# Dossier "Malaria in pregnancy"

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# **Scope**

#### By Petra Mens

Biomedical Research, Royal Tropical Institute

Malaria still claims many victims in the developing world. It is mainly known to affect children under 5 and the disease takes many young lives. However, there is an other important risk group for malaria: pregnant women. When pregnant women become infected with the malaria parasite they often do not have the typical clinical symptoms that make children so ill. But the disease remains a threat not only for the pregnant women, but also for the unborn child, as the parasites continue to perform their devastating work.

Many resources provide information about malaria in general and most have malaria in children or in travelers as a specific target group. This dossier focuses on the issues related to malaria in pregnancy. This group is often neglected in information resources and this dossier tries to bring information about this specific topic together in an understandable manner.

If you would like to make any comments on this dossier or suggest additional resources, please contact the editor, <u>Ilse Egers</u>.

#### Disclaimer:

The information provided in this dossier is only intended to be general summary information to the public. It is not intended to take the place of either professional health care providers or current medical advice and regulations.

# **In-Depth**

# By Petra Mens

Biomedical Research, Royal Tropical Institute.

Approximately one fourth of the world population is at risk of contracting malaria and every year more than 2 million people, mainly young children in sub-Sahara Africa, die due to the complications of malaria. However, not only children are the victim of malaria; also pregnant women in developing countries are a risk group which is threatened by the disease. More than 90% of malaria infections occur in sub-Saharan Africa. There, approximately 30 million women per year become pregnant. Plasmodium falciparum, the most serious form of malaria, is an risk factor in seriously illness is of the pregnant woman, early birth, serious sickness of the child and infant mortality. In areas with stable malaria transmission (e.g. sub-Saharan Africa), P. falciparum infection during pregnancy is estimated to cause as many as 10,000 maternal deaths each year, contributes to approximately 2 – 15% of maternal anemia, 8 – 14% of low birth weight infants (an important contributor to infant mortality), and 3 – 8% of all infant deaths.

Although malaria in pregnancy is often asymptomatic (the patient is infected but does not feel ill or has the typical symptoms of malaria), it nevertheless is the cause of unfavorable pregnancy outcomes both in the mother and in her child. The outcomes of the invasion of the placenta by the malaria parasites, even at low infection rates, leads to ill health for the mother, may cause abortion of the fetus, premature labour, small-for-date babies, low birth weight and post-neonatal infant mortality. The association between maternal malaria and neonatal or infant mortality is not completely clear, but it is evident that chronic malaria during pregnancy causes low birth weight.

Prevention and/or treatment of malaria in pregnancy are major public health challenges and essential components of the obstetrician and antenatal care in endemic areas, but these require special considerations during pregnancy. In particular, only few anti-malaria drugs can be used in this target group and there are some problems with the malaria parasite becoming resistant to these medicines.

Prophylaxis (giving medication to protect pregnant women and the unborn child against malaria without evidence that they are really sick) during pregnancy with anti-malarial drugs has shown that it reduces malaria in the blood and in the placenta of the mother, it has a favourable impact on anaemia of the mother and on the birth weight of the baby. This applies mainly for the first and second pregnancy. This approach is called intermittent preventive treatment or IPT, but is not widely applied yet in many countries where malaria is abundant. This can be caused due to ignorance of the expecting mothers concerning the risk of malaria during pregnancy and/or lack of access to and or knowledge within the medical care. This unfortunately leads to the fact that not everyone takes correct preventive measures (like IPT and sleeping under a bed net). KIT is working on a project to improve IPTp uptake and ANC

attendance in combination with scheduled screening of women by a rapid test and treatment if positive in their own communities by community health workers. See <a href="http://www.cosmicmalaria.eu/">http://www.cosmicmalaria.eu/</a>

An additional problem is the proper treatment of the women when they are infected with malaria. Any medicine in pregnancy should in general be given when it is proven to be safe for the unborn child. For anti-malarials this still poses many problems since not all drugs can be given safely pregnancy. This problem is exacerbated due to the fact that the malaria parasites are or are becoming resistant to several available drugs, which frustrates the treatment of symptomatic malaria.

The increase of anti-malarial drug resistance over the last decades demands continuous research to improve existing treatment and to develop new drugs. Pregnant women and children are the target groups of current global malaria control efforts. However, the antimalarial drugs which are considered safe during pregnancy, chloroquine, quinine and sulfadoxine-pyrimethamine, become increasingly ineffective. The increased inefficacy of these the common affordable anti-malarials prompted many countries to recently shift their treatment guidelines to other, more expensive, medicines , most often combination regimens that contain an artemisinin derivative drug.

In Africa, the most commonly used artemisinin-based treatment (ACT) is Coartem, a combination of artemisinin derivative arthemether with another component called lumefantrine. The introduction of this drug combination drug in national drug policies, including malaria in pregnancy, went faster than drug registration, so that off label prescription is common. Pre-clinical investigations repeatedly showed that artemisinin-based drugs are potentially neurotoxic, and that in high dosages they may also have toxic effects on the unborn child. ACT is currently recommended for drug resistant P. falciparum malaria but usage in the first trimester of pregnancy was recently excluded. The general opinion though is that toxic effects of therapeutic dosages in humans have not been documented yet and that the risks are small and outweighed by the benefits of the artemisinin drugs in the second and third trimester of pregnancy. Recent studies have shown that Coartem can be used safely and effectively in the second trimester of pregnancy for treatment of P. falciparum malaria.

These aspects: treatment, education of pregnant women and effects of different drugs on the unborn child are topics in several research projects of KIT-BR (see KITs involvement).

If you would like to make any comments on this dossier or suggest new resources, please contact the editor, Ilse Egers.

# KIT's Involvement

# By Petra Mens

Biomedical Research, Royal Tropical Institute

The department Biomedical Research, Unit Parasitology, has several research lines in "malaria in pregnancy".

# 2012-2016

Community-based scheduled screening and treatment of malaria in pregnancy for improved maternal and infant health: a cluster-randomized trial COSMIC (European Union FP7 grant) <a href="https://www.cosmicmalaria.eu">www.cosmicmalaria.eu</a>

Preventive treatment with Sulphadoxine-Pyrimethamine can substantially reduce the effects of malaria in pregnancy. This medicine should be taken at every Antenatal care visit starting from the 2nd trimester and should be given at least 1 month apart. This corresponds to at least 3 doses during pregnancy However, as a result of low antenatal care attendance in many countries this strategy is not completely effective. An alternative to protect the women and her child is early detection and treatment. This can be done by rapid diagnostic tests (an approach called scheduled screening and treatment). However as women fail to attend the ANCs regulary other means of devlivering tests and treatments to the women are needed. This study looks at wether Community Health Workers working in the community of the pregnant women can deliver the tests and treatment on regular basis and asseses the health impact of this intervention. Next to this socio-economic fectors, health system factors and health economic factors are being investigated in order to come to a complete picture before policy recommendations will be done.

# Development of diagnostic tools for malaria that can be used in pregnancy (FIND) 2008-2011

Malaria in pregnancy is difficult to diagnose, especially in endemic countries. Often the disease is asymptomatic in mothers who are regularly exposed to malaria and do not show the characteristic symptoms that can be seen in non pregnant persons. One of the reasons is that malaria "hides" in the placenta that is rich of blood and can there do its damage. If the parasite is happy in the placenta it is rarely found in the blood stream of the mother. This makes diagnosis very difficult since most forms of health centers the women go to use a drop of blood for microscopical examination and it is not possible to examine the placenta before the baby is born. Diagnostic tests that make use of the antigens (specific particles of the parasite that are different from the human body, circulate in the bloodstream and are recognized by the human immune system) can be used as an alternative for diagnostics. There are already some of these tests available for diagnostic use but these are not used on regular basis. The Parasitology Unit of Biomedical research is developing new diagnostic tools based on antigen detection that are sensitive and also reliable for diagnostics in pregnant women.

This study has resulted in better insight in the performance of rapid tests and other tests for the detection of malaria and has identified new targets for the development of diagnostic tests

Publications that have arisen through this project:

- PhD thesis: J.H. Kattenberg (Supervisor: Prof. P.A. Kager, Co –supervisors: Dr. P.F. Mens; Dr. H. D.F.H. Schallig) <u>Diagnosis of Malaria in Pregnancy, Evaluation, New developments and Implications</u>
- Kattenberg J.H., Tahita M, Versteeg I., Tinto H, Traore-Coulibaly M, d'Alessandro U., Schallig H.D.F.H., Mens P.F. (2012) <u>Evaluation of antigen detection tests, microscopy and PCR for the diagnosis of malaria in peripheral blood in asymptomatic pregnant women in Nanoro, Burkina Faso.</u> American Journal of Tropical Medicine & Hygiene 87:251-6
- Kattenberg J.H., Tahita M, Versteeg I., Tinto H, Traore-Coulibaly M, Schallig H.D.F.H., Mens P.F. (2012) <u>Antigen persistence of rapid diagnostic tests in pregnant women in Nanoro, Burkina Faso and the implications for the diagnosis of malaria in pregnancy</u>. Tropical Medicine and International Health 5:550-557
- Kattenberg J.H., Versteeg I., Migchelsen S.M., I.J. Gonzales, M.D. Perkins., Mens P.F., Schallig H.D.F.H. (2012) New developments in diagnostics: Monoclonal Antibodies against Plasmodium Dihydrofolate Reductase- Thymidylate Synthase, Heme Detoxification Protein and Glutamate Rich Protein. Mabs 4:120-126

Kattenberg J.H., Ochondo E.A., Boer K.R., Schallig H.D.F.H. Mens. P.F. Leeflang M.M.G (2011)
 Systematic review and meta-analysis: Rapid diagnostic tests versus placental histology,
 peripheral and placental blood microscopy and PCR for malaria in pregnant women. Malaria Journal 10:321

# Malaria in pregnancy in Rwanda (INTERACT Project H) 2006-2012

Rwanda is a country in Africa that also suffers from malaria. In this project a Rwandese PhD student, trained in gynecology, that is supervised by the Parasitology Unit, together with the Academic Medical Centre, Amsterdam, The Netherlands, is studying several aspects of Malaria in pregnancy. In Rwanda the artemisinin based combination drug Coartem is given to all people who are infected with malaria. This is a unique situation since the effects of the drug in pregnancy is not widely studied. Here we study the effects of the drug in 1000 pregnant women in a so called "post marketing surveillance" and compare the pregnancy outcome (the baby) with 1000 women that did not take Coartem during pregnancy. The babies are thoroughly examined directly after delivery and followed up until the age of 9 months.

In addition the effects of the malaria in utero (when the baby is still in the womb) are studied in a smaller group of 100 women. The baby is monitored by ultrasound and a CTG (recording of the hart tones of the baby). The women are compared with a control group of healthy women and women who have fever that is not caused by malaria.

Another aspect of this project is the effects of malaria on the birth weight in Rwanda It is known that malaria has an effect on the birth weight in countries where very high levels of malaria is present. In Rwanda there has been a decline in malaria over the past years and the amount of malaria differs greatly in the different regions of the country. A study in the birth registers and national malaria data showed that malaria does not have the same effect on pregnancy outcome in Rwanda as is found in other African countries.

PhD student Stephen Rulisa expects to defend his thesis on malaria in pregnancy in Rwanda in 2013

Publications that have arisen form this project are:

- Rulisa S., Kaligirwa N., Agaba S., Karangayire P., Karangwa JB, Vyankandondera J., Mens P.F., de Vries P.J. (2012) <u>Fetal and maternal hemodynamics in acute malaria: persistent maternal</u> <u>tachycardia after recovery from malaria</u>. International Journal of Gynecology and Obstetrics <u>119</u>: 66-69
- Rulisa S., Kaligirwa N., Agaba S., Karema C., Mens P.F., de Vries P.J. (2012) <u>Pharmacovigilance of artemether-lumefantrine in pregnant women followed up till delivery in Rwanda</u>. Malaria Journal 11:225
- Rulisa S., Mens P.F., Karema C., Schallig H.D.F.H., Kaligirwa N., Vyankandondera J., de Vries P.J.
   (2009) Malaria has no effect on birth weight in Rwanda. Malaria Journal 8:194

# Malaria in pregnancy in Nigeria (Malaria no More) 2008-2010

Many pregnant women in countries where malaria exists do not know of the dangers of the disease. Most of them know the disease since they experienced it often but do not know the additional effects of malaria during their pregnancy. This is also true for the women in Nigeria. In this project the Parasitology Unit collaborated with the University of Benin City in Edo State, Nigeria to investigate the knowledge,

behavior and subsequent actions of pregnant women with respect to malaria. This was done with validated questionnaires. In the second phase of the study groups of women were educated on the dangers of malaria in pregnancy and were trained to become peer educators, The effects of this method of education was evaluated by doing a second round of questionnaires. Although the study showed that peer education was an effective method to increase the level of education on malaria in pregnancy in the area it did not lead to direct behavioural changes. The study showed that targeted interventions should not only look at education but also invest in active behavioral change.

- Mens P.F. Scheelbeek P., Altabbi H, Enato E.O. (2011) <u>Peer education: The effects on knowledge, of pregnancy related malaria and preventive practice in women of reproductive age in Edo-State</u>, Nigeria. BMC Public Health 11:e610
- Enato, E.F.O, Mens, PF., Okhamafe, A.O., Okpere, E.E., Schallig, H.D.F.H. & Pogoson, E. (2009).
   Plasmodium falciparum malaria in pregnancy: Prevalence of peripheral parasitaemia, anaemia, and malaria care seeking behaviour among pregnant women attending antenatal clinic in Edo
   State, Nigeria. Journal of Obstetrics and Gynaecology 29:301-306

Other publications from KIT-BR on Malaria in Pregnancy

 Mens P.F, Bojtor E.C., Schallig H.D.F.H. (2010) Molecular interactions in the placenta during malaria infection. Review. European Journal of Obstetrics & Gynecology and Reproductive Biology 152:126-132.

# Resources

This <u>Quick Link</u> is a predefined search and offers access to all KIT Library resources in the field of Malaria and Pregnancy.

### **Documents**

# 2013

- Impact of malaria during pregnancy on pregnancy outcomes in a Ugandan prospective cohort with intensive malaria screening and prompt treatment
  - De Beaudrap P., Turyakira E., White L. et al.
  - In this study, the timing, parasitaemia level and number of peripherally-detected malaria infections, but not the presence of fever, were associated with adverse birth outcomes. Hence, prompt malaria detection and treatment should be offered to pregnant women regardless of symptoms or other preventive measures used during pregnancy, and with increased focus on mothers living in remote areas.
  - Malaria Journal | May 2013
- Gender differences in the use of insecticide-treated nets after a universal free distribution campaign in Kano State, Nigeria: post-campaign survey results
  - Garley A., Ivanovich E., Eckert E. et al.
  - Recent expansion in insecticide-treated net (ITN) distribution strategies range from targeting pregnant women and children under five and distributing ITN at antenatal care and immunization programmes, to providing free distribution campaigns to cover an entire population. These changes in strategy raise issues of disparities, such as equity of access and

equality in ITN use among different groups, including females and males.

This study reveals gender disparity in ITN use, with males less likely to use ITNs particularly among ages 15–25 years. The uptake of the intervention among the most at-risk group (females) is higher than males, which may be reflective of earlier strategies for malaria interventions. Further research is needed to identify whether gender disparities in ITN use are related to traditional targeting of pregnant women and children with malaria interventions; however, results provide evidence to design gender-sensitive messaging for universal ITN distribution campaigns to ensure that males benefit equally from such communications and activities.

• Impact of malaria during pregnancy on pregnancy outcomes in a Ugandan prospective cohort with intensive malaria screening and prompt treatment

De Beaudrap P., Turyakira E., White I. et al.

This study followed a prospective cohort of pregnant women who had access to intensive malaria screening and prompt treatment to identify factors associated with increased risk of MiP and to analyse how various characteristics of MiP affect delivery outcomes.

In this study, the timing, parasitaemia level and number of peripherally-detected malaria infections, but not the presence of fever, were associated with adverse birth outcomes. Hence, prompt malaria detection and treatment should be offered to pregnant women regardless of symptoms or other preventive measures used during pregnancy, and with increased focus on mothers living in remote areas.

Malaria Journal | April 2013

World Malaria Day 2013

Progress and gaps in the treatment for malaria

• <u>Uncomplicated malaria among pregnant women in the Brazilian Amazon: Local barriers to prompt and effective case management</u>

Borges Luz T., Suárez-Mutis M., Miranda S. et al.

This study aims to identify the local barriers to prompt and effective case management of malaria in pregnancy and was carried out in health facilities located in three endemic municipalities of the Brazilian Amazon. The study design combined both qualitative and quantitative descriptive methods. Flaws were detected in diagnosis and treatment. Training, knowledge and counseling were also sub-optimal. These results indicated the need to improve the health-worker performance through training.

Acta Tropica | 2013

# 2012

• <u>Prevalence, pattern, and determinants of placental malaria in a population of southeastern</u>
Nigerian parturients

Ezebialua I., Eke A., Ezeagwuna D. et al.

Placental malaria is a complication of malaria in pregnancy and is associated with adverse outcomes. Its burden is highest in Sub-Saharan Africa, but despite this, data based on histological analysis are scarce from this region. This study showed that the prevalence of placental malaria in southeastern Nigeria is high, and demonstrated that the mean parasite density was inversely related to parity. Significant factors associated with placental malaria were also identified. Appreciation of these significant factors will assist program managers in implementing the strategies for the prevention of malaria in pregnancy. International Journal of Infectious Diseases | 2012

 Malaria Policy Advisory Committee to the WHO: conclusions and recommendations of September 2012 meeting

WHO Malaria Policy Advisory Committee and Secretariat

This article provides a summary of the discussions, conclusions and recommendations from the meeting.

Malaria Journal | 2012

• A population pharmacokinetic model of piperaquine in pregnant and non-pregnant women with uncomplicated Plasmodium falciparum malaria in Sudan

Hoglund R., Adam I., Hanpithakpong W. et al.

Pregnancy is associated with an increased risk of developing a malaria infection and a higher risk of developing severe malaria. The pharmacokinetic properties of many anti-malarials are also altered during pregnancy, often resulting in a decreased drug exposure. Piperaquine is a promising anti-malarial partner drug used in a fixed-dose combination with dihydroartemisinin. The aim of this study was to investigate the population pharmacokinetics of piperaquine in pregnant and non-pregnant Sudanese women with uncomplicated Plasmodium falciparum malaria.

Malaria Journal | 2012

• Peripheral blood cell signatures of plasmodium falciparum infection during pregnancy Ibitokou S., Oesterholt M., Brutus L. et al.

Sequestration of Plasmodium falciparum-infected erythrocytes in placental intervillous spaces causes inflammation and pathology. Knowledge of the profiles of immune cells associated with the physiopathology of pregnancy-associated malaria (PAM) is scarce. The authors conducted a longitudinal, prospective study, both in Benin and Tanzania, including ~1000 pregnant women in each site with systematic follow-up at scheduled antenatal visits until delivery. Findings emphasize the prominent role played by B cells during PAM whenever it arises during pregnancy, whilst also revealing signature changes in other circulating cell types that primarily reflect the relative duration of the infections. Thus, the acute, recently-acquired infections present at delivery were marked by changes in DC and Teff frequencies, contrasting with infections at inclusion, considered chronic in nature, that were characterized by an abundance of immature monocytes and a paucity of Treg in PBMC.

PLoS ONE | 2012

• <u>Biomarkers of Plasmodium falciparum infection during pregnancy in women living in</u> northeastern Tanzania

Boström S., Ibitokou S., Oesterholt M., et al.

In pregnant women, Plasmodium falciparum infections are an important cause of maternal morbidity as well as fetal and neonatal mortality. Erythrocytes infected by these malaria-causing parasites accumulate through adhesive interactions in placental intervillous spaces, thus evading detection in peripheral blood smears. Sequestered infected erythrocytes induce inflammation, offering the possibility of detecting inflammatory mediators in peripheral blood that could act as biomarkers of placental infection. In a longitudinal, prospective study in Tanzania, the authors quantified a range of different cytokines, chemokines and angiogenic factors in peripheral plasma samples, taken on multiple sequential occasions during pregnancy up to and including delivery, from P. falciparum-infected women and matched uninfected controls. The results show that during healthy, uninfected pregnancies the levels of most of the panel of molecules they measured were largely unchanged except at delivery.

PLoS ONE | 2012

• WHO updates guidance on intermittent preventive treatment of malaria in pregnancy Intermittent preventive treatment for pregnant women (IPTp) with sulfadoxine-pyrimethamine (SP) remains a powerful tool against malaria in countries with moderate to high stable malaria transmission. Yet there has been confusion, lapses and very poor coverage with this intervention with little progress toward the Roll back malaria target of 80% coverage with two doses during pregnancy. WHO has recently revisited this strategy and has issued revised

recommendations, reproduced in this Update. Importantly, according to the WHO, these also address some of the myths about IPTp with SP.

World Health Organization | October 2012

• The Malaria in Pregnancy Library: a bibliometric review

Van Eijk A., Hill J., Povall S. et al.

The last decade has seen a dramatic increase in publications related to malaria in pregnancy, and an increasing proportion of these are publically available online. The MiP Library is a useful, scholarly source for literature and systematic reviews related to malaria in pregnancy. Malaria Journal | 2012

• <u>Sub-optimal delivery of intermittent preventive treatment for malaria in pregnancy in Nigeria:</u> influence of provider factors

Onoka C., Onwujekwe O., Hanson K. et al.

The level of access to intermittent preventive treatment for malaria in pregnancy (IPTp) in Nigeria is still low despite relatively high antenatal care coverage in the study area. This paper presents information on provider factors that affect the delivery of IPTp in Nigeria. Malaria Journal | 2012

• <u>Validity of self-reported use of sulphadoxinepyrimethamine intermittent presumptive treatment</u> during pregnancy (IPTp): a cross-sectional study

Namusoke F., Ntale M., Wahlgren M. et al.

The results of this study question the accuracy of self-reported data in estimating IPTp coverage in the population. More studies on validity of self reported data are recommended. Since the validity of IPTp self reports is vital for guiding policy on malaria control in pregnancy, ways should be sought to improve accuracy of the information from such reports.

Malaria Journal | 2012

 New insights into acquisition, boosting, and longevity of immunity to malaria in pregnant women

Fowkes F., McGready R., Cross N. et al.

How antimalarial antibodies are acquired and maintained during pregnancy and boosted after reinfection with Plasmodium falciparum and Plasmodium vivax is unknown. A nested case-control study of 467 pregnant women (136 Plasmodium-infected cases and 331 uninfected control subjects) in northwestern Thailand was conducted.

Results. Antibodies to P. falciparum and P. vivax were highly variable over time, and maintenance of high levels of antimalarial antibodies involved highly dynamic responses resulting from intermittent exposure to infection. There was evidence of boosting with each successive infection for P. falciparum responses, suggesting the presence of immunological memory. However, the half-lives of Plasmodium antibody responses were relatively short, compared with measles, and much shorter for merozoite responses, compared with PfVAR2CSA responses. These findings may have important practical implications for predicting the duration of vaccine induced responses by candidate antigens and supports the development of malaria vaccines to protect pregnant women.

Journal of Infectious Diseases | 2012

 Plasmodium falciparum parasitaemia in the first half of pregnancy, uterine and umbilical artery blood flow, and foetal growth: a longitudinal Doppler ultrasound study
 Griffin J., Lokomba V., Landis S. et al.

Early pregnancy malaria parasitaemia affects uterine and umbilical artery blood flow, possibly due to alterations in placentation and angiogenesis, respectively. Among primigravidae, early pregnancy malaria parasitaemia increases the risk of intrauterine growth restriction. The findings support the initiation of malaria parasitaemia prevention and control efforts earlier in

pregnancy.

Malaria Journal | 2012

• Effect of malaria in pregnancy on foetal cortical brain development: a longitudinal observational study

Rijken M., de Wit M., Mulder E. et al.

Malaria in pregnancy has a negative impact on foetal growth, but it is not known whether this also affects the foetal nervous system. The aim of this study was to examine the effects of malaria on foetal cortex development by three-dimensional ultrasound. The percentage of images that could be graded was similar to other neuro-sonographic studies. Maternal malaria does not have a gross effect on foetal brain development, at least in this population, which had access to early detection and effective treatment of malaria.

Malaria Journal | 2012

- Africa: Malaria Policy Center Launches New Website to Provide in-Depth and Up to Date Information On Progress in the Malaria Fight allAfrica | June 2012
- Essential malaria actions guide for Kenyan families

This guide is designed to assist district health managers, health workers, and NGO partners in planning and implementing malaria social and behaviour change communication activities at community level. The guide seeks to ensure harmonisation of communication approaches and promotes seven essential malaria actions that fall into four categories: long-lasting insecticide-treated nets use, malaria case management, indoor residual spraying, and prevention of malaria during pregnancy. The guide seeks to enable district health teams, partners, and stakeholders implementing advocacy, communication and social mobilisation activities.

Division of Malaria Control Kenya | 2012 | 30 pp.

• A systematic review of the safety and efficacy of artemether-lumefantrine against uncomplicated Plasmodium falciparum malaria during pregnancy

Manyando C., Kayentao K., D'Alessandro U. et al.

There is evidence to suggest that the pharmacokinetics of anti-malarial drugs may change in pregnancy, although the impact on efficacy and safety needs to be studied further, especially since the majority of studies report high cure rates and adequate tolerability. As there are fewer reports of AL safety in the first trimester, additional data are required to assess the potential to use AL in the first trimester. Though the available safety and efficacy data support the use of AL in the second and third trimesters, there is still a need for further information. These findings reinforce the WHO recommendation to treat uncomplicated falciparum malaria with quinine plus clindamycin in early pregnancy and ACT in later pregnancy.

Malaria Journal | 2012

<u>Temporal trends of sulphadoxine-pyrimethamine (SP) drug-resistance molecular markers in</u>
 <u>Plasmodium falciparum parasites from pregnant women in western Kenya</u>
 Iriemenam N., Shah M., Gatei W. et al.

Resistance to sulphadoxine-pyrimethamine (SP) in Plasmodium falciparum parasites is associated with mutations in the dihydrofolate reductase (dhfr) and dihydropteroate synthase (dhps) genes and has spread worldwide. SP remains the recommended drug for intermittent preventive treatment for malaria in pregnancy (IPTp) and information on population prevalence of the SP resistance molecular markers in pregnant women is limited.

Malaria Journal | 2012 | 30 pp.

• Malaria in Pregnancy: A solvable problem

At the end of June 2012, doctors, public health professionals, researchers, and scientists convened in Istanbul to attend "Malaria in Pregnancy: A Solvable Problem," a conference organized by the Harvard School of Public Health's Maternal Health Task Force. The objective of

the meeting was to share successes and challenges in MiP coverage from different countries, with the goal of identifying steps to improve coverage and reduce malaria in pregnancy. Coverage of the conference can be accessed at the Maternal Health Task Force's blog and at the Malaria Matters blog

• Malaria in Pregnancy Blog Series

Maternal Health Task Force's Blog

• The President's Malaria Initiative

Sixth Annual Report to Congress

PMI supports operations research projects designed to inform and improve program implementation and contribute to global malaria control efforts.

USAID | 2012

• The epidemiology of postpartum malaria: a systematic review

Boel M., Rijken M., Brabin B. et al.

The results of this review have to be carefully interpreted, as the majority of studies were not designed to study postpartum malaria, and there was large variability in study designs and reported outcomes. Current evidence suggests an effort should be made to detect and radically cure malaria during pregnancy so that women do not enter the postpartum period with residual parasites.

Malaria Journal | 2012 | 17 pp.

• Low coverage of intermittent preventive treatment for malaria in pregnancy in Nigeria: demandside influences

Onoka C., Hanson K., Onwujekwe O.

Nigeria instituted intermittent preventive treatment for malaria (IPTp) using sulphadoxinepyrimethamine (SP) for pregnant women in 2001, but coverage remains low. This study examined the influence of demand side factors on IPTp coverage.

Malaria Journal | 2012 | 15 pp.

• An analysis of timing and frequency of malaria infection during pregnancy in relation to the risk of low birth weight, anemia and perinatal mortality in Burkina Faso

Valea I., Tinto H., Drabo M. et al.

A prospective study aiming at assessing the effect of adding a third dose sulphadoxine-pyrimethamine (SP) to the standard two-dose intermittent preventive treatment for pregnant women was carried out in Hounde, Burkina Faso. Malaria infection during first trimester of pregnancy is associated to a higher risk of low birth weight. Women should be encouraged to use long-lasting insecticidal nets before and throughout their pregnancy.

Malaria Journal | 2012 | 12 pp.

• Supply-related drivers of staff motivation for providing intermittent preventive treatment of malaria during pregnancy in Tanzania: evidence from two rural districts

Mubyazi, G., Bloch, P., Byskov, J. et al.

This paper describes the supply-related drivers of motivation and performance of HWs in administering IPTp doses among other ANC services delivered in public and private health facilities (HFs) in Tanzania, using a case study of Mkuranga and Mufindi districts. Malaria Journal | 2012 | 23 pp.

#### 2011

• World Malaria Report 2011

The World Malaria Report 2011 summarizes information received from 106 malaria-endemic countries and a range of other sources. It analyses prevention and control measures according to a comprehensive set of indicators, and highlights continued progress towards global malaria

targets.

World Health Organization | 2011 | 259 pp.

• Systematic review and meta-analysis: rapid diagnostic tests versus placental histology, microscopy and PCR for malaria in pregnant women

Kattenberg J., Ochodo E., Boer K., Schallig H. et al.

The findings suggest that rapid diagnostic tests (RDTs) and molecular techniques (PCR) may have good performance characteristics to serve as alternatives for the diagnosis of malaria in pregnancy, besides any other limitations and practical considerations concerning the use of these tests. Nevertheless, more studies with placental histology as reference test are urgently required to reliably determine the accuracy of RDTs and PCR for the diagnosis of placental malaria. P. vivax infections have been neglected in diagnostic test accuracy studies of malaria in pregnancy.

Malaria Journal | 2011

• <u>Intermittent preventive treatment regimens for malaria in HIV-positive pregnant women</u> (Review)

Mathanga D., Uthman O., Chinkhumba J.

Intermittent preventive treatment is recommended for pregnant women living in malaria endemic countries due to benefits for both mother and baby. However, the impact may not be the same in HIV-positive pregnant women, as HIV infection impairs a woman's immunity. The objectives is to compare intermittent preventive treatment regimens for malaria in HIV-positive pregnant women living in malaria-endemic areas.

Cochrane Database of Systematic Reviews | 2011

• Community case management of malaria using ACT and RDT in two districts in Zambia: achieving high adherence to test results using community health workers

Chanda P., Hamainza B., Moonga H. et al.

Community Health Workers are effective delivery points for prompt and effective malaria case management at community level. Adherence to test results is the best ever reported in Zambia. Further areas of implementation research are discussed.

Malaria Journal | 2011

Patterns of anti-malarial drug treatment among pregnant women in Uganda

Sangare L., Weiss N., Brentlinger P. et al.

The study objective was to determine the degree to which presumed episodes of uncomplicated symptomatic malaria in pregnancy were treated with a recommended anti-malarial regimen in a region of Uganda. Self-reported malaria was extremely common in this population (women living in Jinja, Uganda who had been pregnant in the past year). Adherence to treatment guidelines for the management of malaria in pregnancy was poor.

Malaria Journal | 2011

• The President's Malaria Initiative. Fifth annual Report to congress

This report describes the role and contributions of the US Government to reduce the burden of malaria in Africa and its impact on health systems.

Chapter Three focuses on malaria in pregnancy.

USAID | April 2011

• Claims about the misuse of insecticide-treated mosquito nets: Are these evidence-based? Eisele T., Thwing J., Keating J.

While it is clear there is room for improving the level of ITN use among those who have them, and that misuse of nets occasionally occurs, the authors of the article found very little evidence to support claims of widespread misuse.

PLoS Medicine | 2011

 Reported reasons for not using a mosquito net when one is available: a review of the published literature

Pulford J., Hetzel M., Bryant M. et al.

Discomfort, primarily due to heat, and perceived (low) mosquito density were the most widely identified reason for non-use. Social factors, such as sleeping elsewhere, or not sleeping at all, were also reported across studies as were technical factors related to mosquito net use (i.e. not being able to hang a mosquito net or finding it inconvenient to hang) and the temporary unavailability of a normally available mosquito net (primarily due to someone else using it). However, confidence in the reported findings was substantially undermined by a range of methodological limitations and a dearth of dedicated research investigation. Malaria Journal | 2011

• Malaria associated symptoms in pregnant women followed-up in Benin Huynh B., Fievet N., Gbaguidi G. et al.

This study found that pregnant women infected with Plasmodium only had symptoms related to malaria when infection was detected at unscheduled visits, generally at distance from the last dose of intermittent preventive treatment during pregnancy (IPTp). A third dose of IPTp administered at the end of pregnancy might avoid such late infections.

Malaria Journal | 2011

Successes and challenges for Malaria in Pregnancy Programming: A three-country analysis
 This brief provides ministries of health, donors, and malaria and reproductive health
 implementing partners with a synthesis of lessons learned in malaria in pregnancy programming
 in three relatively high-performing countries—Malawi, Senegal, and Zambia—highlighting best
 practices and successful strategies that can be applied to other malaria-endemic countries
 throughout Africa.

USAID | 2011

Natural products as starting points for future anti-malarial therapies: going back to our roots?
 Wells T.

The relative paucity of new herbal medicinal product scaffolds active against malaria results discovered in recent years suggest it is time to re-evaluate the 'smash and grab' approach of randomly testing purified natural products and replace it with a patient-data led approach. This will require a change of perspective form many in the field.

Malaria Journal | 2011

• Guidelines for the treatment of malaria. Second edition

The WHO Guidelines for the treatment of malaria, which were first published in 2006, provide global, evidence-based recommendations on the case management of malaria, targeted mainly at policy-makers at country level, providing a framework for the development of specific and more detailed national treatment protocols that take into account local antimalarial drug resistance patterns and health service capacity in the country. This second edition of the guidelines revisits the recommendations based on updated evidence. You will also find information on malaria in pregnancy in these guidelines.

WHO | 2010

Reduced risk for placental malaria in iron deficient women

Senga E., Harper G., Koshy G. et al.

Women with either acute, or acute and chronic placental malaria were less likely to have iron deficiency than women without placental malaria infection There is a priority to establish if reversing iron deficiency through iron supplementation programs either prior to or during pregnancy enhances malaria risk.

Malaria Journal | 2011

• Parasitological efficacy of antimalarials in the treatment and prevention of falciparum malaria in pregnancy 1998 to 2009: A systematic review

McGready R., White N., Nosten F.

The objective was to review the therapeutic efficacy of antimalarials used for treatment and intermittent preventive treatment (IPT) in pregnancy. The author's conclusions: Drugs used in pregnancy should aim for 95% efficacy but many currently deployed regimens are associated with much lower cure rates.

BJOG | 2011

• Malaria control in pregnancy: still a long way to go (Comment)

Gutman J., Slutsker L.

In the Lancet Infectious Diseases, Anna Maria van Eijk and colleagues report the progress of coverage with malaria control interventions in pregnant women in sub-Saharan Africa. Van Eijk and colleagues' analysis is a reminder that cost-effective techniques to scale up malaria control interventions are needed. High rates of attendance at antenatal clinic can provide an effective platform to deliver these services; success will require strengthened systems through training of health workers, education of clients, and robust supply chains to ensure goals are achieved. The Lancet Infectious Diseases | 2011

• Coverage of malaria protection in pregnant women in sub-Saharan Africa: a synthesis and analysis of national survey data

Eijk van A., Hill J., Alegana V. et al.

Despite success in a few countries, coverage of insecticide-treated nets and intermittent preventive treatment in pregnant African women is inadequate; increased efforts towards scale-up are needed.

The Lancet | 2011

 Intermittent preventive treatment of malaria with sulphadoxine-pyrimethamine during pregnancy in Burkina Faso: effect of adding a third dose to the standard two-dose regimen on low birth weight, anaemia and pregnancy outcomes

Valea, I.; Tinto, H.; Drabo, M. et al. Intermittent preventive treatment with sulphadoxine-pyrimethamine (IPTp-SP) is being implemented in most malaria endemic countries as a standard two-doses regimen as it reduces the risk of low birth weight (LBW) and the prevalence of maternal anaemia. Nevertheless, where the risk of infection close to delivery is high because of intense transmission, a third IPTp-SP dose may further reduce the negative effects of malaria on pregnancy outcome. The risk of LBW and severe anaemia tended to be lower in the SP3 group, though this was not statistically significant, probably due to the low uptake of the intervention which reduced the power of the study. Further studies are needed for establishing whether a third SP dose has a real benefit in preventing the negative effects of malaria in pregnancy in settings where transmission is markedly seasonal.

Malaria Journal | 2010

 Anti-bacterial activity of intermittent preventive treatment of malaria in pregnancy: comparative in vitro study of sulphadoxine-pyrimethamine, mefloquine, and azithromycin Capan M., Mombo-Ngoma G., Makristahtis A. et al.

In this study, the intrinsic anti-bacterial activity of mefloquine and azithromycin was assessed in comparison to sulphadoxine-pyrimethamine against bacterial pathogens with clinical importance in pregnancy in a standard microdilution assay.

Malaria Journal | 2010

• Saving lives with malaria control: Counting down to the Millennium Development Goals

This report aims to introduce to the Roll Back Malaria (RBM) community the Lives Saved Tool, or
LiST model, and its appropriate use and value in estimating lives saved through malaria

prevention both retrospectively and prospectively.

World Health Organization | 2010

• Comparison of real-time PCR and microscopy for malaria parasite detection in Malawian pregnant women

Rantala A., Taylor S., Trottman P. et al.

Although microscopy remains the most appropriate method for clinical malaria diagnosis in field settings, molecular diagnostics such as real-time PCR offer a more reliable means to detect malaria parasites, particularly at low levels. Determination of the possible contribution of these submicroscopic infections to poor birth outcomes and maternal health is critical. Malaria Journal | 2010

• <u>Possession and usage of insecticidal bed nets among the people of Uganda: Is BRAC Uganda</u> Health Programme pursuing a pro-poor path?

Masud A., Zerihun A.

The BRAC Uganda's bed nets distribution at a subsidized price appeared to be inadequate and inequitable, and BRAC's knowledge dissemination is insufficient for initiating preventive actions such as proper use of insecticidal bed nets to interrupt malaria transmission. Findings contribute to the on-going debate on bed nets distribution in Africa and make a strong case for its free distribution.

PLoS One | 2010

• <u>Decreasing burden of malaria in pregnancy in Malawian women and its relationship to use of</u> intermittent preventive therapy or bed nets

Feng G., Simpson J., Chaluluka E. et al.

Increased bednet coverage explains changes in parasitemia and birth weight among pregnant women better than sulfadoxine-pyrimethamine use. High bed net coverage, and sulfadoxine-pyrimethamine resistance, may be contributing to its apparent loss of effectiveness. PLoS One | 2010

• Perceptions on the use of insecticide treated nets in parts of the Imo River Basin, Nigeria: Implications for preventing malaria in pregnancy

Chukwuocha U.M., Dozie I., Onwuliri C. et al.

This study aimed at assessing perceptions on use of ITNs in parts of the Imo River Basin, Nigeria and its implications in preventing malaria in pregnancy. Data was collected using focus group discussions, key informant interviews and structured questionnaires. Results showed high awareness on the benefits of ITNs. Factors affecting use of ITNs included its high cost, perceptions of chemicals used to treat them as having dangerous effects on pregnancy, low utilization of antenatal care, husband's lack of interest in malaria prevention and perceptions that adolescent girls are at low risk of getting malaria.

African Journal of Reproductive Health | 2010

• Bottlenecks for high coverage of intermittent preventive treatment in pregnancy: The case of adolescent pregnancies in rural Burkina Faso

Peeters Grietens K., Gies S., Coulibaly S.O. et al.

This study shows that adolescents need to be targeted specifically, prior to their first pregnancy and with measures adapted to their social context, addressing their structural constraints and needs and going beyond standard health promotion campaigns.

PLoS One | 2010

• Effects of Malaria in pregnancy on newborn anthropometry

Falade C., Tongo O., Ogunkunle O. et al.

During a cross-sectional study of 983 mothers delivering in a secondary health care facility in Ibadan, southwestern Nigeria, an area of high malaria transmission, the effect of maternal and placental malaria parasitaemia on newborn anthropometry was evaluated. Malaria in pregnancy

results in symmetric foetal growth restriction and the effect is more marked among primigravid mothers.

The Journal of Infection in Developing Countries | 2010

Availability and utilization of malaria prevention strategies in pregnancy in eastern India
 Wylie B., Hashmi A., Singh N. et al.

A disconnect remains between routine antenatal practices in India and known strategies to prevent and treat malaria in pregnancy. Prevention strategies, in particular the use of insecticide-treated bednets, are underutilized. Gaps highlighted by this study combined with recent estimates of the prevalence of malaria during pregnancy in these areas should be used to revise governmental policy and target increased educational efforts among health care workers and pregnant women.

BMC Public Health | 2010

• The potential role of the educational system in addressing the effect of inadequate knowledge of mosquitoes on use of insecticide-treated nets in Ghana

Kudom A., Mensah B.

This study was undertaken to get a better understanding of perceptions of malaria, knowledge on mosquitoes among secondary and tertiary students in Cape Coast, Ghana.

Malaria Journal | 2010

• <u>Safety of artemether-lumefantrine in pregnant women with malaria: results of a prospective</u> cohort study in Zambia

Manyando C., Mkandawire R., Puma L. et al.

Safety data regarding exposure to artemisinin-based combination therapy in pregnancy are limited. This prospective cohort study conducted in Zambia evaluated the safety of artemether-lumefantrine in pregnant women with malaria.

Malaria Journal | 2010

• Which family members use the best nets? An analysis of the condition of mosquito nets and their distribution within households in Tanzania

Tsuang A., Lines J., Hanson K.

Two main findings emerge from the analysis of the survey data. First, small decreases in the household person-to-net ratio resulted in proportionately large increases in within-household net coverage levels. Second, infants were more likely to use intact ITNs than any other household member. More generally, this study suggests that the more vulnerable-to-malaria members of the family are given priority for use of the most protective nets in the household. Malaria Journal | 2010

• <u>Sleeping arrangement and house structure affect bed net use in villages along Lake Victoria</u> Iwashita H., Dida H. et al.

The objectives of this study were to explore whether an individual's sleeping arrangements and house structure affect bed net use in villages along Lake Victoria in western Kenya.

Malaria Journal | 2010

• Effect of training on the use of long-lasting insecticide-treated bed nets on the burden of malaria among vulnerable groups, south-west Ethiopia: baseline results of a cluster randomized trial Deribew A. et al.

The availability and utilization of treated bednets was low in the study area. The prevalence of malaria and anaemia was high. Intervention strategies of malaria should focus on high risk population and vulnerable groups.

Malaria Journal | 2010

• <u>Intermittent screening and treatment versus intermittent preventive treatment of malaria in pregnancy: user acceptability</u>

Smith L., Jones C. et al.

The conclusion of this study is that intermittent screening and treatment and intermittent preventive treatment are equally acceptable to pregnant women. The women were more concerned about quality of services received, in particular the polite and patient attitude of health staff, and positive health implications for themselves and their babies than about the nature of the intervention.

Malaria Journal | 2010

<u>Women's experiences and views about costs of seeking malaria chemoprevention and other antenatal services: a qualitative study from two districts in rural Tanzania</u>

Mubyazi G. et al.

Strengthening of user-fee exemption practices and bringing services closer to the users, are urgently needed measures for increasing equity in health services in Tanzania.

Malaria Journal | 2010

• Placental malaria, anaemia and low birthweight in Yemen

Albiti A., Adam I.et al.

Conclusion of this study is that preventive measures (bednets and intermittent preventive treatment) should be employed for pregnant women regardless of their age or parity. Transactions of the Royal Society of Tropical Medicine and Hygiene | 2010

World Malaria Report 2009

This report demonstrates that funding has resulted in steady increases in the coverage with malaria control interventions, especially insecticide-treated mosquito nets. It also shows that where these interventions have been fully scaled up, the malaria burden falls dramatically. World Health Organization | 2009

• Quantifying the number of pregnancies at risk of malaria in 2007: A demographic study Dellicour S., Tatem A. et al.

Comprehensive and contemporary estimates of the number of pregnancies at risk of malaria are not currently available, particularly for endemic areas outside of Africa. We derived global estimates of the number of women who became pregnant in 2007 in areas with Plasmodium falciparum and P. vivax transmission.

PLoS Medicine | 2010

• Quinine for the treatment of malaria in pregnancy

Matthew C., Chandramohan D.

The authors of this reaction in the Lancet call for the discontinuation of quinine monotherapy in sub-Saharan Africa. However, combination therapies using quinine for the treatment of uncomplicated malaria in pregnancy were discounted. They agree that artemether with lumefantrine, azithromycin, artesunate with mefloquine, or dihydroartemisinin with piperaquine should be investigated for their potential use in the treatment of pregnant women with uncomplicated malaria.

The Lancet Infectious Diseases | 2010

### 2009

Intermittent preventive treatment of malaria in pregnancy

<u>Can Prenatal Malaria Exposure Produce an Immune Tolerant Phenotype? A Prospective Birth Cohort</u> Study in Kenya

- Estimating the burden of malaria in pregnancy: a case study from rural Madhya Pradesh, India
- Rural Gambian women's reliance on health workers to deliver sulphadoxine pyrimethamine as recommended intermittent preventive treatment for malaria in pregnancy

- Prevalence of Malaria in Pregnant Women in Lagos, South-West Nigeria
- <u>Structural insights into chondroitin sulphate A binding Duffy-binding-like domains from Plasmodium falciparum: implications for intervention strategies against placental malaria</u>
   Plasmodium falciparum malaria in pregnancy: Prevalence of peripheral parasitaemia, anaemia and malaria care-seeking behaviour among pregnant women attending two antenatal clinics in Edo State, Nigeria (full text available through Ilse Egers i.egers@kit.nl)
- A review on high burden of malaria during pregnancy: Need of social science intervention

#### 2008

- Access and barriers to measures targeted to prevent malaria in pregnancy in rural Kenya
- Malaria in pregnancy in an area of stable and intense transmissions: is it asymptomatic?
- <u>Prevention and control of malaria in pregnancy in the African Region. A program implementation</u> guide
- <u>Intermittent preventive therapy with SP for the prevention of malaria in pregnancy: Regimen</u> optimisation studies in Africa
- Malaria in Pregnancy in the Solomon Islands: Barriers to prevention and control
- Malaria in pregnancy pilot projects nationally adopted in Kenya and Malawi
- Control measures for malaria in pregnancy in India
- An autopsy study of maternal mortality in Mozambique: The contribution of infectious diseases

### 2007

- The effect of health care worker training on the use of intermittent preventive treatment for malaria in pregnancy in rural western Kenya
- Estimation of effectiveness of interventions for malaria control in pregnancy using the screening method
- <u>Intermittent preventive treatment of malaria in pregnancy: the effect of new delivery approaches on access and compliance rates in Uganda</u>
- Malaria and anaemia among pregnant women at first antenatal clinic visit in Kisumu, western Kenya
- Seasonal variations in maternal mortality in Maputo, Mazambique: the role of malaria
- Impact of Placental Plasmodium falciparum Malaria on Pregnancy and Perinatal Outcome in Sub-Saharan Africa

#### Websites

- Roll Back Malaria (RBM)
- The Malaria in Pregnancy Library
- Malaria no More
- WHO Malaria in Pregnancy
- USAID Malaria in Pregnancy
- Medicines for Malaria
- Malaria in Pregnancy Consortium
- Malaria Prevention and Treatment
- Shoklo Malaria Research Unit
- GLOBAL NETWORK Neglected Tropical Diseases

# **KIT Library Queries**

# Malaria in Pregnancy

# **Glossary**

# ACT = Artemisinin-based Combination Therapy

Over the past decade, a new group of antimalarials – the artemisinin compounds, especially artesunate, artemether and dihydroartemisinin – have been deployed on an increasingly large scale. These compounds produce a very rapid therapeutic response (reduction of the parasite biomass and resolution of symptoms), are active against multidrugresistant *P. falciparum*, are well tolerated by the patients and reduce gametocyte carriage (and thus have the potential to reduce transmission of malaria). To date, no resistance to artemisinin or artemisinin derivatives has been reported, although some decrease in sensitivity in vitro has been detected in China and Viet Nam. As a response to increasing levels of resistance to antimalarial medicines, WHO recommends that all countries experiencing resistance to conventional monotherapies, such as chloroquine, amodiaquine or sulfadoxine—pyrimethamine, should use combination therapies, preferably those containing artemisinin derivatives (ACTs – artemisinin-based combination therapies) for falciparum malaria (source: Facts on ACTs, Artemisinin-based Combination Therapies, World Health Organization).

#### • IPT = Intermittent Preventive Treatment

Intermittent preventive treatment involves providing all pregnant women with at least two preventive treatment doses of an effective antimalarial drug during routine antenatal clinic visits. This approach has been shown to be safe, inexpensive and effective (source: World Health Organization).

### • MiP = Malaria in Pregnancy

Malarial infection during pregnancy is a major public health problem in tropical and subtropical regions throughout the world. The burden of malaria infection during pregnancy is caused chiefly by *Plasmodium falciparum*, the most common malaria species in Africa. The impact of the other three human malaria parasites (P. *vivax*, P. *malariae*, and P. *ovale*) is less clear (source: World Health Organization).

# • Plasmodium falciparum

Malaria is caused by parasites of the species *Plasmodium*. The parasites are spread to people through the bites of infected mosquitoes. There are four types of human malaria: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*. *Plasmodium falciparum* and *Plasmodium vivax* are the most common. *Plasmodium falciparum* is the most deadly (source: World Health Organization).

### • RDT = Rapid Diagnostic Tests

Malaria rapid diagnostic tests, sometimes called "dipsticks" or malaria rapid diagnostic devices (MRDDs), assist in the diagnosis of malaria by providing evidence of the presence of malaria parasites in human blood. RDTs are an alternative to diagnosis based on clinical grounds or microscopy, particularly where good quality microscopy services cannot be readily provided (source: World Health Organization).