+), the WHO, primarily through its WHO Africa Regional Office, and the ACCESS Program. MAC supports the RBM initiative by providing technical assistance to African countries at the regional, sub-regional and national levels to promote adoption of malaria policies, use of antimalarial drugs and services, and knowledge of and demand for appropriate services at the community level.

The President's Malaria Initiative (PMI), which began in 2005, is a U.S. Government collaboration led by the USAID that includes the CDC, the Department of State, the White House and others. Its objective is to decrease deaths due to malaria by 50% in 15 African countries.

In addition to these global partnerships, countries are establishing local partnerships to implement national policies and link to other initiatives, such as Integrated Management of Childhood Illnesses, Making Pregnancy Safer and the Global Fund to Fight AIDS, Tuberculosis and Malaria. Two regional networks are the Malaria in Pregnancy Coalition for East and Southern Africa (MIPESA) and RAOPAG, the Reseau d'Afrique de l'Ouest contre le paludisme pendant la grossesse (West African Network against Malaria during Pregnancy).

RESOURCES AVAILABLE FROM THE ACCESS PROGRAM

Malaria during Pregnancy Resource Package: Tools to Facilitate Policy Change and Implementation. 2003. JHPIEGO/MNH Program: Baltimore, MD.

Home and Community-Based Health Care for Mothers and Newborns. 2006. ACCESS Program: Baltimore, MD.

Household-to-Hospital Continuum of Maternal and Newborn Care. 2005. ACCESS Program: Baltimore, MD.

For more information on MIP, please visit the ACCESS Web site at: www.accesstohealth.org.

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