Policy

Clinical Guideline

Malaria in Pregnancy

Policy developed by: SA Maternal & Neonatal Clinical Network
Approved SA Health Safety & Quality Strategic Governance Committee on: 24 June 2015
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Summary Guideline for the management of the pregnant woman with Malaria

Keywords fever, malaise, abdominal discomfort, muscle, joint aches, chills, sweats, rigors, gastrointestinal illness, mosquito, permethrin-emulsifiable, mosquito repellent, mefloquine, malaria, malarial parasites, quinine, clindamycin, mefloquine, nausea, dizzines, anxiety, vivid dreams, visual disturbances, anaemia, Malaria in Pregnancy clinical guideline

Policy history Is this a new policy? **N**
Does this policy amend or update an existing policy? **Y v3.0**
Does this policy replace an existing policy? **N**

Applies to All Health Networks

Staff impact All Clinical, Medical, Nursing, Allied Health, Emergency, Dental, Mental Health, Pathology

PDS reference CG131

Version control and change history

Version	Date from	Date to	Amendment
1.0	19 May 04	25 Jan 10	Original version
2.0	25 Jan 10	05 Aug 13	reviewed
3.0	05 Aug 13	24 Jun 15	reviewed
4.0	24 Jun 15	current	

Government of South Australia
SA Health

South Australian Perinatal Practice Guidelines

malaria in pregnancy

Note

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:
The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown prior to the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet we experience the worst health outcomes in comparison. Our Aboriginal women are 2-5 times more likely to die in childbirth and our babies are 2-3 times more likely to be low birth weight. Despite these unacceptable statistics the birth of an Aboriginal baby is an important Cultural event and diverse protocols during the birthing journey may apply.

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Contact: South Australian Perinatal Practice Guidelines Workgroup at:
cywhs.perinatalprotocol@health.sa.gov.au

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Introduction

- Malaria occurs mainly in the tropical areas of Africa, Asia, and Latin America
- Malaria is a parasitic disease spread by the bite of the female *Anopheles* mosquito, which is active between dusk and dawn
- Five main species of the malaria parasite infect humans:
    - *Plasmodium falciparum* (most severe form)
    - *Plasmodium vivax*
    - *Plasmodium ovale*
    - *Plasmodium malariae*
    - *Plasmodium knowlesi*
- Malaria can be a life threatening for non-immune women during pregnancy. Severe malaria may lead to fetal loss and high maternal mortality due to hypoglycaemia and acute respiratory distress syndrome
- Australia was declared malaria-free by the World Health Organization in 1981, and since then, only a small number of cases of locally acquired malaria have been reported from North Queensland (in Cape York, Cairns and Badu Island in the Torres Strait)[2]
- Pregnant women should be advised to avoid travel to malaria-endemic areas
- For pregnant women who cannot avoid travelling to malaria-risk areas (in South America, Africa, the Indian subcontinent, Asia, and the South Pacific) the medical officer should consult with an Infectious Diseases specialist or doctor experienced in Travel medicine to determine the appropriate chemoprophylaxis agent (www.cdc.gov/travel/mal_preg_pub.htm)
- Malaria in pregnancy adversely affects the mother and fetus. The main complications are:
    - Miscarriage
    - Stillbirth
    - Preterm birth
    - Low infant birthweight[4,5]
    - Severe maternal and neonatal anaemia[4,5]
- Drug treatments for malaria during pregnancy reduce severe antenatal anaemia, and are associated with higher birthweight in the baby, particularly for low parity women[5]

Clinical symptoms

- Fever
- Malaise
- Headache
- Abdominal discomfort
- Muscle and joint aches
- Chills, sweats, rigors
- May present as a respiratory or gastrointestinal illness

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Incubation period

- 95 % of cases develop symptoms within one month
- Incubation period depends on the species[5]
    - *P. falciparum* 9-14 days
    - *P. vivax* and *P. ovale* 12-18 days
    - *P. malariae* 18-40 days
    - *P. knowlesi 9-12 days*

Route of transmission

- Malaria is caused by the bite of the female *Anopheles* mosquito, which results in infection of the red blood cell[10,11]

Infection precautions

- Standard precautions

Prevention

- Minimise exposure to mosquitoes in malarial risk areas
    - Avoid outdoor night time activities
    - Use mosquito nets preferably impregnated with Permethrin-emulsifiable concentrate. Permethrin is an insecticide but not a repellent (not recommended for skin application)
    - Wear clothing that covers the arms and legs
    - Use a mosquito repellent (a solution of 20 to 50% DEET has been in widespread use with no apparent effects, however, there is no specific data on the safety of DEET in the first trimester of pregnancy)[11]
- There is no 100 % effective malaria chemoprophylaxis regimen for women planning pregnancy or during pregnancy. Malaria chemoprophylaxis should **only** be prescribed in consultation with an Infectious Diseases specialist or experienced Travel medicine doctor

Diagnosis

- Malaria should be considered in pregnant women with a fever who have travelled to malaria-endemic areas

Laboratory diagnosis

- Collect blood in an EDTA tube for 'thick and thin films' to detect malarial parasites. Also a malarial antigen assay is available in South Australia
    - In a febrile patient, 3 negative malaria smears 12 to 24 hours apart rules out the diagnosis of malaria[12]
- Rapid diagnostic tests for malaria antigens should also be requested[12] (a negative antigen test does not exclude malaria)[22]
- Other tests should include complete blood examination, urea, creatinine, electrolytes, liver function tests, serum glucose, venous pH, serum lactate and coagulation studies

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Notification

- Malaria is a **notifiable disease**. Notification should be made to the Communicable Disease Control Branch of SA Health as soon as possible and at least within three days of suspicion of diagnosis by fax, post or telephone (1300 232 272)[6]
- The appropriate notification form for reporting a notifiable disease or related death in South Australia may be downloaded and is available from URL: http://www.sahealth.sa.gov.au/NotifiableDiseaseReporting

Antepartum[12]

- Regular antenatal care including assessment of maternal haemoglobin, platelets, glucose and fetal growth scans is advised following recovery from an episode of malaria
    - If growth restriction is identified, follow management as per 'Fetal growth restriction' guideline (in the A to Z index at www.sahealth.sa.gov.au/perinatal)

Intrapartum[12]

- Uncomplicated malaria in pregnancy is not a reason for induction of labour
- Vertical transmission to the fetus can occur particularly when there is infection at the time of birth and the placenta and cord are blood film positive for malaria
- Send placenta for histopathology
- Send additional cord and infant blood films to detect congenital malaria

Antimalarial treatment

- Early treatment of malaria in the woman reduces the systemic effects of parasitaemia and reduces the adverse effects on the fetus

Advice should be sought from an Infectious Diseases specialist or experienced Travel medicine doctor before prescribing antimalarials for prophylaxis or treatment. The choice of agent depends on many factors including the area to which the woman has or is travelling and reported antimalarial drug resistance patterns

Severe malaria in pregnancy

- Treat as complicated malaria if one or more of the following:
    - Unable to tolerate oral medication
    - Parasitaemia >2% of red blood cells
- Any signs of severe malaria:
    - altered mental state
    - jaundice
    - renal impairment
    - oliguria
    - unable to sit unaided
    - respiratory distress
    - severe anaemia
    - hypoglycaemia
    - acidosis

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First trimester

- Expert advice should be obtained from an Infectious Diseases specialist for management of severe malaria
- ***Artesunate*** 2.4 mg / kg IV, on admission and repeat at 12 hours and 24 hours, then once daily until oral therapy is tolerated
- **OR** (if parenteral artesunate is not immediately available) ***Quinine dihydrochloride*** 20 mg / kg IV over 4 hours as a loading dose, then 10 mg / kg IV over 4 hours (starting 4 hours after the loading dose is completed), 8-hourly until oral therapy is tolerated
- The IV loading dose of quinine is not required if the patient has received:
    - 3 or more doses of quinine or quinidine in the last 48 hours
    - Mefloquine prophylaxis in the last 24 hours or a treatment dose of mefloquine in the last 3 days
    - For patients receiving IV quinine, measure blood pressure and blood glucose concentration frequently (because quinine stimulates insulin secretion and can cause hypoglycaemia). Cardiac monitoring is also necessary. If treatment with IV quinine continues for longer than 48 hours, dose adjustment may be necessary, especially in patients with renal impairment

Second and third trimester

- IV artesunate as above
- IV quinine ***should be avoided*** in the second and third trimesters as it is associated with recurrent hypoglycemia [3]

Uncomplicated malaria in pregnancy

- Refers to mild cases and excludes criteria listed above in severe malaria

First trimester

- Quinine sulfate 600 mg (adult less than 50 kg: 450 mg) orally, 8-hourly for 7 days, PLUS clindamycin 300 mg orally, 8-hourly for 7 days

Second and third trimester

- artemether+lumefantrine tablets 20+120 mg
    - 4 tablets per dose orally with fatty food or full-fat milk (to ensure adequate absorption of lumefantrine), at 0, 8, 24, 36, 48 and 60 hours, making a total adult dose of 24 tablets in 6 doses
- **If unable to tolerate oral therapy, treat as for severe malaria as above**

Adverse effects of uncomplicated malaria

- Anaemia is one of the principal adverse effects of uncomplicated malaria in pregnancy and all women with malaria should be screened for anaemia. If anaemia is detected, iron and folic acid supplementation should be considered after completion of a course of antimalarials[10,11]

Resistance[21]

- **Artemisinin resistance** has been reported in some areas of the Greater Mekong Sub region (Thailand, Vietnam, Cambodia, Laos and Myanmar [Burma]), resulting in reduced efficacy of artemisinin-based combination therapy against **P. falciparum** (but not other malaria species)
- For patients with malaria caused by P. falciparum (either alone or with other species) acquired from this region and who respond slowly to artemether+lumefantrine (i.e. persisting parasitaemia after 72 hours of therapy), switch to oral quinine sulfate 600 mg (adult less than 50 kg: 450 mg) orally, 8-hourly for 7 days PLUS clindamycin 300 mg orally, 8-hourly for 7 days

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Eradication treatment for dormant parasites in the liver

- **P. vivax** and **P. ovale** can exist as dormant parasites (hypnozoites) in the liver, which can reactivate to cause relapsed malaria. The regimens above for the blood-stage of malaria (see above) do not eliminate hypnozoites, so continued treatment with chloroquine throughout pregnancy is required for both P.vivax and P.ovale
- ***Primaquine for the treatment of hypnozoites should not be given during pregnancy***
- Pregnant women with these species should be maintained on chloroquine prophylaxis for the duration of their pregnancy
    - The dose of chloroquine phosphate 500mg orally once per week (available via the Special Access Scheme) equivalent to 400mg of hydroxychloroquine sulphate [20,22]

Postpartum

- After delivery, patients with **P. vivax** or **P. ovale** infections may be treated with primaquine providing glucose-6-phosphate dehydrogenase (G6PD) deficiency has been excluded in both the mother and her breastfed infant
- For **P. vivax** infection, once G6PD deficiency has been excluded for mother and breastfed infant, use:
    - Primaquine 30 mg orally, daily, or if nausea occurs 15 mg orally, 12-hourly. Treat for a minimum of 14 days or, in adults more than 70 kg, until a total cumulative dose of 6 mg/kg is reached
- For **P. ovale** infection, once G6PD deficiency has been excluded, for mother and breastfed infant, use:
    - Primaquine 15 mg orally, daily for 14 days
- Primaquine can cause severe haemolysis in patients who are glucose-6-phosphate dehydrogenase (G6PD) deficient. If the patient is G6PD deficient, seek expert advice. For persons with borderline G6PD deficiency or as an alternate to the above regimen, primaquine may be given at the dose of 45 mg (base) orally one time per week for 8 weeks, seek Infectious Diseases specialist advice. See reference below

Antimalarial medications

Chloroquine*/ Hydroxychloroquine

- There has been no evidence of harmful effects on the fetus when chloroquine / hydroxychloroquine is used in the recommended doses for the prevention or treatment of malaria in pregnancy[13,16]
- There have been cases reports describing an association with fetal effects including neurological disturbances and interference with hearing, balance and vision when chloroquine is used in high doses and long term therapy for other indications. However, causation has not been established[13,16]
- *Chloroquine is not registered in Australia but is available via the Special Access Scheme

Mefloquine

- Melfoquine registries and surveillance data have recorded thousands of exposures (mainly in the first trimester of pregnancy) with no increase rate of malformations or spontaneous abortions[15]
- Mefloquine may be used throughout pregnancy for the prophylaxis and treatment of malaria if there is no resistance[13]

Primaquine

- Primaquine should not be used during pregnancy because of the potential risk of haemolytic effects in the fetus[13]

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- Primaquine may be used during breastfeeding but should be avoided in breastfed infants who have glucose-6-phosphate dehydrogenase (G6PD) deficiency, are less than one month old or have hyperbilirubinaemia, as there is a risk of haemolysis in these infants[20]

Quinine

- Quinine has not been associated with an increased risk of birth defects when used in doses for the treatment of malaria,[17] however when used in the last part of pregnancy severe maternal hypoglycaemia has been reported[13]
- A small number of case reports have suggested that eye, ear, CNS and limb defects may be associated with quinine use[16], however these results have not been replicated in a larger surveillance study[18]
- Quinine may be used in pregnancy[13]

Clindamycin

- Clindamycin is used in combination with oral quinine for the treatment of uncomplicated *P. falciparum* infection. It has not been associated with an increased risk of malformations or complications when used in pregnancy

Artermether+Lumefantrine(Riamet®) or Atovaquone+Proguanil (Malarone®)

- Artermether+Lumefantrine (Riamet®) or Atovaquone+Proguanil (Malarone®) may be used on advice from an Infectious Diseases Specialist if other treatment options are not available or are not being tolerated[19]
- Experience regarding the use of artemisinin based therapy in pregnancy is limited to less than 1,000 reported cases (250 exposures to artermether+lumefantrine) and the majority of exposures have been in the second and third trimesters. No difference in the incidence of birth defects or birth outcomes has been observed when compared to controls[18]
- There have been a limited number of pregnancies exposed to atovaquone+proguanil and there has been no significant association with increased risk of birth defects[19]

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Abbreviations

CDC	Centers for Disease Control
DEET	N,N-diethyl-meta-toluamide
EDTA	Ethylenedinitrilotetraacetic acid
e.g.	For example
G6PD	glucose-6-phosphate dehydrogenase
RCOG	Royal College of Obstetricians and Gynaecologists
WHO	World Health Organization

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