

Malaria during pregnancy: New study assesses risks during first trimester

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The largest ever study to assess the effects of malaria and its treatment in the first trimester of pregnancy has shown that the disease significantly increases the risk of miscarriage, but that treating with antimalarial drugs is relatively safe and reduces this risk.

In the study, carried out at the Shoklo <u>Malaria</u> Research Unit (SMRU), in Thailand and funded by the Wellcome Trust, researchers examined medical records of women attending the unit's antenatal clinic over the 25 years since it was founded.

Malaria kills around one million people each year, mainly children and pregnant women. Malaria in pregnancy is a major cause of <u>maternal</u> <u>mortality</u>, and <u>low birth weight</u> which predisposes to <u>neonatal mortality</u>. The disease is caused by infection with the <u>malaria parasite</u>, with two major species Plasmodium <u>falciparum</u> and Plasmodium vivax commonly infecting pregnant women in the South East Asia region The parasites are transmitted into the blood stream through the bite of infected mosquitos. They proceed to enter the liver where they multiply before leaving and infecting <u>red blood cells</u>. P. vivax is able to re-emerge from the liver stage which cannot be treated in pregnancy.

The most effective drug for treating malaria is <u>artemisinin</u>, which is usually given as part of a combination therapy, a cocktail of drugs aimed at treating the disease whilst reducing the risk of the emergence of parasites resistant to one particular drug. Artemisinin combination therapies (ACT) are recommended by the <u>World Health Organization</u>



for the treatment of malaria except in the first trimester. This is because animal studies have indicated that the drugs can be toxic to embryos.

Despite the risks to pregnant women, there is very little published evidence on the effects of malaria and antimalarial <u>drug exposure</u> during the first trimester of pregnancy. This is in part because antenatal clinic services are often unavailable in the rural tropics and if they are, women rarely attend the clinics before their second trimester. Also, <u>pregnant</u> <u>women</u> are usually excluded from clinical trials of new drugs because of the risks of adverse effects; no randomised controlled trial has ever been carried out on how best to treat malaria in the first trimester.

In a study published today in the journal *Lancet Infectious Diseases*, researchers at the SMRU, part of the Wellcome Trust-Mahidol University-Oxford University Tropical Medicine Research Programme, examined the records of all women attending antenatal clinics at the unit. Of these, 16,668 had no malaria during pregnancy, whilst 945 had only a single episode during their first trimester and no episodes later in pregnancy.

Around one in five pregnancies resulted in miscarriage when malaria was not a factor. Symptomatic malaria increased the risk of miscarriage to one in two pregnancies; for asymptomatic malaria, the risk of miscarriage was one in three pregnancies. In women with malaria, more severe disease, higher levels of parasites in the blood and infection at an earlier stage of pregnancy increased the risk of miscarriage further. The risks associated with miscarriage were similar for P. falciparum and P. vivax infections.

P. falciparum infections were treated with quinine or artesunate, or inadvertently with ACT, and P. vivax with chloroquine. Of the women treated (irrespective of symptoms), 26% miscarried following chloroquine, 27% following quinine and 31% following artesunate.



After inadvertent treatment with an ACT the miscarriage rate was 24%, comparable to the rate associated with other treatments.

"Malaria is a potentially deadly disease and is particularly dangerous during pregnancy, both to the health of the mother and to the health of her unborn child," explains Dr Rose McGready from the Shoklo Malaria Research Unit. "Understanding the risks is essential for weighing up the treatment options. Our work has highlighted the particular risk factors with malaria infection during pregnancy. Particularly worrying is the risk of miscarriage even when the disease is asymptomatic. However, whilst the dangers of miscarriage are considerable, our study offers some good news, that the most common drugs reduce this risk significantly."

Combating infectious diseases is one the strategic priorities of the Wellcome Trust. Much of this work is carried out at a local level in regions where disease is endemic. This includes several major overseas programmes, including the Wellcome Trust-Mahidol University-Oxford University Tropical Medicine Research Programme.

Dr Jimmy Whitworth, Head of International Activities at the Wellcome Trust, says: "This is a very important observational study on the risks of treating malaria in women in early pregnancy, a key high-risk group for this infection. These results, which come from the research group that has done the majority of studies of malaria in pregnancy anywhere in the world, show that antimalarial treatment with standard first-line drugs reduces the risk of <u>miscarriage</u> in the first trimester. These findings are likely to change practice guidelines worldwide and to save the lives of many women and unborn children."

Provided by Wellcome Trust

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