Control of malaria in pregnancy: an elusive target

High risk – but not prioritised in management programmes. Prof William Brieger reports

Women are at high risk for malaria in pregnancy (MIP). While adults in environments with stable malaria transmission develop some immunity, pregnant women present a special situation – their placentas – which are new territory for the malaria parasites.

MIP leads to a number of problems.[1] In the woman herself malaria causes anaemia,[2] which threatens the life of the pregnant woman. The foetus and newborn are also at risk as MIP leads to retarded foetal growth, miscarriage, stillbirth, and low birthweight. Should the child of a mother with malaria be born alive, he/she is at greater risk of neonatal and infant mortality.

Recent research has expanded on the known and suspected dangers of MIP. A suspected role of malaria in post-partum haemorrhage (PPH) was found in Papua New Guinea where PPH was higher in the malarious lowlands than in the highlands.[3] A later study in Tanzania found that post-partum, the odds ratio for a 'blood loss of 400 ml or greater was significantly increased for women with placental malaria.'[4] The problem showed seasonal variation, and was worse in the peak malaria transmission months.

Pre-eclampsia is life threatening condition for pregnant women. Studies have begun to associate MIP with increased risk of this problem. In an unstable transmission area of Sudan, research showed that, 'family history of hypertension and placental malaria were significantly associated with pre-eclampsia.'[5] In Senegal, researchers also found an association between placental malaria infection and gestational hypertension.[6]

Finally, while placental malaria has long been associated with intra-uterine growth retardation (IUGR) of the foetus, a recent article has helped to explain the process.[7] The study based in Thailand showed that, 'Most placenta volumes in the infected women were below the 50th centile for gestational age; most of those with *Plasmodium falciparum* were below the 10th centile.' More study along these lines will help us to better understand how placental malaria infection causes IUGR.

Fortunately, MIP and the concomitant risks can be controlled and prevented. Three main interventions have been designed and tested to protect pregnant women against the damage that malaria causes. These received highlighted focus at the Roll Back Malaria (RBM) Abuja Summit in 2000[8] and include:

- Intermittent Preventive Treatment in pregnancy (IPTp) that entails giving at least two doses of an effective antimalarial drug (sulphadoxine–pyrimethamine) at least 1 month apart after quickening in order to clear malaria parasites from the placenta.
- Insecticide-treated bednets, most commonly now found in the long-lasting insecticide-treated nets (LLINs) form, with women encouraged to sleep under them every night from as early in pregnancy as possible (if not before).
- Prompt diagnosis and accurate treatment with an effective artemisinin-based combination therapy (ACT) drug whenever a woman actually experiences an episode of malaria.

IPTp is the only pregnancy-specific intervention of the three and is ideally delivered during focused antenatal care (ANC) visits as part of a full package

This pregnant woman has hung her insecticide-treated bednet

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of pregnancy care services. Although the African Regional Office of the World Health Organization issued its 'Strategic Framework for Malaria Control during Pregnancy in the WHO Africa Region' in draft in 2002 and finalised in 2004,[9] countries were slow to adopt IPTp. This slowness was ironic because the ANC platform was readily available with high levels of attendance and the drug itself is cheap. The use of IPTp eventually caught on after several research efforts proved its effectiveness in reducing anaemia, placental malaria and low birthweight.[1,10]

Using IPTp and LLINs together has a synergistic effect, and nets themselves are quite valuable as they can be used in the first trimester of pregnancy, when IPTp is not recommended. Like IPTp, LLINS should be an integral part of the services provided at ANC. Recent efforts to achieve universal coverage (UC) of LLINs has meant in theory that a woman has LLINs in the house and can start using them, thus ensuring protection whenever she becomes pregnant.

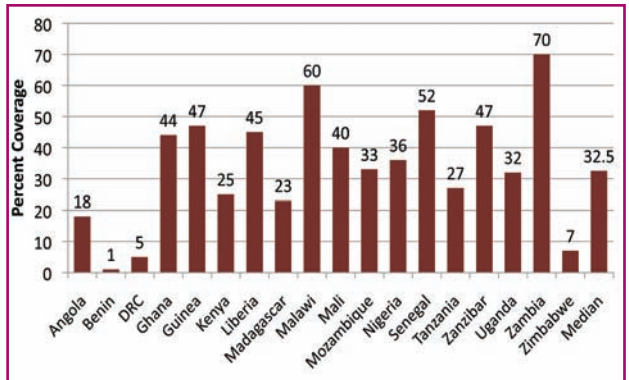
Because the level of malaria transmission varies across Africa, interventions for pregnant women also vary. IPTp is most effective in areas of stable, nearly year-round transmission, like Nigeria or Tanzania, where women may have developed some immunity to the disease and may not exhibit frank signs of malaria, even though their placentas may be infected. In areas of unstable, seasonal, or epidemic malaria, such as Namibia or Ethiopia, adults do not acquire immunity and their malaria episodes are quite noticeable and dangerous. In this situation prompt diagnosis, with either a rapid diagnostic test or microscopy, identifies the parasite and prompts quick treatment with ACTs.

As we hopefully move closer to malaria elimination, the experience of low-transmission countries will become the norm, and there will be more reliance on prompt case management than IPTp. In the meantime, we are unfortunately not close to the Abuja 2000 targets for 2010 of 80% coverage of pregnant women with two doses of IPTp (IPTp2), LLINs and where applicable, prompt case management.

The US President's Malaria Initiative (PMI) now works in 19 countries on the basis of their having a functional national malaria control programme and the presence of other donors like the Global Fund. Therefore, the additional inputs provided by PMI should help put these countries over the top in terms of coverage targets, and are being used to formulate the charts in this article. The actual data in the charts come primarily from Demographic and Health Surveys (DHS) and their sister efforts, the Malaria Indicator Surveys (MIS).[11] Most of the data are from 2008–2010, but since these surveys are not done every year in every country, data from Benin date from 2006.

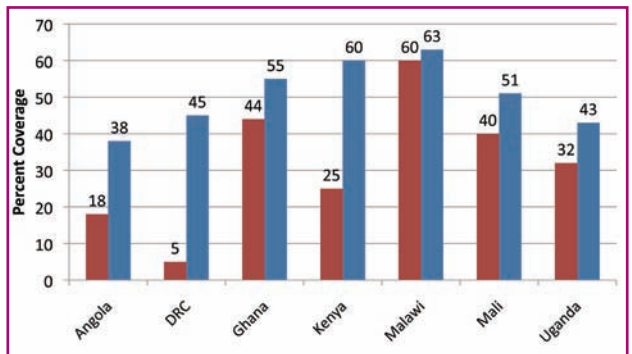
Figure 1 shows the average IPTp2 coverage in the 17 countries where IPTp is part of national policy (Rwanda and Ethiopia are in the low-transmission category where IPTp is not used). The median coverage figure for these countries is only 32.5%. Only two countries, Malawi (60%) and Zambia (70%), had achieved RBM's 2005 target of 60% coverage, and were far from closing in on the 80% goal for 2010 (of

Figure 1 IPTp coverage: two doses



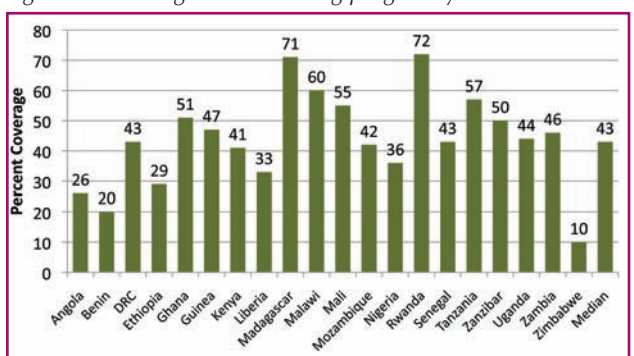
Roll Back Malaria coverage target was 80% for 2010

Figure 2 IPTp coverage: household surveys vs ANC clinic data



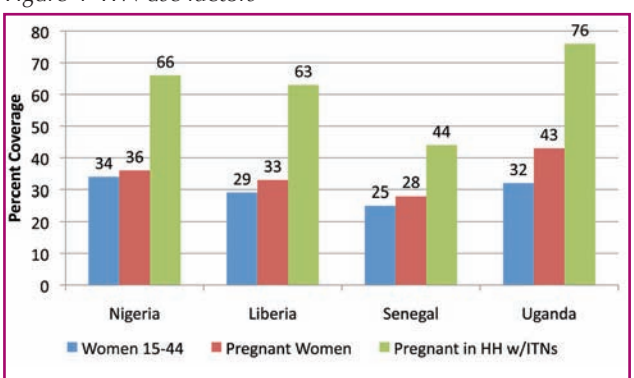
ANC data from World Malaria Report 2011; ANC coverage (blue) uses ANC registration as denominator, so coverage appears greater than household surveys (brown)

Figure 3 Coverage of ITN during pregnancy



Roll Back Malaria coverage target was 80% for 2010

Figure 4 ITN use factors



DHS malaria indicator surveys 2009–2010. (HH=households)

note, PMI sets an 85% target for 2010).

Since large national surveys cannot be done every year, it is recommended that we look at data on IPTp collected at ANC clinics. The denominator in this case would be the number of women registering for ANC, which in most countries is usually a large proportion ranging between 80 and 95% of pregnant women; however even with this more exclusive denominator, we seen in Figure 2 that targets are still difficult to achieve.[12] What the ANC data reveal are possible missed opportunities where 20% or more of pregnant women who do register do not get the desired two doses.

Why are these figures low? A number of health system deficiencies and community concerns may be at play. The health system components include integration/coordination of services, policy development and dissemination, finance, commodities, community involvement, monitoring and evaluation, and human resource capacity. The USAID Maternal and Child Health Integrated Project recently conducted MIP implementation case studies in Malawi, Senegal, and Zambia and found that integration, finance, and commodities were the weakest links and in fact made successes in other health system components of MIP services difficult.[13]

Concerning treated bednet use in pregnancy, Figure 3 shows that only three countries had achieved the 2005 target of 60% at their most recent national survey. Here again the median among the 19 PMI countries is low, only 43% of pregnant women surveyed. Receiving multiple donor support (PMI, Global Fund, etc.) does not seem to be the answer to achieving high coverage of interventions to prevent MIP.

Efforts to provide nets through UC campaigns and ANC may have met roadblocks. Figure 4 looks more closely at LLIN use by pregnant women. First we see that women may not be using nets prior to the time they become pregnant. Because of procurement problems, countries have had to redefine UC as two nets per household, when in many African settings a household has five or more residents. Even when nets are available in a household, the pregnant woman may not use them. Figure 4 also shows that even in homes with nets possibly only two-thirds of pregnant women sleep under them. We also need to think about household dynamics that occur when there are not enough nets to go around.

What can we do to meet our targets? A recent study addressed the

A pregnant woman receiving a rapid diagnostic test in Burkina Faso

Intermittent Preventive Treatment in pregnancy (IPTp) clears malaria parasites from the placenta

Follow-up monitoring by the volunteer community-directed distributors (CDDs). Will the insecticide-treated bednet remained unopened?

Providing a valuable role: CDDs are a link between the clinic and the community

problems of inadequate net use, even when a household owns nets. An implementation trial was organised in 11 intervention and 11 control villages in southwest Ethiopia, where household heads in the intervention group received tailored training about the proper use of LLINs.[14] The two most important results of this intervention were:

- symptomatic malaria steadily declined in the intervention villages compared with the control villages in the follow-up periods;
- children in the intervention arm were less likely to be anaemic compared with those in the control arm both in the high- and low-transmission seasons.

Another net promotion study took place in Ghana using a community-based participatory research approach. The researchers provided hands-on training for village volunteers who in turn gave instructions and assistance in hanging of nets, in-home small group education, and monthly follow-up.[15] The intervention resulted in rates of individual LLIN usage that increased significantly from 29% at baseline to 88.7% at 6 months and to 96.6% at 12 months.

Community volunteers can play a valuable role in providing IPTp, under the training and supervision of ANC health staff. In Akwa Ibom State, Nigeria, there was a very slow uptake of IPTp programming by local government primary health clinics. There were also social and cultural reasons why pregnant women did not attend ANC in a timely manner. ANC staff in intervention local government areas were trained in the community-directed intervention (CDI) approach and in turn reached out to surrounding villages and kin groups to encourage them to select volunteer community-directed distributors (CDDs).[16] The ANC staff not only trained the volunteers, but also maintained basic stocks of sulphadoxine pyrimethamine (SP) at the clinics. They supervised monthly CDD meetings where refresher training and problem solving occurred. Together the ANC staff and the CDDs maintained a community-to-clinic monitoring and evaluation system that ensured all service provision was properly reported. To ensure comparability, the project provided adequate stocks of SP at ANC clinics in the control areas, but not the capacity building for CDI.

After 18 months of intervention, in the control group, the fraction of women taking the proper two doses of IPTp increased from 6 percentage points to 27 percentage points. In the treatment group, the corresponding percentage of women increased from 9 percentage points to 66 percentage points. Contrary to fears of health programme managers that CDI would detract from ANC attendance, the proportion of women attending ANC actually increased, since part of the job of the CDD was to actively encourage ANC visits so that women would receive the comprehensive package of services.

In conclusion, pregnant women appear to be a high-risk, but possibly neglected, target group when it comes to rolling back malaria. It is not enough for national malaria control programmes to purchase drugs and nets and promulgate guidelines. As we can see, malaria protection happens at the grass roots level. There should be strong community-clinic partnerships and village- and household-based health education that ensures uptake and use of all MIP control interventions.

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