Republic of Sudan
Federal Ministry of Health

Sudan
Malaria Diagnosis and Treatment Protocol
2017

Directorate of Communicable and Non-communicable Diseases Control

Khartoum, Sudan

June 2017
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**Abbreviations**

- **ACTs**: Artemisinin-based Combination Therapies
- **AL**: Artemether-lumefantrine
- **An**: Anopheles
- **ARDS**: Adult respiratory distress syndrome
- **ARF**: Acute renal failure
- **AS**: Artesunate
- **AS+SP**: Artesunate+Sulfadoxine / Pyrimetahmine
- **BF**: Blood film
- **BFFM**: Blood film for malaria
- **CFR**: Case Fatality Rate
- **CNCDCD**: Communicable and Non-communicable Diseases Control Directorate
- **DHAP**: Dihydroartemisinin-piperaquine
- **EMRO**: East Mediterranean Regional Office
- **FDPs**: Fibrin degradation products
- **FFP**: Fresh frozen plasma
- **FMOH**: Federal Ministry of Health
- **G6PD**: Glucose-6-Phosphate Dehydrogenase Deficiency
- **Hb**: Haemoglobin
- **IM**: Intramuscular
- **IUGR**: Intra-uterine growth retardation
- **IV**: Intravenous
- **LFTs**: Liver function tests
- **MIP**: Malaria in Pregnancy
- **MIS**: Malaria Indicator Survey
- **P.**: *Plasmodium*
- **PCV**: Packed cell volume
- **Pf**: *P. falciparum*
- **PT**: Prothrombin time
- **PTT**: Partial thromboplastin time
- **Pv**: *P. vivax*
- **RBCs**: Red Blood Cells
- **RDTs**: Rapid Diagnostic Tests (malaria)
- **SC**: Subcutaneous
- **SM**: Severe Malaria
- **SP**: Sulfadoxine /pyrimetahmine
- **TWBC**: Total white blood cells
- **UM**: Uncomplicated Malaria
- **WHO**: World Health Organization
Acknowledgement

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Introduction

Malaria in Sudan:
Malaria constitutes a major public health problem in Sudan. Almost, 75% of population is at risk of developing malaria. Malaria transmission is unstable putting the whole country under the risk of malaria epidemic. The possibility of epidemic increased with heavy rains, floods and in case of interruption of control activities.

In 2015, 586,827 confirmed cases were reported from public health facilities out of the estimated 1,400,000 cases (970,000; 1,900,000). As well, 868 deaths were reported out of the estimated 3,500 deaths (130; 6800). The reported malaria cases represent 8.7% and 12.2% of the total outpatient attendance and of hospital admissions respectively. The disease proportional mortality was 4.3% in 2015 putting malaria as one of the main causes of death in Sudan.

Results of the Sudan Malaria Indicators Survey in 2016 (Sudan MIS 2016), showed an overall parasite prevalence of 5.9%. The prevalence is range between<1 in Red Sea, Northern, River Nile and Khartoum States to >20% in Central Darfur State. In South and West Darfur, Blue Nile and South Kordofan states the prevalence approached or exceeded 10% (Table 1). The prevalence correlates with age, as children are 3 times more likely to get malaria than adults. Apparently there was no difference between male and female. Similarly, the lowest economic class is at higher risk. Internally displaced people and refugee camps reported prevalence doubled that in rural areas and 3 times higher than that in urban areas. The main species is the *P. falciparum (pf)* representing 87.6% of cases. However, the *P. vivax (pv)* unexpectedly reaches 8.1% and mixed infection (*pf & pv*) approached 5%. *P. vivax* alone plus mixed infection exceeded 15% in North Darfur, West Darfur, South Darfur, River Nile and Khartoum states. The main vector species is *An.arabiensis* besides *An. Gambia* and *An. funestus*.

Epidemiological strata:
Malaria transmission in Sudan is highly linked with climatic conditions. There are two peaks of transmissions; one during the rainy season and the other during winter season. Malaria during the rainy season involves most of the areas in Sudan. In urban areas and in irrigated schemes the transmission is throughout the year with a noticeable peak during the winter time. Six malaria epidemiological strata could be identified: irrigated schemes, seasonal, man-made urban, desert-fringe, riverine and emergency and complex situation malaria.
### Main strategies for malaria control in Sudan:

The Communicable and Non-communicable Disease Control Directorate (CNCDCD) lead the response to malaria toll in Sudan. Sudan is still in the control phase but efforts to move towards elimination in Red Sea, Northern, River Nile and Khartoum States are under way. In line with the malaria global strategy, 2016 -2030, the CNCDCD together with partners emphasize the importance of ensuring:

- Early diagnosis and prompt treatment of malaria,

- Vector control response (including insecticide treated nets, indoor residual spraying and larval source management etc.),

- Forecasting, early detection and containment of the epidemics,

- Capacity building and strengthening of malaria control activities through improvement of the information system, operational research and partnership

- Raising the public awareness and knowledge on malaria prevention and control.

### Table 1: Malaria parasite prevalence using RDT according to residence and state, Sudan MIS, 2016

<table>
<thead>
<tr>
<th>Residence</th>
<th>No. tested</th>
<th>No. positive</th>
<th>% Positive</th>
<th>Total pf</th>
<th>% Pf</th>
<th>Total pv</th>
<th>% pv</th>
<th>Total mixed</th>
<th>% Mixed</th>
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<td>Urban</td>
<td>11062</td>
<td>455</td>
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<td>4.3</td>
</tr>
</tbody>
</table>
Early diagnosis and prompt treatment of malaria:

Since 2004, the treatment of uncomplicated malaria in Sudan has changed from *mono-therapy* to artemisinin-based combination therapies (ACTs). Combination therapy “is the simultaneous use of two or more schizonticidal drugs with independent mode of action and different biochemical targets in the parasite”. Combination therapy is more effective than monotherapy as it delays the emergence of resistance.

The treatment outcome of malaria depends on appropriate management with the recommended ACTs. However, delay in providing adequate care will eventually lead to poor outcome. Adherence of health care providers to treatment policy is necessary to ensure good treatment outcome and to delay the emergence of resistance. The presence of quality assured laboratory diagnosis as well as the availability of adequate, quality assured, safe, and affordable antimalarial medicines at all levels of health service delivery are critical for provision of effective malaria case management. Efforts also should be directed to raise the awareness of patients and communities about the importance of early diagnosis and safety of antimalarial drugs as well as compliance to treatment.

Sudan Malaria Treatment Protocol, 2017:

Many efficacy studies were carried out during the past few years in different regions of the Sudan. Findings showed a decreasing efficacy to artesunate + sulphadoxine-pyremethamine (AS+SP), particularly in Gedarif State (>10%). Findings also showed high efficacy (>95%) of artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DHAP). Moreover, the Sudan MIS 2016 showed irrational use of artemether intramuscular for treatment of uncomplicated malaria. Some published studies showed higher rate of non-adherence of health care providers to the treatment guidelines and self-treatment.

In response to this situation, the malaria technical advisory committee (formed from national experts and partners) recommended the use of AL as a first-line and DHAP as a second-line treatment for malaria in Sudan. The committee also recommended the use of quinine or intravenous artesunate for treatment of severe malaria at hospital level. Artesunate suppository and intramuscular quinine are recommended for pre-referral treatment. The committee recommended banning the use of intramuscular
artemether in Sudan. The recommendations of the committee were endorsed by the “Council of Undersecretary in Federal Ministry of Health” and were issued by the “Ministerial Decree no. 17/2017”. Necessary implementation arrangements are taking place at all levels following this decree.

The CNCDCD established a technical committee to update the malaria national treatment protocol and the training materials. This document “Sudan Malaria Diagnosis and Treatment Protocol, 2017” was written and revised by the committee members taking into consideration the “National Technical Committee Recommendations”, the “Ministerial Decree” and the best practice in malaria treatment as reflected in the “WHO Guidelines for Malaria Treatment, 2015”.

Following this introduction the “Sudan Malaria Diagnosis and Treatment Protocol, 2017” is arranged in 6 units as follow:

- Unit 1: Diagnosis of uncomplicated malaria
- Unit 2: Treatment of uncomplicated malaria
- Unit 3: Management of severe malaria
- Unit 4: Malaria in pregnancy
- Unit 5: Malaria in children
- Unit 6: Malaria in special situations

The diagram below summarizes the general plan for malaria diagnosis and treatment with more details in the following sections.
Patient presents with fever or history of fever (+/- Other symptoms or signs suggestive of malaria)

Yes, and there is no other obvious cause of fever and no danger signs

Ask for BF for malaria or RDT

Positive

This is malaria – Classify to UM or SM (look for signs and symptoms suggestive for SM)

Severe Malaria

General management + Specific treatment

Condition worse with development of severe malaria manifestations

Uncomplicated Malaria

Give the 1st line

Fever but no parasitemia within 4 weeks

Fever and parasitemia not resolved or recurred within 4 weeks

Consider giving 2nd line or its alternative

Negative

Look for other causes (history/examination, investigations)

Possibility of malaria still there

Repeat malaria test and decide accordingly

Malaria excluded

Treat the other causes

No

Look for causes other than malaria

Yes, and there is other obvious cause of fever

Treat the cause

General Plan for Malaria Diagnosis and Treatment
Unit 1: Diagnosis of Uncomplicated Malaria

1.1. Case definition of Uncomplicated Malaria (UM):

Suspected malaria:

Malaria is suspected when a patient presents with fever (or history of fever within 48 hours) with or without other symptoms and signs suggestive of malaria (e.g. headache, vomiting, sweating). The health care worker should consider other common causes of fever in the area as a cause of the current presentation and as co-infection with malaria. In Sudan, these could be pneumonia, tonsillitis, chest infection, measles, abscess, urinary tract infection, etc....

Confirmed malaria:

Malaria is confirmed by demonstration of asexual stages (ring stage, late trophozoite and schizont) of the parasite by microscopy or by detection of the parasite antigens using rapid diagnostic tests (RDTs) in suspected cases.

1.2. Laboratory diagnosis of malaria:

1.2.1 Microscopy:

Whenever asked to do microscopy for suspected malaria cases, laboratory personnel have to prepare thick and thin blood films and stain with Giemsa. In the result form, laboratory personnel should state clearly the following:

- Presence of malaria parasite (seen or unseen)
- Parasite species (Pf, Pv, P. ovale, P. malariae and P. knowlesi)
- Parasite stages (ring stage, trophozoite, schizont and gametocytes)
- Parasite count

Reporting of parasite count:

Two methods are commonly used in reporting blood smear results, the parasite per micro-litre and the “plus” system.

Parasite per micro litre of blood:

This is the preferred methods of reporting in which it is assumed that 1 microliter of blood contains 8,000 white blood cells (WBC). The number of parasites counted relative to the number of leucocytes counted can thus be converted to the number of parasites per microliter of blood by the uncomplicated formula given below:

\[
\text{(Parasite count per µl of blood)} = \frac{\text{(Number of parasites} \times 8000 \text{ WBC})}{\text{(Number of leucocytes counted})}
\]
In practice, this means that if 200 leucocytes are counted (denominator in the formula), the number of the parasites should be multiplied by 40 and if 500 are counted the number of parasites is multiplied by 16 to give parasite per micro litre of blood.

The “Plus” system:
This is a semi-quantitative method. Table 2 below shows the correlation between the crosses (+ +) and the parasite count.

Table (2): The correlation between the degree of parasitemia (crosses) and the parasite estimate per fields

<table>
<thead>
<tr>
<th>Degree of parasitemia</th>
<th>Parasite estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>1-10 parasites per 100 fields</td>
</tr>
<tr>
<td>++</td>
<td>11-100 parasites per 100 fields</td>
</tr>
<tr>
<td>+++</td>
<td>1-10 parasites per one fields</td>
</tr>
<tr>
<td>++++</td>
<td>&gt;10 parasites per one fields</td>
</tr>
</tbody>
</table>

1.2.2 Rapid diagnostic tests (RDTs):
Antigen-based RDTs (NOT antibody-based RDTs) for both *P. falciparum* and *P. vivax* (*pf* and *pv*) or *P. falciparum* with other species (*Pf-PAN*) are recommended for use in Sudan. RDTs are recommended for use all over the Sudan and at all levels of healthcare including home-based malaria management.
Unit 2: Treatment of Uncomplicated Malaria

The objectives of treating uncomplicated malaria cases (UM) are to cure the infection as rapidly as possible, to prevent progression to severe complicated malaria, to prevent onward transmission of infection and to delay the emergence as well as spread of resistance to anti-malarial drugs.

2.1 Treatment of uncomplicated falciparum malaria:
The Federal Ministry of Health recommends the use of Artemether-lumefantrine and Dihydroartemisinin + piperaquine as 1st and 2nd line treatment respectively and the use of Quinine tablets as the third line with dosage and regimens indicated.

2.2.1 First-line treatment:
The "first-line treatment" in Sudan is Artemether-lumefantrine (AL) in form of tablets.

Artemether-Lumefantrine (AL) is a highly effective "fixed dose combination" antimalarial treatment. Each tablet contains artemether and lumefantrine. It has a high clinical and parasitological cure rate and rapid gametocyte clearance.

The total recommended dose is “5 -24 mg/kg body weight artemether and 29 -144 mg/kg body weight lumefantrine”. The recommended dosage regimen of the AL is six doses: twice per day for three days. The dose regimen is as follows:

- First dose after confirmation of malaria,
- Second dose 8 hours after the first dose.
- The 3rd dose 24 hours after the first dose.
- The remaining doses should be taken every 12 hours (Table 3).

The dose should be repeated if the drug is vomited within 30 minutes.

Formulation available: AL in Sudan is currently available as dispersible tablets containing 20 mg artemether and 120 mg lumefantrine (AL 20/120) for children and in standard tablets containing 80 mg artemether and 480 mg lumefantrine (AL 80/480) for adult.

Side effects: There are no serious adverse reactions documented. Studies have shown no risk of cardiotoxicity.

Contraindications: AL should not to be administered to patient known to have hypersensitivity to artemether or lumefantrine. AL is contraindicated in first trimester of pregnancy.
Table (3): Dosage schedule for “artemether–lumefantrine” tablets (AL)

<table>
<thead>
<tr>
<th>Weight in Kg</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Total number of tablets</th>
<th>Tablet strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initially</td>
<td>8 hours after the 1st dose</td>
<td>24 hours after the 1st dose</td>
<td>12 hours after the 3rd dose</td>
<td>12 hours after the 4th dose</td>
<td>12 hours after the 5th dose</td>
</tr>
<tr>
<td>&lt;5</td>
<td>Adjust the dosing considering the weight</td>
<td></td>
<td></td>
<td></td>
<td>AL “20/120” dispersible tablets</td>
</tr>
<tr>
<td>5 - 14</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>15 - 24</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>25 - 34</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>Children &gt;34 kg and adults</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

2.2.2 Second-line treatment:
Treatment failure:
Consider treatment failure when fever and parasitemia persist or recurs within 4 weeks after initial treatment. Treatment failure is not always due to parasite resistance. More time should be spent to revisit history and examination and check the adequacy of AL dose before shifting to the second line treatment.

Dihydroartemisinin + piperaquine tablets (DHAP):
The second line treatment is “Dihydroartemisinin + piperaquine” tablets shortly known as “DHAP”. This is a highly effective fixed dose combination antimalarial treatment.
The recommended dosage regimen of the DHAP is 3 doses over 3 consecutive days: once daily taken at the same time each day. Dosing should be based on body weight.
The daily dose for adult and children weighing 25 kg or more is 4 mg/kg body weight (2-10) per day of dihydroartemisinin + 18 mg/kg body weight (16-26) per day of piperaquine once a day. The dose for children weighing <25 kg is 4 mg/kg body weight (2.5-10) per day of dihydroartemisinin + 24 mg/kg body weight (20-32) per day of piperaquine (Table 4).
Formulations available: Two strengths are currently available for DHAP: for paediatrics cases use 20/160 DHAP (20 mg DHA + 160 mg P) and for adults use 40/320 DHAP (40 mg DHA + 320 mg P).
Table (4): Dosage schedule for “Dihydroartemisinin + pipraquine” tablets (DHAP)

<table>
<thead>
<tr>
<th>body weight (Kg)</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>total no of tablets</th>
<th>DHAP Tablet strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DHAP “20/160” dispersible tablets</td>
</tr>
<tr>
<td>5 - 6</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>7-12</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>13-23</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>24-35</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>36-74</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>75 and above</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

2.2.3 Third line treatment:

*Oral Quinine*: Quinine dihydrochloride, quinine hydrochloride or quinine sulphate orally should be used as a third line drug in case of non-response to DHAP. The oral quinine dose for uncomplicated malaria is 10 mg /kg body weight, 8-hourly for 7 days (Table 5).

Table (5): Dosage schedule for quinine tablet

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight/kg</th>
<th>Number of tablets/dose (300 mg tab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>5 – 6</td>
<td>¼</td>
</tr>
<tr>
<td>1 – 4 years</td>
<td>11-14</td>
<td>½</td>
</tr>
<tr>
<td>5 – 7 years</td>
<td>19 -24</td>
<td>1</td>
</tr>
<tr>
<td>8 – 10 years</td>
<td>25 -35</td>
<td>1 ¼</td>
</tr>
<tr>
<td>11-15 years</td>
<td>37 -50</td>
<td>1 ½</td>
</tr>
<tr>
<td>Above 15 years</td>
<td>&gt;50</td>
<td>2</td>
</tr>
</tbody>
</table>

2.2 Treatment of uncomplicated vivax malaria:

Cases of *P. vivax malaria* constitute about 8% of the total cases and in some states this may exceed 20%. *P. vivax* is susceptible to the first-line treatment (AL) with the same dosage prescribed in case of infection with *P. falciparum* (Table 3). For radical cure of *P. vivax* AL must be followed by primaquine.

Primaquine is used in all cases of *P. vivax* malaria except pregnant women, infant age less than 6 months, breastfeeding mothers and people with known G6PD deficiency.

The dose of primaquine for adult is 15 mg daily for 14 days. The dose for children is 0.25 mg/kg body weight for 14 days.
Unit 3: Management of Severe Malaria

3.1 Case definition of severe malaria (SM):

Severe malaria is defined as malaria due to *P. falciparum* or *P. Vivax* infection that is sufficiently serious to be an immediate threat to life. It is a medical emergency, which requires hospitalization.

The health care providers should regard a patient as having severe malaria if he or she has one or more (mostly seen in combination) of the conditions listed in table 6 below. See the chart on the next page also.

### Table (6): Clinical and laboratory features of severe malaria

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Laboratory findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Impaired level of consciousness (cerebral malaria…)</td>
<td>• Severe anaemia: (Hb&lt;5 g/dl, PCV &lt; 15% in children; &lt; 7g/dl, PCV &lt; 20% in adults)</td>
</tr>
<tr>
<td>• Respiratory distress (acidotic breathing)</td>
<td>• Hypoglycemia: (&lt;2.2 mmol/l - &lt;40 mg/dl)</td>
</tr>
<tr>
<td>• Repetitive convulsions (more than one in 24 hours)</td>
<td>• Metabolic Acidosis (Plasma bicarbonate &lt; 15 mmol/l)</td>
</tr>
<tr>
<td>• Circulatory collapse</td>
<td>• Hyperlactataemia (lactate&gt;5 mmol/l)</td>
</tr>
<tr>
<td>• Pulmonary oedema</td>
<td>• Hyperparasitemia: Parasite count &gt;100 000/μl in low transmission and &gt;250,000/μl in high transmission (≥5% parasitaemia of the RBCs)</td>
</tr>
<tr>
<td>• Abnormal bleeding</td>
<td>• Renal impairment (Serum creatinine&gt; 265 μmol/l)</td>
</tr>
<tr>
<td>• Jaundice</td>
<td></td>
</tr>
<tr>
<td>• Haemoglobinuria</td>
<td></td>
</tr>
<tr>
<td>• Prostration</td>
<td></td>
</tr>
<tr>
<td>• Continuous vomiting</td>
<td></td>
</tr>
<tr>
<td>• Acute kidney injury</td>
<td></td>
</tr>
</tbody>
</table>

Any infection with *P. falciparum* or *P. vivax* can become severe if treatment is delayed or inadequate. All Sudanese are at risk to develop severe malaria as transmission is unstable. Some categories have higher risk eg:

- Pregnant women, especially primigravidae.
- People returning to endemic areas after a few years absence.
- Visitors (of any age) from non-endemic areas.
- Children < 5 years
- Splenectomised individual
Flowchart for Diagnosis and Management of Severe Malaria

Suspect **Severe Malaria** if the patient present with one or more of the following feature:

- Repeated vomiting
- Prostration
- Impaired consciousness (cerebral malaria)
- Respiratory distress (acidotic breathing)
- Multiple convulsions
- Circulatory collapse
- Pulmonary oedema
- Abnormal bleeding
- Jaundice
- Haemoglobinurea

**Start General management as required with:**

- Proper Nursing
- Diazepam
- Dextrose
- Cardiac bed + O₂
- Blood transfusion
- Plasma expanders & life-saving drugs
- Management of ARF
- Fresh blood or FFP

**Treat SEVERE MALARIA with:**

- IV Quinine
- OR
- IV Artesunate

**Ask for relevant investigations:**

- Blood film or RDTs
- Random blood Sugar
- TWBC
- Hb/ PCV
- Lumber puncture
- Chest X-Ray
- Blood Urea & electrolytes
- PT – PTT, platelets count
- LFTs (serum bilirubin)
- FDPs Or DIMER

**Excluding other possible causes:** history, examination, investigations (TWBC, LP…)

**Determine patient recovery by assessing:**

- Body temperature
- Parasite count
- Coma scale
- Patient ability to drink, eat, talk, sit, stand, walk...

**Assess possible sequelae of disease & treatment:**

- Improved
- Not improved

- Perform neurological examination
- Assess vision & hearing
- Repeat Haematocrit on Day 7, Day 14 & 1 month later

Not improved

Think & exclude possible other causes: history, examination, investigations (TWBC, LP…)

Improved
3.2 Important remarks:

- Severe malaria cases should be managed at hospitals. So health workers at the peripheral units should refer patients immediately. Pre-referral treatment is recommended at peripheral units.
- Attention should be given to the general management (good nursing care) of the patient as for the specific treatment.
- Early recognition, referral and early institution of the appropriate management at hospital are of paramount importance in the reduction of deaths attributed to malaria.
- Case fatality rate (CFR) is a useful indicator for hospital management i.e. higher CFR indicates inadequate case management at hospital level or delayed presentation.

3.3 General management of the patient with SM:
The health care providers on duty at any level of health care services should consider the following (8 + 8 + 4) points in the management of patient with severe malaria

Do the following 8 immediate measures:

1. Start resuscitation, particularly maintenance of a patent ABCs.
2. Establish IV line.
3. Make a thick blood smear for immediate malaria parasite count. RDTs can be useful in certain areas
4. Classify the degree of dehydration; assess patient’s fluid requirements and correct accordingly.
5. Control fever if the axillary temperature is 38.5°C or above: Tepid sponge, fanning and oral or rectal paracetamol (15mg/kg every 4 to 6 hours)
6. Control convulsions: Maintain airway, treat with rectal diazepam (0.5mg/kg) or slow IV diazepam (0.3mg/kg, maximum 10mg in an adult). Also correct hypoglycaemia if it is present.
7. Detect and treat Hypoglycaemia: Hypoglycaemia can be induced by high parasitemia, fasting and quinine therapy. Hypoglycaemia can recur especially in pregnant women and children. If blood glucose ≤ 2.2mmol/l or ≤ 40mg/dl; give 1ml/kg of 50% dextrose IV, diluted with an equal volume of 0.9% Saline, give
slowly over 3-5 minutes. Follow with 10% dextrose infusion at 5ml/kg/hr. If there is no test for blood glucose, treat as if the patient is hypoglycaemic;

8. **Start Quinine IV or Artesunate IV** (if not accessible, Quinine IM or Artesunate suppositories can be administered; notably in case of hyperparasitemia).

**Look and deal with the following 8 complications:**

1. **Shock, algid malaria:** if Systolic Bp <50mmHg in children 1-5 yrs or <80 mmHg in >5yrs, suspect Gram-negative septicaemia. In such case take blood samples for culture. Give parenteral broad-spectrum antimicrobials. Correct hemodynamic disturbances. **Treat with:** 30ml/kg 0.9% Saline IV in 1hour, then, reassess. Give oxygen if possible.

2. **Consider the need for blood transfusion:** Assess the degree of palor (nopalor, some pallor or severe pallor). Look for signs of severe anaemia such as very pale mucous membranes, respiratory distress and a rapid pulse.

   **Note:** The decision to transfuse with blood should not only be based on low laboratory values but as a guide Hct<15% or Hb<5 g/dL

   **Transfuse blood if there is:**
   1. Cardio respiratory symptoms e.g. severe anaemia.
   2. PCV<20 or Hb<5g/dL.

3. **In case of metabolic acidosis:** Exclude and treat hypovolaemia and gram negative septicaemia. Give isotonic saline 20 ml/Kg of body weight rapidly or screened whole blood 10ml/Kg over 30 minutes if haemoglobin is <5 g/dl.

4. **If there is spontaneous bleeding and coagulation disorder:** Transfuse screened fresh whole blood or clotting factors; give vitamin K 10 mg IV per day for adult, 1 mg/day for infant, 2-3 mg/day for children, and 5-10 mg/day for adolescent. Vitamin K should be given SC or IV.

5. **Acute renal failure:** Special efforts should be given to detection of symptoms and signs suggestive of renal failure. Exclude dehydration; maintain strict fluid balance; carry out dialysis if indicated.

6. **Malarial haemoglobinuria (black-water fever):** Continue with suitable antimalarial treatment; transfuse screened fresh blood if needed.

7. **Acute pulmonary oedema:** Prevent by avoiding excessive rehydration. Treatment
Monitor considering the following 4 points:

1. **Level of consciousness**: If there is an altered level of consciousness use Glasgow or Blantyre coma scales to assess progress every 6 hours until the patient retained full consciousness.

2. **Fluid input/output**: Detect dehydration and avoid fluid overload. Prevent pulmonary oedema.

3. **Vital signs**: Monitor vital signs every 6 hours to detect complications of severe malaria. If pulmonary oedema develops (rapid respiratory rate and deep laboured breathing) stop all IV fluids except quinine and call medical officer/clinical officer for management.

4. **Level of parasitemia**: Determine the parasite count daily to monitor the therapeutic effect of treatment. Stop when there is no detectable parasitemia.

Educate the patient and relatives about compliance with a full course of treatment, home prevention of malaria and the sequel of severe malaria. Wait for the patient to recover before counselling.

### 3.4 Specific treatment of patients with SM:

#### 3.4.1 Pre-referral treatment at peripheral units:

In most of the rural settings of the Sudan, it is usual to see patients with SM seeking care at the primary health care units. The health personnel in these units should refer the patients to the nearest hospital. Pre-referral treatment should be given. This could be **Quinine IM** or **artesunate suppositories** as follows:

**Quinine** given by intramuscular route can be a valuable initial treatment for a patient with complicated malaria as pre-referral treatment. The dose of IM quinine is 10 mg /kg body weight given after dilution with normal saline or distilled water to a concentration...
of 60 mg/ml; the dose is divided into 2 halves and each injected into anterior upper thighs (table 7 and 8).

**Table (7): Dosage dilution schedule for intra-muscular quinine (600 mg/2 ml) using insulin syringe**

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight (kg)</th>
<th>Quinine injection (ml)</th>
<th>Normal saline or distilled water for dilution (ml)</th>
<th>Total injection volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 month</td>
<td>5-6</td>
<td>0.2</td>
<td>0.8</td>
<td>1</td>
</tr>
<tr>
<td>4-11 year</td>
<td>7-10</td>
<td>0.3</td>
<td>1.2</td>
<td>1.5</td>
</tr>
<tr>
<td>1-2 year</td>
<td>11-14</td>
<td>0.4</td>
<td>1.6</td>
<td>2</td>
</tr>
<tr>
<td>3-4 year</td>
<td>15-18</td>
<td>0.6</td>
<td>2.4</td>
<td>3</td>
</tr>
<tr>
<td>5-7 year</td>
<td>19-24</td>
<td>0.8</td>
<td>3.2</td>
<td>4</td>
</tr>
<tr>
<td>8-10 year</td>
<td>25-35</td>
<td>1.1</td>
<td>4.9</td>
<td>6</td>
</tr>
<tr>
<td>11-15 year</td>
<td>36-50</td>
<td>1.3</td>
<td>5.7</td>
<td>7</td>
</tr>
<tr>
<td>16 and above</td>
<td>50 and above</td>
<td>2</td>
<td>8</td>
<td>10</td>
</tr>
</tbody>
</table>

The dose should be divided into halves and injected into anterior upper thighs.

**Table (8): Dosage dilution schedule for intra-muscular quinine (600 mg/2 ml) using 5 ml syringe**

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight (kg)</th>
<th>Volume of Quinine injection in lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 month</td>
<td>5-6</td>
<td>1 ml</td>
</tr>
<tr>
<td>4-11 year</td>
<td>7-10</td>
<td>1 ½ ml</td>
</tr>
<tr>
<td>1-2 year</td>
<td>11-14</td>
<td>2 ml</td>
</tr>
<tr>
<td>3-4 year</td>
<td>15-18</td>
<td>3 ml</td>
</tr>
<tr>
<td>5-7 year</td>
<td>19-24</td>
<td>4 ml</td>
</tr>
<tr>
<td>8-10 year</td>
<td>25-35</td>
<td>6 ml</td>
</tr>
<tr>
<td>11-15 year</td>
<td>36-50</td>
<td>7 ml</td>
</tr>
<tr>
<td>16 and above</td>
<td>50 and above</td>
<td>10</td>
</tr>
</tbody>
</table>

**NB:** each 1 ml of standard 5 ml syringe contains 5 lines

(Total recommended dosage is 10 mg/Kg, 8-hourly for 7 days)

Using standard 5 ml syringe:
- Take 1 ml of Quinine (300 mg)
- Add 4 ml of distilled water or normal saline
- The result is: a 5 ml diluted Quinine of 60 mg/ml concentration (12 mg/line)

**Artesunate suppositories:**

Artesunate rectal capsules/suppositories, 10 mg/Kg (available in form of 50 mg or 200 mg per recto-cap), should be given rectally as soon as possible, once the diagnosis of malaria is made. If the rectal capsule is expelled within the first hour, another rectal capsule should be inserted immediately. Artesunate rectal capsules are recommended only for children, for adult IM Quinine is the option for pre-referral.

If after 24 hours the patient has not been referred to hospital and is still unable to take oral medication, a second dose should be repeated
3.4.2 Treatment of SM at hospital settings:

3.4.2.1 Treatment with IV quinine:

IV Quinine can be given in one of the 3 ways depending on the patient condition and according to the level of health facility.

Quinine for 7 days:

Initial treatment with Quinine should be in infusion, preferably in 5% Glucose and 5% glucose in normal saline. The dose is 10 mg salt/kg body weight administered 8-hourly over four hours duration (slow infusion in a rate of 32 drops/min for adult) for at least 2 days and shift to the oral quinine as soon as the patient can take oral medication (Table 4) to complete the 7 days.

Table 9: Dilution schedule and drop rate for intravenous quinine administration

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Weight(kg)</th>
<th>Quinine dose</th>
<th>Volume of undiluted quinine solution (300mg/ml)</th>
<th>Amount of fluid to be infused (in 4 hours)</th>
<th>Drop rate per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 month</td>
<td>≤6</td>
<td>60 mg</td>
<td>0.2 ml</td>
<td>50 ml</td>
<td>4 drops</td>
</tr>
<tr>
<td>4 &lt;12 months</td>
<td>6_10</td>
<td>90 mg</td>
<td>0.4 ml</td>
<td>100 ml</td>
<td>8 drops</td>
</tr>
<tr>
<td>1&lt;3yrs</td>
<td>11 _14</td>
<td>150 mg</td>
<td>0.5 ml</td>
<td>100 ml</td>
<td>8 drops</td>
</tr>
<tr>
<td>3 &lt; 5</td>
<td>15 _18</td>
<td>180 mg</td>
<td>0.6 ml</td>
<td>150 ml</td>
<td>13 drops</td>
</tr>
<tr>
<td>5 &lt;8</td>
<td>19 _ 24</td>
<td>210 mg</td>
<td>0.7 ml</td>
<td>200 ml</td>
<td>17 drops</td>
</tr>
<tr>
<td>8 &lt; 12</td>
<td>25 _ 35</td>
<td>300 mg</td>
<td>1.0 ml</td>
<td>250 ml</td>
<td>21 drops</td>
</tr>
<tr>
<td>12&lt; 14</td>
<td>36 _49</td>
<td>420 mg</td>
<td>1.4 ml</td>
<td>350 ml</td>
<td>30 drops</td>
</tr>
<tr>
<td>14 &lt;16</td>
<td>50 - 60</td>
<td>540 mg</td>
<td>1.8 ml</td>
<td>500 ml</td>
<td>42 drops</td>
</tr>
<tr>
<td>16 and above</td>
<td>&gt;60</td>
<td>600 mg</td>
<td>2.0 ml</td>
<td>500 ml</td>
<td>42 drops</td>
</tr>
</tbody>
</table>

Quinine IM:

If the IV route is not possible, Quinine can be given in the same dose by intramuscular injection diluted with sterile normal saline or distilled water to a concentration of 60 mg/ml. The dose should be divided into two halves and injected into both anterior upper thighs (Tables 5 and 6). Shift to the oral Quinine as soon as the patient can take oral medication.
Quinine for at least 3 days and then first-line:
It is observed that compliance to oral quinine sometimes is not good. Alternative option is to give quinine IV or IM for at least 3 days at hospital and then shift to the oral quinine to complete 7 days treatment. Alternatively shift to first-line treatment (AL). Ensure patient takes full oral course of AL.

Quinine side effects:
Rapid intravenous administration of Quinine can precipitate hypoglycaemia, hypotension and fatal cardiovascular toxicity.

3.4.2.2 Treatment with intravenous artesunate (AS IV):
IV Artesunate (shortly known as AS/IV) is a short-acting antimalarial drug that clears Plasmodium parasites more rapidly than conventional antimalarial. The drug acts against both the sexual and asexual stages of the parasite.

Dose and regimen: Artesunate 2.4 mg/kg body weight (3.0mg/kg in children less than 20kg) given by IV injection:
- on admission (time = 0),
- After 12 hours.
- After 24 hours from the first dose,

At least 24 hours of parenteral artesunate (3 doses) should be given irrespective of the ability to tolerate oral medication before switching to full course of AL.
- Continue using Artesunate IV every 24 hour for 7 days when the patients can’t take oral.

Drug formulations: The drug is available in three strengths: 30, 60 and 120 mg vial containing artesunate powder. The drug is packed together with sodium bicarbonate for reconstitution and normal saline for dilution. The health care providers need to prepare the drug for use carefully as in the box below.
### Calculate and prepare the artesunate IV for intravenous administration:

1. Weight the patient (in kg)
2. Calculate the dose
   - For patients weighing ≤20 kg: 3.0 mg x body weight (kg)
   - For patients weighing >20 kg: 2.4 mg x body weight (kg)
3. Calculate the needed number of artesunate vials (30, 60 and 120 mg) for each patient guided by the following estimate:

<table>
<thead>
<tr>
<th>Weight in Kg</th>
<th>Vials of artesunate powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 – 10</td>
<td>One vial 30 mg</td>
</tr>
<tr>
<td>11 – 25</td>
<td>One vial 60 mg</td>
</tr>
<tr>
<td>26 – 50</td>
<td>One vial 120 mg</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Two vials 120 mg</td>
</tr>
</tbody>
</table>

4. Prepare the drug for the administration (table below):
   - Add the attached 5% sodium bicarbonate solution to artesunate powder
   - Shake the vial for 2–3 minutes for better dissolution.
   - Add the attached 5% normal saline (not a distilled water) to make the concentration of artesunate as 10 mg/ ml

<table>
<thead>
<tr>
<th>Artesunate injection preparation</th>
<th>30 mg</th>
<th>60 mg</th>
<th>120 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bicarbonate solution volume</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Saline solution volume</td>
<td>2.5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total volume in ml</strong></td>
<td>3</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Artesunate concentration</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5. Calculate the required **dose in ml** for each patient using the equation:

   \[ \text{Dose in ml} = \text{weight in kg} \times \frac{\text{recommended dose}}{10} \]

   (round to the higher figure)

   - For patient weighing 15 kg, the dose in ml is: \(15 \times \frac{3}{10} = 4.5\) give 5 ml
   - For patient weighing 60 kg, the dose in ml is: \(60 \times \frac{2.4}{10} = 14.4\) give 15 ml

6. Administer by slow injection (4 ml per minute).
7. Schedule the next dose.

**The solution should be prepared for each administration and should not be stored.**
**Artesunate side effects:** Artesunate is generally well-tolerated and has a better safety profile than quinine in severe malaria. Its side-effects include hypersensitivity reactions, gastrointestinal disturbances, cough, rash, arthralgia and dizziness. Clinically, the most significant side effect is haemolysis, which has been reported up to weeks after treatment.

**Contraindications:** Artesunate is contraindicated in patients with known hypersensitivity to artesunate or artemisinin derivatives.

### 3.4.3 Treatment of severe *P. vivax* malaria:

Although *P. vivax* malaria is considered to be benign malaria, with a very low case-fatality ratio, it may still cause a severe and debilitating febrile illness. It can also occasionally result in severe disease, as in *P. falciparum* malaria. Severe *P. vivax* malaria manifestations that have been reported are cerebral malaria, severe anemia, severe thrombocytopenia or pancytopenia, jaundice, spleen rupture, acute renal failure and acute respiratory distress syndrome. Severe anemia and acute pulmonary edema are not uncommon. The underlying mechanisms of severe manifestations are not fully understood. Prompt and effective treatment and case management should be the same as for severe and complicated falciparum malaria.
Malaria in pregnancy is one of the most common medical diseases. It causes high morbidity and mortality to the mother, her foetus, the neonate and the infant. According to WHO, the infection contributes to as much as 15% of maternal anaemia, 14% of low birth weight infants, 30% of preventable low birth weight, 70% of intrauterine growth retardation, 36% of premature deliveries, and 8% of infant mortality. It is a leading indirect cause of maternal mortality in Sudan. The Best practices of malaria control during pregnancy include effective management of malaria cases for women in the reproductive age and using of insecticide treated nets.

4.1 What is special about malaria in pregnancy?

Malaria in pregnancy (MIP) is a peculiar disease in many ways:

- The mortality and morbidity of MIP is higher than in non-pregnant women. The risk is even more increased in primigravidae.
- There is evidence of maternal Immuno-suppression in the second half of pregnancy which is caused by many factors (hormonal, placental and lymphocytic) in addition to malaria infection itself.
- Reduced immunity to malaria in pregnancy leads to more relapses of malaria and more parasitaemia and so worsens clinical manifestations.
- MIP is a risk to both pregnant women and the baby:
  - Primigravidae and HIV positive pregnant women are at greater risk of malaria and therefore anaemia, severe malaria and death.
  - Placental infection leads to low birth weight which is a major risk for malaria, other illnesses and deaths in infants.
- *P. falciparum* is the commonest malaria infection and can lead to acute renal failure, pulmonary oedema or cerebral malaria with convulsions and coma.
- Transplacental infection to the foetus can occur.
- The risks of MIP are high so prompt chemotherapy for malaria is mandatory.
- Antimalarial drug options are not always safe or well tested in relation to pregnancy trimesters.
4.2 Clinical features of MIP:

- MIP could be confused by early pregnancy features and sometimes has atypical presentation so **it is important to base the diagnosis and management on clinical evaluation in addition to blood film or RDTs.**
- The common manifestations of MIP include the following:
  - **Fever** with more paroxysms in the second half of pregnancy.
  - **Anaemia** is a common presentation and it could be due to: haemolysis of parasitized RBCs; increased demands of pregnancy; or profound haemolysis that may aggravate folate deficiency. Anaemia is more common and severe between 16-29 weeks, and pre-existing iron and folate deficiency can exacerbate it and vice versa. Anaemia increases the risk of prenatal mortality and maternal morbidity and mortality, the risk of pulmonary oedema, and the risk of postpartum haemorrhage is also higher.
  - **Splenomegaly** may be present but variable in size; and pre-existing large spleen may regress in size in pregnancy.
  - **Acute pulmonary oedema** is a more common and serious complication of MIP compared to non-pregnant population. It is more common in the second and third trimesters. However, it can occur immediately postpartum due to: the auto-transfusion of placental blood with high proportion of parasitized RBCs and the sudden increase in the peripheral vascular resistance after delivery.
  - **Hypoglycaemia** due to:
    - Increased demand of glucose due to hyper-catabolic state and infecting parasite
    - Hypoglycaemic response to starvation
    - Increased response of pancreatic islets to secretory stimuli.

  Hypoglycaemia presents with symptoms similar to those of malaria. Abnormal behaviour, convulsions and sudden loss of consciousness are also symptoms of cerebral malaria.
    - Secondary infections such as urinary tract infection, pneumonias...etc. are more common due to Immuno-suppression.
4.3 Complications and effects of MIP:

4.3.1 Maternal:

- **During pregnancy:**
  - Frequency and severity are greater than in non-pregnant particularly among primigravidae
  - Severe anaemia is common
  - Hyperpyrexia.
  - Hypoglycaemia
  - Transplacental infection leading to congenital malaria and neonatal death.

- **During labour:**
  - Precipitated labour
  - Postpartum haemorrhage

- **During puerperium:**
  - Puerperal pyrexia
  - Difficulty in lactation.

4.3.2 Foetal:

High grade fever, placental insufficiency, hypoglycaemia, anaemia and other complications can adversely affect the foetus. Spontaneous abortions, premature birth, stillbirth, IUGR, low birth weight, and foetal distress are problems observed during foetal growth. Transplacental spread to the foetus can result in congenital malaria. Congenital malaria was previously thought to be uncommon especially in indigenous populations. More recent studies, however, suggest that incidence has increased and values between 0.3 to 33% have been observed from both endemic and non-endemic areas.

The placental barrier and maternal IgG antibodies, which cross the placenta, may protect the foetus to some extent. Congenital malaria is more common in the non-immune population and the incidence goes up during the epidemic of malaria. Foetal antimalarial levels are usually sub-therapeutic to cure the infection in the foetus. Foetal chloroquine and Quinine levels are about one third of simultaneous maternal levels and these sub-therapeutic drug levels do not cure the infection in the foetus. All four species can cause congenital malaria. The newborn can present with fever, irritability, feeding
problems, hepatosplenomegaly, anaemia, and jaundice. The diagnosis can be confirmed by smear for malaria parasite. Febrile illness in the first week in the newborn is usually bacterial; however, think about malaria.

4.4 Management of MIP:
This includes: diagnosis, supportive measures, antimalarial drugs, management of complications, and management of labour and special neonatal care

4.4.1 Diagnosis:
- Clinical assessment to exclude early pregnancy features and other common causes.
- Confirmed the diagnosis by microscopy or RDTs.

4.4.2 Supportive measures:
- Ideally the patient should be admitted when it is possible. Assess the severity of the condition by general examination: pallor; jaundice; blood pressure; temperature, haemoglobin level, and parasite count.
- Platelets count, SGPT, serum bilirubin, serum creatinine and blood sugar may also need to be assessed.
- Monitor the maternal and foetal vital parameters 3-4 hourly and monitor the fluid intake/output daily.
- Avoid overdosing and under dosing with the drugs

4.4.3 Anti-malarial drugs:
The following should be considered when malaria diagnosed during pregnancy or labour:
- Treatment of MIP should be initiated as early as possible.
- Treatment varies according to the gestational age as.

4.4.3.1 Treatment of uncomplicated MIP
In the first trimester:

**Oral Quinine** can be safely used in the first trimester of pregnancy. The dose is 10 mg/Kg body weight, administered 8-hourly for 7 days (2 tablets tds).

In the second and third trimester:

**AL, DHAP and quinine** can be used safely as 1st line, 2nd line and third line treatment for UM respectively. For the dosage see table 3 and table 4 in unit 2.

4.4.3.2 Management of severe MIP:
- In the management of severe malaria in pregnancy especial concern must be paid to: anaemia, hypoglycaemia and pulmonary oedema.
- Two options are available: quinine or artesunate IV.
Quinine: Quinine in a dose of 10 mg/Kg body weight 8-hourly for 7 days. Start with IV Quinine in 10% glucose infusion or 5% glucose in normal saline; if for some reason Quinine cannot be given by infusion, Quinine dihydrochloride can be given in the same dosage by IM injection diluted with sterile normal saline to a concentration of 60 mg/ml (Table 5 and 6), and shift to oral as soon as possible. In case there is no 10% glucose concentration give one bottle of 5% glucose before administration of Quinine; be careful not to induce pulmonary oedema. Random blood sugar should be done before and after Quinine administration.

Or Quinine 10 mg/Kg body weight 8 hourly for at least 3 days (IV or IM) and shift to oral quinine as soon as the patient can take orally.

Intravenous artesunate in the dose of 2.4 mg/kg body weight per dose for at least 24 hours or until the patient tolerate oral then shift to oral quinine in the first trimester or full dose of first line in the second and third trimester.

Table11: Antimalarial Drugs for malaria in pregnancy and puerperium

<table>
<thead>
<tr>
<th>Pregnancy in weeks</th>
<th>Uncomplicated malaria</th>
<th>Severe malaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>Quinine</td>
<td>Quinine or IV artesunate followed by oral quinine</td>
</tr>
<tr>
<td>13-36</td>
<td>AL, DHAP or quinine</td>
<td>Quinine or IV artesunate followed by AL</td>
</tr>
<tr>
<td>37–delivery</td>
<td>AL, DHAP or quinine</td>
<td>Quinine or IV artesunate followed by AL</td>
</tr>
<tr>
<td>Puerperium</td>
<td>AL, DHAP or quinine</td>
<td>Quinine or IV artesunate followed by AL</td>
</tr>
</tbody>
</table>

- Mefloquine is the drug of choice and evidence suggests it is not associated with an increased risk to the foetus. The dose is 250 mg orally once a week after the main meal. Start 1 to 2 weeks before arrival and continue for 4 weeks after leaving.
4.4.4 Management of complications:
- **Pulmonary oedema:** careful fluid management, back rest elevation, diuretics and ventilation if needed.
- **Hypoglycaemia:** 25%-50% dextrose, 50-100 ml IV (1ml/kg) followed by 10% dextrose as a continuous infusion. Blood sugar should be monitored every 4-6 hours where possible.
- **Anaemia:** packed cell should be transfused if Hb<5 g/dL.
- **Renal failure:** it could be pre-renal due to unrecognized dehydration or renal due to severe parasitaemia. Management involves careful investigations, diuretics and dialysis if needed.
- **Septicaemia shock or algid malaria:** administration of third generation of cephalosporin, monitoring of vital parameters (blood pressure) and fluid replacement when required (systolic<90mmHg).

4.4.5 Management in labour:
Falciparum malaria and higher fever induce uterine contractions, resulting in **preterm labour**. The frequency and intensity of the contractions is related to the degree of the fever. Foetal distress is the commonly recognized complication. Lower the temperature of the woman by using tepid sponging or antipyretics such as paracetamol. Adequate fluid management and careful monitoring in labour are mandatory.

4.4.6. Especial neonatal care:
Is needed when there is prematurity, low birth weight, foetal distress or neonatal fever, or where the mother experience repeated infection of malaria during pregnancy. Table 11 summaries the use of antimalarial drugs for MIP and puerperium.

4. 5. Important notes:
- The following drugs are contraindicated in pregnancy: primaquine, halofantaine and doxycycciline.
- Treatment of *P. vivax* and *P. ovale*: Treatment of the liver cycle and eradication of *P. vivax* or *P. ovale* hypnozoites using Primaquine is contraindicated in pregnancy and during lactation (until the G6PD status of child is known). Hypnozoite eradication must be deferred till after delivery and cessation of breastfeeding. Confirmed cases of *P. vivax* or *P. ovale* in pregnancy should take prophylaxis until after delivery.
Unit 5: Malaria In Children

Malaria is a major contributor to child ill health. There are three principal ways in which malaria can contribute to death in young children;

- An overwhelming acute infection, which frequently presents as seizures or coma (cerebral malaria), may kill a child directly and quickly.
- Repeated malaria infections contribute to the development of severe anaemia, which substantially increases the risk of death.
- Low birth weight – frequently the consequence of malaria infection in pregnant women - is the major risk factor for death in the first month of life.

5.1 Uncomplicated malaria in children:

5.1.1 Diagnosis of uncomplicated malaria in children

- Health care providers should suspect uncomplicated malaria in:
  - Any child with fever, headache, aches and pains.
  - A young child who is irritable, refuse to eat and who is vomiting.
  - Children with palmar pallor or a haemoglobin concentration of < 8 g/dl.

- In any case laboratory confirmation with microscopy of RDTs is mandatory as diagnosis based only on clinical features has very low specificity and results in over treatment and may be misleading.

- Other possible causes of fever (acute respiratory infections, tonsillitis, measles, abscess, urinary tract infection ...etc.) and whether alternative or additional treatment is required must always be carefully considered.

5.1.2 Management of uncomplicated malaria in children

- Delay in treating *P. falciparum* malaria in infants and young children can have fatal consequences, particularly for more severe infections.

- In treating young children, it is important to ensure accurate dosing and retention of the administered dose, as infants are more likely to vomit or regurgitate antimalarial treatment than older children or adults.

- Mothers often need advice on techniques of drug administration and the importance of administering the drug again if it is regurgitated within 30 minutes of administration.

- The recommended treatment for uncomplicated malaria in children is AL (Table 3) as first line, DHAP (Table 4) as a second line and quinine as a third line (Table 5).
- Adjust the dose for infants weighing < 5 kg with uncomplicated *P. falciparum* malaria with AL or DHAP considering the dose for children weighing 5 kg.
- The only antimalarial drug that is currently contraindicated for infants (<6 months) is primaquine.

5.2 Severe malaria in children:

5.2.1 Diagnosis and general management of severe malaria in children:
- The severe malaria criteria mentioned in the severe malaria unit can be applied for children. The most common and important manifestations of *P. falciparum* infection in children are:
  - Severe anaemia (may be presented as anaemic heart failure)
  - Cerebral malaria
  - Repeated convulsions
  - Hypoglycaemia
  - Respiratory distress (acidosis).
- Key aspects of the assessment of children with severe malaria are:
  
  **Assess the:**
  - Level of consciousness (using the Blantyre coma scale)
  - State of hydration, and
  - Presence of anaemia

  **Vital signs:**
  - Temperature
  - Pulse rate
  - Rate and depth of respiration (acidotic breathing) Rate and depth of respiration and
  - Oxygen saturation (using pulse oximeter)

  **Immediate tests must include:**
  - Thick and thin blood films or RDTs
  - PCV.
  - Random blood glucose
  - Lumbar puncture (if indicated).

- Proper nursing care should be immediately instituted.
- Emergency measures include:
- Assess ABC (Airway, breathing and circulation) hydration
- Abort convulsions with intra-rectal diazepam in a dose of 0.5 mg/Kg.
- Correct hypoglycaemia
- Use tepid sponging, fanning and/or paracetamol trying to keep the temperature at normal range
- Treat severe anaemia
- Insert nasogastric tube to minimize the risk of aspiration pneumonia if the child is unconscious.

- IV fluids should be given with caution and should be always guided by the level of dehydration.

### 5.2.2 Specific treatment of severe malaria in children:
- Initiate specific management as soon as possible. Weigh the patient and calculate the dose of antimalarial treatment according to body weight.
- **Quinine or artesunate are the recommended drugs** and should be given initially as below:
  - **Quinine** should be given through intravenous infusion preferably in 5 or 10% glucose. The dose is 10 mg salt/kg body weight administered 8-hourly for 7 days. If IV Quinine is not possible, Quinine (the same dose) can be given intramuscularly diluted with normal saline or distilled water to a concentration of 60 mg/ml into anterior upper thigh.
  - **Intravenous artesunate** for at least 24 hours and until the patient tolerate oral dose. The dose is 2.4 mg/kg body weight per dose. In children weighting <20 kg give a higher dose of artesunate than larger children and adult (3 mg/kg body weight per dose) to ensure equivalent exposure to the drug. When you shift to oral dose of AL give a 3 days treatment.

### 5.3 Malaria in neonates and infants:
**New-borns and infants** less than 12 months of age are one of most the vulnerable groups affected by malaria. In malaria-endemic areas, infants become vulnerable to *P. falciparum* and to *P. vivax* malaria at approximately 3 months of age (when immunity acquired from the mother starts to wane). Infants are at increased risk of rapid disease progression, severe malaria and death. Severe anaemia is particularly common in this age group.
**Congenital malaria** is defined as presence of Plasmodium parasites in the erythrocytes of newborns aged less than seven days’. It is an important consequence of malaria in pregnancy but clinically apparent congenital malaria is rare in areas in which malaria is endemic and levels of maternal antibody are high. Clinical features of congenital malaria include:

- Most common features: fever, anaemia and splenomegaly
- Other features: include hepatosplenomegaly, jaundice, regurgitation, loose stools, and poor feeding
- Do not confuse with neonatal infection
- Fever during the first 3 weeks of life is mostly due to bacterial infection

Prompt diagnosis and effective treatment for malaria in neonate and infants should be initiated early and as follows:

- Confirm using microscopy or RDTs
- Artemisinin derivatives are safe and well tolerated by young.
- Use ACTs for uncomplicated malaria and use quinine or artesunate IV for severe malaria
- A single dose of rectal artesunate as pre-referral treatment reduces the risk of death.
Unit 6: Malaria In Special Situations

6.1 Treatment of malaria caused by *P. ovale* and *P. malariae*:
*P. ovale* and *P. malariae* are rare in Sudan. They give rise to mild clinical disease. Death from these species is very rare. Relapse is expected with *P. ovale*. Treat cases of *P. malariae* with the AL (Artemether-lumefantrine) using the same dosage in table 2. Treat cases of *P. ovale* as you deal with *P. Vivax* using AL and primaquine as recommended for *P. vivax*.

6.2 Malaria prophylaxis and prevention:
In Sudan the whole population is at risk to malaria but the following special groups are at higher risk to malaria infection:

- Travellers from malaria free areas (visitors).
- People with sickle cell disease.
- Splenectomised individuals.
- Children on steroids or immunosuppressive drugs.
- Expatriates and Sudanese returning from non-malarious areas

For the above special groups the recommended prophylactic regimen is mefloquine: For adult the dose is 250 mg (one tab) every 7 days, starting one week before entering the area, once weekly while in the area, and once weekly for 4 weeks after leaving the area. For children it is 5 mg/Kg with the same interval as for adults. Atovaquone- proguanil (Malarone®) offers an alternative for chemoprophylaxis in those person travelling to Chloroquine-resistant *P. falciparum* areas who cannot take Mefloquine. The prophylactic dose for adults is 250 mg of atovaquoneplus 100 mg of proguanil (one adult tablet) daily beginning one day before entering the malarious area and for seven days after leaving. Prophylactic dosage schedules for children are shown in table 12.

Table 12: Dosage schedules for atovaquone (A)+ proguanil(P) (62.5 mg A + 25 mg P) chemoprophylaxis in children:

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Number of tablets per day (Paediatric strength)</th>
<th>Daily dose Atovaquone (A) + proguanil(P) (62.5 mg A + 25 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;11</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>11 – 20</td>
<td>1</td>
<td>62.5 mg A + 25 mg P</td>
</tr>
<tr>
<td>21 – 30</td>
<td>2</td>
<td>125 mg A + 50 mg P</td>
</tr>
<tr>
<td>31 – 40</td>
<td>3</td>
<td>187.5 mg A + 75 mg P</td>
</tr>
</tbody>
</table>

NB. The drug should be taken with food or a milky drink

The CNCDCD advice to the whole population and to these special groups is to reduce mosquito contact by the use of insecticide treated nets and repellents.
Bibliography


### Summary tables

#### Dosage schedule for “artemether – lumefantrine” (AL)

<table>
<thead>
<tr>
<th>Weight in Kgs</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Total number of tablets</th>
<th>Tablet strength</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initially</td>
<td>8 hours after the 1st dose</td>
<td>24 hours after the 1st dose</td>
<td>12 hours after the 3rd dose</td>
<td>12 hours after the 4th dose</td>
</tr>
<tr>
<td>&lt;5</td>
<td>Adjust the dosing considering the weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 - 14</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1  1  1</td>
<td>6</td>
</tr>
<tr>
<td>15 - 24</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2  2  2</td>
<td>12</td>
</tr>
<tr>
<td>25 - 34</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3  3  3</td>
<td>18</td>
</tr>
<tr>
<td>Children &gt;34 kg and adults</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1 1 1</td>
<td>6</td>
</tr>
</tbody>
</table>

#### Dosage schedule for Dihydroartemisinin + piperaquine tablets (DHAP)

<table>
<thead>
<tr>
<th>body weight (Kg)</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>total no of tablets</th>
<th>DHAP Tablet strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>Use the same dose per kg as more than five kg</td>
<td></td>
<td></td>
<td></td>
<td>DHAP “20/160” dispersible tablets</td>
</tr>
<tr>
<td>5 - 6</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>7-12</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>DHAP “40/320” tablets</td>
</tr>
<tr>
<td>13-23</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>24-35</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>36-74</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>75 and above</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>