SUDAN MALARIA CASE MANAGEMENT PROTOCOL 2023

FEDERAL MINISTRY OF HEALTH SUDAN

ACKNOWLEDGMENT

The Federal Ministry of Health would like to acknowledge the efforts carried out by the dedicated members of the malaria Technical Advisory Committee and the protocol writing team.

The ministry also acknowledges the World Health Organization, The Global Fund, and the United Nations Development Programme for their valuable contribution to this document, as well as their consistent support for Sudan's National Malaria Control Programme.

WRITING TEAM

| Name | Affiliation/Position | Status in the committee |
|---|-------------------------------------|-------------------------|
| Dr. Samah Isam Abdalla Elhassan | Case Management Officer, NMCP, FMOH | Head |
| Dr. Ahmed Abdulgadir Noureddin | Case Management Officer, NMCP, FMOH | Member |
| Dr. Ayat Mustafa Mohamed Osman | Case Management Officer, NMCP, FMOH | Member |
| Dr. Khansa Albdelmonaem Elsoni Ahmed | Head of Case Management, NMCP, FMOH | Member |
| Dr. Khlood Fathi Hassan Alnaeem | Case Management Officer, NMCP, FMOH | Member |
| Dr. Mariam Adam Babiker Adam | Malaria Officer, WHO | Member |
| Dr. Sahar Khalid Mohamed Mohamed | Case Management Officer, NMCP, FMOH | Member |
| Dr. Samah Kamaleldeen Bakri Abass | Case Management Officer, NMCP, FMOH | Member |

PECHNICAL ADVISORY COMMITTEE MEMBERS

| Name | Affiliation/Position | Status in the committee |
|----------------------------------|---|-------------------------|
| Dr. Dalya Eltayeb | Director General, PHC, FMOH | Member |
| Dr. Sara Azhari Hassan Abdulla | Director, DCD, FMOH | Member |
| Dr. Fadwa Mohammed Saad | Director, NMCP, FMOH | Head |
| Prof. Elfatih Mohamed Malik | Professor of Community Medicine, University of Khartoum | Member |
| Dr. Abdalla Hamadelsyed Ahmed | Senior Technical Advisor, GFA | Member |
| Dr. Fahad Awad Ali Elnour | Malaria Grant Manage, GF | Member |
| Dr. Mariam Adam Babiker | Malaria Officer, WHO | Member |
| Mr. Sayed Ali Mustafa Masaad | National Public Health Laboratory | Member |
| Mr. Tarig Mohamed Elfaki Alabass | National Public Health Laboratory | Member |
| Prof. Bakri Yousif M. Nour | Professor of Medical Parasitology, University of Gezira | Member |
| Prof. Musa Mohammed Kheir | Professor of Internal Medicine, University of Khartoum | Member |
| Prof. Omer Zayid Baraka | Professor of Internal Medicine, University of Khartoum | Member |
| Prof. Ali Babiker Haboor | Professor of Child Health, University of Gezira | Member |
| Prof Elmuntasir Taha | Professor of Pediatrics, University of Alrebat | Member |
| Prof. Duria Abdulwahab Rayis | Professor of Obs & Gyne, University of Khartoum | Member |
| Prof. Mohammed Elsanousi | Professor of Obs & Gyne, University of Gezira | Member |
| Prof. Ishag Adam | Professor of Obs & Gyne, University of Khartoum | Member |
| Dr. Mukhtar Mohamed Salih | Registrar of Internal Medicine, SMSB. Al Tababa | Member |
| Dr. Esmahan Elkheir Babeker | Director, MCH, FMOH | Member |
| Dr. Sakhr Badawi Omar Elsheikh | Senior malaria M&E, PMU, GF | Member |
| Dr. Layla Hamadelnile Abdalradi | Head, response department, HEEC | Member |
| Dr Asma Hashim Elhassan Eltohami | Malaria Program Officer, PMU, GF | Member |
| | | |

Professor of Community Medicine, Wedmedani College

Member

Prof. Samira Hamid Abdelrahman

| Abbreviations | 6 |
|---|----|
| Preface | 7 |
| Introduction | 8 |
| Unit 1: Malaria Diagnosis | 10 |
| Unit 2: Management of Uncomplicated Malaria | 13 |
| Unit 3: Management of Severe Malaria | 24 |
| Unit 4: Malaria in Pregnancy | 42 |
| Unit 5: Malaria in Children | 46 |
| Unit 6: Malaria Prevention and Prophylaxis | 50 |
| References | 52 |

ABBREVIATIONS

ACT

AL

AS

DHAP

G6PD

HRP2

IPTp

ITN

MIP

RDT

SM

SP

UM

WHO

Artemisinin-based combinaton therapy

Artemether-lumefantrine

Artesunate

Dihydroartemisinin-piperaquine

Glucose-6-phosphate dehydrogenase

Histidine-rich protein 2

Intermittent preventive treatment in pregnancy

Insecticide-treated net

Malaria in pregnancy

Rapid diagnostic test

Severe malaria

Sulfadoxine pyrimethamine

Uncomplicated malaria

World Health Organization

PREFACE

The protocol of malaria case management in Sudan was last updated in 2017 in response to the findings of the therapeutic efficacy study. Artesunate + sulphadoxine-pyremethamine (AS+SP) efficacy was found to be decreasing, particularly in Gedarif State, where treatment failure exceeded 10%. The study also demonstrated the high efficacy (>95%) of artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DHAP). Furthermore, the Sudan Malaria Indicators Survey 2016 revealed irrational use of intramuscular artemether for the treatment of uncomplicated malaria. In light of these findings, AL and DHAP were recommended as firstand second-line for the treatment of uncomplicated malaria, respectively. The aforementioned recommendations remain endorsed by the Federal Ministry of Health. However, the Malaria Program Review 2018 recommended an update for the management of severe malaria in Sudan. In response, the national malaria control program (NMCP) called for a Technical Advisory Committee (TAC) meeting to update the Sudan Malaria Protocol and its related training materials. The TAC recommendations were used along with the WHO Guidelines for Malaria, issued on 25 November 2022, to develop the Sudan Malaria Case Management Protocol 2023.

Dr. Dalya Eltayeb Director General of PHC Prof. Heitham M. I. Awadallah Undersecretary of Federal Ministry of Health

INTRODUCTION

Malaria is a major public health problem in Sudan. In 2021, malaria was the leading cause of outpatient attendance, hospital admissions and inpatient deaths in Sudan.

Plasmodium falciparum (P. falciparum) is the most common infective species, accounting for more than 87.6% of the cases. Plasmodium vivax (P. vivax) infections reached 8.1%, while mixed infections (P.falciparum and P.vivax) totaled 4.3%. Recent statistical reports, however, indicate that the prevalence of P.vivax is currently higher than previously reported.

The Sudan Malaria Case Management Protocol 2023 emphasizes the importance of early diagnosis and prompt treatment of malaria. As uncomplicated falciparum malaria can rapidly progress to severe forms of disease, the aim is to provide effective treatment within 24-48 hours of the onset of malaria symptoms.

The rational use of antimalarial agents is important to reduce drug resistance.

Antimalarial agents should only be prescribed to patients who truly have malaria, and full treatment courses should be strictly followed. Incorrect treatment approaches, such as prescription without parasitological testing, inadequate dosing, and the continued use of injectable artemether, will all select for drug resistance.

To ensure that all patients achieve rapid clinical and parasitological cure, antimalarial drugs must be given at optimal dosage based on the patient's weight.

As malaria preventive measures account for more than 80% of the reductions in malaria cases in Africa, the updated protocol builds on this knowledge by expanding the role of healthcare practitioners in health promotion.

UNIT 1: MALARIA DIAGNOSIS

Malaria is suspected when a patient presents with fever (or history of fever) with or without other symptoms and signs suggestive of malaria. In all settings, suspected malaria must be confirmed with a parasitological test.

1.1 Parasitological Diagnosis

Two methods can be used to make a parasitological diagnosis: quality-assured microscopy and rapid diagnostic tests (RDTs).

1.1.1 Quality-assured microscopy

Quality-assured light microscopy is the gold standard for the diagnosis of malaria.

Giemsa-stained thick and thin blood films should be examined and the following clearly stated:

- Presence of malaria parasite (seen or not seen)
- Parasite species
- Stages of the parasite
- Parasite count by micro liter (μL)

Advantages of light microscopy include high sensitivity and specificity, the ability to determine parasite species and density, and the ability to monitor response to therapy.

The disadvantage of microscopy is the difficulty of maintaining good performance due to the requirements of adequate training and supervision of laboratory staff, as well as provision and maintenance of quality microscopes, stains and slides.

1.1.2 Rapid diagnostic tests

Rapid diagnostic tests (RDTs) are highly sensitive and specific for malaria diagnosis. They are immuno-chromatographic tests used for detecting parasite-specific antigens (not antibodies) in a blood sample. Some tests allow detection of only one species (P. falciparum),

while others allow the detection of more than one species. Advantages of RDTs are rapid provision of results, extension of diagnostic services to lowest-level health facilities and communities, and fewer requirements for training and skilled personnel.

Potential disadvantages of RDTs include:

- Inability, in the case of PfHRP2-based RDTs, to distinguish new infection from recently and effectively treated infections, due to the persistence of the antigen in the blood 1-5 weeks after effective treatment.
- The emergence of P.falciparum strains with HRP2 deletions.
- The heterogeneous quality of available RDTs kits.

UNIT 2: MANAGEMENT OF UNCOMPLICATED MALARIA

2.1 Case definition of uncomplicated malaria (UM)

Uncomplicated malaria is defined as a patient who presents with symptoms of malaria and a positive parasitological test (microscopy or RDTs), with no features of severe malaria (see Unit 3 for the definition of severe malaria).

2.2 Therapeutic objectives

- To cure the infection as rapidly as possible.
- To prevent progression to severe malaria.
- To prevent onward transmission of infection to others.
- To prevent the emergence and spread of resistance to antimalarial drugs.

2.3 First-line treatment

The first-line treatment for uncomplicated malaria in Sudan

is artemether-lumefantrine (AL) in the form of tablets.

AL is a highly effective fixed-dose combination antimalarial

treatment. Each tablet contains both artemether

lumefantrine. It has high clinical and parasitological cure

rates.

Formulations available: in Sudan, AL is currently available as

dispersible or standard tablets containing 20 mg artemether

and 120 mg lumefantrine (AL 20/120), and standard tablets

containing 80 mg artemether and 480 mg lumefantrine (AL

80/480) in fixed-dose combinations.

Dosage regimen: AL is given twice a day for three days (the

total is six doses).

The second dose should be taken 8 hours after the first dose.

The 3rd dose should be taken 24 hours after the first dose.

The remaining doses should be taken every 12 hours (Table

1).

Additional considerations: To maximize absorption, AL

14

should be taken with fatty food or milk. The dose should be repeated if the drug is vomited within 30 minutes.

Side effects: AL is generally well-tolerated. Reported adverse effects include gastrointestinal upset, headache, dizziness and muscle pain.

Contraindications: Hypersensitivity to artemether or lumefantrine.

Drug interactions: Decreased exposure to lumefantrine has been documented in young children, pregnant women, large adults, smokers and patients taking rifampicin. As these target groups may be at increased risk for treatment failure, their responses to treatment should be monitored more closely and their adherence ensured.

Table (1): Dosage schedule for artemether-lumefantrine (AL)

| | Day 1 | | Da | ay 2 | Da | ay 3 | | |
|-----------------------------------|-----------|---|--|--|--|--|-------------------------------|---------------------------------|
| Weight (Kg) | Initially | 8 hours after the 1st dose | 24 hours after the 1st dose | 12 hours after the 3rd dose | 12 hours after the 4th dose | 12 hours after the 5th dose | Total number of tablets | Tablet strength |
| < 5 | | | | Seek co | nsultar | nt advid | ce | |
| 5 – 14 | 1 | 1 | 1 | 1 | 1 | 1 | 6 | AL "20/120" |
| 15 – 24 | 2 | 2 | 2 | 2 | 2 | 2 | 12 | dispersible |
| 25 – 34 | 3 | 3 | 3 | 3 | 3 | 3 | 18 | AL"20/120" standard tablets |
| Children > 34 kg and adults | 1 | 1 | 1 | 1 | 1 | 1 | 6 | AL "80/480" standard tablets |

2.3.1. Treatment failure

- Treatment failure is considered when fever and parasitemia persist or recur within 4 weeks after initial treatment.
- Treatment failure is not always due to parasite resistance. Other causes include sub-optimal dosing, poor adherence, vomiting, unusual pharmacokinetics in an individual or substandard medicines.
- Revisit the history to determine whether the patient vomited the previous treatment or did not complete a full course of treatment.
- Treatment failure must be confirmed parasitologically.
 The use of RDTs is contraindicated in suspected treatment failure, as they remain positive for weeks after initial infection, even with effective treatment.
- After exclusion of alternative causes, the second-line treatment should be used (see 2.4 Second-line treatment).
- Recurrence of fever and parasitemia more than 4
 weeks after treatment should be considered new
 infections and treated with first-line treatment (AL).

2.4 Second-line treatment

The second-line treatment is indicated in the case of treatment failure or when the first-line treatment is contraindicated or unavailable.

Second-line treatment: dihydroartemisinin + piperaquine (DHAP) is the second-line treatment. DHAP is a highly effective fixed-dose combination antimalarial treatment.

Formulations available: Two strengths are currently available as fixed-dose combination tablets: 20/160 DHAP (20 mg DHA + 160 mg P) for pediatric cases, and 40/320 DHAP (40 mg DHA + 320 mg P) for adults.

Dosage regimen: DHAP is given once daily for three consecutive days (a total of three doses). The dose should be taken at the same time every day (Table 2).

Additional considerations: High-fat meals should be avoided with DHAP as they alter the absorption of piperaquine.

Side effects: Side effects are uncommon. Gastrointestinal upset and dizziness may occur in a minority of patients.

Contraindications:

- Hypersensitivity to dihydroartemisinin or piperaquine.
- Patients with congenital or acquired QT prolongation

Drug interactions: Malnourished children are at an increased risk of DHAP treatment failure. Their response to treatment should be monitored closely.

Table (2): Dosage schedule for dihydroartemisinin + piperaquine (DHAP)

| DHAP | body | | | | total no |
|----------|---------|-------|----------|------------|----------|
| Tablet | weight | Day 1 | Day 2 | Day 3 | of |
| strength | (Kg) | | | | tablets |
| | < 5 | Se | ek consu | ltant advi | ce |
| 20/160 | 5 - 8 | 1 | 1 | 1 | 3 |
| Tablet | 8 - 11 | 1.5 | 1.5 | 1.5 | 4.5 |
| | 11 - 17 | 1 | 1 | 1 | 3 |
| | 17 - 25 | 1.5 | 1.5 | 1.5 | 4.5 |
| 40/320 | 25 - 36 | 2 | 2 | 2 | 6 |
| | 36 - 60 | 3 | 3 | 3 | 9 |
| Tablet | 60 - 80 | 4 | 4 | 4 | 12 |
| | >80 | 5 | 5 | 5 | 15 |

2.5 Treatment of uncomplicated vivax malaria

The treatment of choice for uncomplicated vivax malaria is AL plus primaquine.

The objectives of treatment of vivax malaria are twofold: to cure the acute blood stage infection and to clear hypnozoites from the liver to prevent relapses. This is known as radical cure.

The blood stage of P. vivax is susceptible to the first-line treatment (AL) and should be treated with the same dosage prescribed in cases of infection with P. falciparum (Table 1).

For hypnozoite clearance, AL must be followed by primaquine.

Formulations available: Tablets containing 15 mg and 30 mg of primaquine are available.

Dosage regimen: The dose of primaquine for adults is 15 mg daily for 14 days. The dose for children is 0.25 mg/kg body weight daily for 14 days.

Side effects: Primaquine is known to cause hemolysis in people with G6PD deficiency.

In people with G6PD deficiency, relapse is prevented by giving primaquine at 0.75 mg/kg body weight once a week for 8 weeks, with close medical supervision for potential primaquine-induced hemolysis.

Contraindications:

- Pregnant and breastfeeding women
- Infants aged less than 6 months

2.6 Malaria caused by P. ovale and P. malaria

P. ovale and P. malariae are relatively uncommon in Sudan. They cause mild clinical disease. Treat cases of P. malariae with AL using the same dosage as in Table 1.

Since P. ovale can form hypnozoites like P. vivax, P. ovale should be treated with AL and primaquine.

2.7 Mixed infections

Mixed malarial infections are common in endemic areas like Sudan. AL is effective against all malaria species and

is the treatment of choice for mixed infections. If P.vivax and/or P.ovale are involved, primaquine should be prescribed in addition to AL.

UNIT 3: MANAGEMENT OF SEVERE MALARIA

3.1 Case definition of severe malaria

Severe malaria is defined as parasitologically confirmed malaria plus one or more of the manifestations listed in Table 3.

It is a medical emergency that should be managed at hospitals. Healthcare workers at peripheral units should refer patients immediately. Pre-referral treatment is recommended at peripheral units before referral to the hospital (See section 3.5. Pre-referral treatment).

Table (3): Manifestations of severe malaria

| Clinical manifestations | Laboratory findings |
|--|--|
| Impaired consciousness (Glasgow Coma score of < 11 in adults or Blantyre coma score < 3 in children) Multiple convulsions (more than two episodes within 24 hours) Jaundice Pulmonary edema Respiratory distress (acidotic breathing) Abnormal bleeding Ø Shock Haemoglobinuria or myoglobinuria Prostration i.e. severe generalized weakness Continuous vomiting | Severe anemia: (Hb ≤ 5 g/dl, PCV ≤ 15% in children; Hb < 7g/dl, PCV < 20% in adults) Hypoglycemia: (<2.2 mmol/l or <40 mg/dl) Ø Metabolic Acidosis (Plasma bicarbonate < 15 mmol/l) Hyperlactatemia (lactate ≥ 5 mmol/l) Hyperparasitemia (P. falciparum > 10%) Renal impairment (Serum creatinine > 265 µmol/l, or blood urea > 20 mmol/L) |
| • Continuous vomiting | |

3.2 Specific treatment of severe malaria

Intravenous artesunate is the treatment of choice for severe malaria.

Drug formulations: The drug is available as artesunate powder in three strengths: 30, 60, and 120 mg vials. The drug is packed together with sodium bicarbonate for reconstitution and normal saline for dilution.

Dose and regimen: Artesunate 2.4 mg/kg body weight (or 3.0 mg/kg in children less than 20 kg) is given by intravenous injection on admission (time = 0), repeated at 12 hours and 24 hours, then once a day until the patient can tolerate oral medication. After at least 24 hours of parenteral treatment and if the patient can tolerate oral medication, complete the treatment with a full course of artemether-lumefantrine. At least 3 doses of parenteral artesunate should be given within the first 24 hours of treatment. These should be given irrespective of the patient's ability to tolerate oral medication.

If intravenous administration is unavailable, artesunate

may be administered intramuscularly.

Healthcare providers need to prepare parenteral artesunate for use carefully as in the instructions below:

- 1- Weigh the patient (in kg)
- **2-** Calculate the needed number of artesunate vials (30, 60, or 120 mg) for each patient guided by the following:

| Weight in Kg | Vials of artesunate powder |
|--------------|----------------------------|
| 4 – 10 | One vial of 30 mg |
| 11 – 25 | One vial of 60 mg |
| 26 – 50 | One vial of 120 mg |
| > 50 | Two vials of 120 mg |

3- The solution should be prepared freshly for each administration as follows:

Add the attached 5% sodium bicarbonate solution to artesunate powder

- Shake the vial gently for 2-3 minutes for better dissolution.
- Add the attached 5% normal saline (not distilled water) to make the concentration of artesunate 10 mg/ ml for intravenous administration.
- Regardless of strength (30, 60 or 120 mg), the final concentration of artesunate after mixing will be 10 mg/ml. The total volume, however, will differ as follows:

| Artesunate injection preparation | | | | |
|----------------------------------|----|-------------|-----|--|
| Mode of Administration | | Intravenous | | |
| Strength (mg) | 30 | 60 | 120 | |
| Total volume (ml) | 3 | 6 | 12 | |
| Artesunate concentration (mg/ml) | | 10 | | |

4. Calculate the required dose in ml for each patient using the following table :

| | Dose to be administered | | | | |
|--------------|---|------------|--|--|--|
| | immediately (0), after 12 hours, 24 hours then once a day until the | | | | |
| Weight in kg | | | | | |
| | patient can take orally | | | | |
| | Dose in mg | Dose in ml | | | |
| < 4 | 10 | 1 | | | |
| 4 - 6 | 20 | 2 | | | |
| 7 -10 | 30 | 3 | | | |
| 11 - 13 | 40 | 4 | | | |
| 14 - 16 | 50 | 5 | | | |
| 17 - 25 | 60 | 6 | | | |
| 26 - 29 | 70 | 7 | | | |
| 30 - 33 | 80 | 8 | | | |
| 34 - 37 | 90 | 9 | | | |
| 38 - 41 | 100 | 10 | | | |
| 42 - 45 | 110 | 11 | | | |
| 46 - 50 | 120 | 12 | | | |
| 51 - 54 | 130 | 13 | | | |
| 55 - 58 | 140 | 14 | | | |
| 59 - 62 | 150 | 15 | | | |
| 63 - 66 | 160 | 16 | | | |
| 67 - 70 | 170 | 17 | | | |
| 71 - 75 | 180 | 18 | | | |
| 76 - 79 | 190 | 19 | | | |
| 80 - 83 | 200 | 20 | | | |
| 84 - 87 | 210 | 21 | | | |
| 88 - 91 | 220 | 22 | | | |
| 92 - 95 | 230 | 23 | | | |
| ≥ 96 | 240 | 24 | | | |

5- Administer intravenously as a slow bolus over 1–2 minutes.

Note: Artesunate may be administered intramuscularly if intravenous administration is not possible

- To prepare artesunate for IM administration, the same aforementioned preparatory steps should be followed. However, the concentration should be 20 mg/ml. To make the concentration 20 mg/ml, the amount of 5% normal saline added should be modified as follows: 1 ml for 30 mg vials, 2 ml for 60 mg vials, and 4 ml for 120 mg vials.
- The dosage in ml will be half that of the dose provided in the 'dosage schedule for IV artesunate' table.
- The IM preparation should be injected slowly into the anterior thigh. If the dose is more than 2 ml for babies or more than 5 ml for adults, split the dose between the two thighs.

Side effects: Artesunate is generally well-tolerated and has a better safety profile than quinine. Artesunate 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: Hypersensitivity to artesunate or artemisinin derivatives.

3.2.1 Treatment with quinine

Use IV quinine for treating severe malaria when artesunate is not available or contraindicated.

Formulations available: intravenous quinine is available as 300 mg/ml (or 600 mg/2ml) vials.

Dose and regimen: Rapid intravenous administration of quinine is dangerous. Each dose (10 mg/kg) of parenteral quinine must be diluted in 5% dextrose and administered as a slow infusion over 4 hours (Table 4). The dose is administered at 8-hour intervals. IV quinine should be

continued for at least 24 hours and until the patient can take oral medication. A full course of oral artemether-lumefantrine should be prescribed as soon as the patient can tolerate oral medication. If artemisinin derivatives are contraindicated, a 7-day course of oral quinine can be used instead.

Table (4): Dilution schedule and drop rate for IV quinine administration

| Weight (kg) | Quinine dose (mg) | Volume of undiluted quinine solution (ml) | Amount of fluid to be infused in 4 hours (ml) | Drop rate per minute |
|----------------|----------------------|---|---|----------------------------|
| ≤ 6 | 60 | 0.2 | 50 | 4 |
| 6 - 10 | 90 | 0.4 | 100 | 8 |
| 11 - 14 | 150 | 0.5 | 100 | 8 |
| 15 - 18 | 180 | 0.6 | 150 | 13 |
| 19 - 24 | 210 | 0.7 | 200 | 17 |
| 25 - 35 | 300 | 1.0 | 250 | 21 |
| 36 - 49 | 420 | 1.4 | 350 | 30 |
| 50 - 60 | 540 | 1.8 | 500 | 42 |
| ≥ 60 | 600 | 2.0 | 500 | 42 |

If the IV route is not possible, IM quinine can be given in the same dosage as IV quinine. Intramuscular injection must be diluted with sterile normal saline or distilled water to 60 mg/ml, split to halves, and administered into the anterior upper aspect of the each thigh.

Side effects: hypoglycaemia is the most serious and frequent adverse effect. Other side effects include hypotension and cinchonism.

3.2.2 Specific treatment of severe P. vivax malaria

Although P. vivax malaria is considered benign with a very low case-fatality rate, it can occasionally cause severe disease. Prompt and effective treatment and case management should be the same as for severe and complicated P.falciparum malaria. Parenteral treatment should be followed by full courses of artemether-lumefantrine and primaquine.

3.2.3 Adjustment of dosing in renal failure or hepatic dysfunction

The dosage of artesunate does not have to be adjusted for patients with vital organ dysfunction. However, quinine accumulates in severe vital organ dysfunction. If a patient with severe malaria has persisting acute kidney injury or there is no clinical improvement by 48 h, the dose of quinine should be reduced by one-third, to 10 mg salt/kg body weight every 12 h. Dosage adjustments are not necessary if patients are receiving either hemodialysis or hemofiltration.

3.3 General management of patients with severe malaria

Attention should be paid to the patient's general management as well as specific treatment.

The healthcare providers on duty at any level of healthcare services should consider the following points in the management of a patient with severe malaria.

Do the following immediate measures

1. Start resuscitation, particularly maintenance of the

airway, breathing, and circulation (ABCs)

- 2. Make a thick blood smear for immediate malaria parasite
- **3.** Establish the patient's hydration status, assess the patient's fluid requirements and replace accordingly.
- **4.** 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).
- **5.** Control convulsions: Maintain airway, treat with rectal diazepam (0.5mg/kg) or slow IV diazepam (0.3mg/kg, maximum 10mg in an adult). Correct hypoglycemia if is present.
- **6.** Detect and treat hypoglycemia: If blood glucose ≤ 2.2 mmol/l (or ≤ 3 mmol/L for children < 5 years); give 5 ml/kg of 10% dextrose IV 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 hypoglycemic.
- **7.** Start intravenous artesunate (see 3.2. Specific treatment of severe malaria).

Look and deal with the following complications

- **1.** Shock, algid malaria: if systolic BP <50mmHg in children 1-5 yrs. or <80 mmHg in >5yrs, suspect Gram-negative septicemia. In such cases, take blood samples for culture. Give parenteral broad-spectrum antimicrobials. Correct hemodynamic disturbances. Treat with 30ml/kg 0.9% Saline IV in 1 hour, then, reassess. Give oxygen if possible
- 2. Consider the need for blood transfusion: Assess the degree of pallor (no pallor, some pallor or severe pallor). Look for signs of severe anemia 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. Transfuse blood if there is:

- **A.** Cardio respiratory symptoms e.g. cardiac failure or decompensation.
- **B.** PCV<15% or Hb <5g/dL.
- **3.** In case of metabolic acidosis: Exclude and treat hypoglycemia, hypovolemia, and septicemia. Give

isotonic saline 20 ml/Kg of body weight rapidly or screened. If severe, add hemofiltration or haemodialysis.

- **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 adults, 1 mg/day for infants, 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: Exclude dehydration; maintain strict fluid balance; carry out dialysis if indicated.
- **6.** Malarial hemoglobinuria (black-water fever): Continue with suitable anti-malarial treatment; transfuse screened fresh blood if needed.
- **7.** Acute pulmonary oedema: Prevent by avoiding excessive IV fluids. Treatment raise the bed to an angle of 450; give oxygen. If pulmonary oedema is due to overhydration, stop intravenous fluids, and give a diuretic (furosemide I.V. in a dose of 40 mg for adults and 0.5 -1 mg/Kg/dose for children). In life-threatening hypoxemia intubate the patient.

- **8.** Exclude common infections/conditions that present like severe malaria:
 - Perform urinalysis for urinary tract infection.
 - Diagnostic lumbar puncture should be performed
 (unless contraindicated) for unconscious patients.

 Coma and fever may be due to meningoencephalitis or malaria. Cerebral malaria is not associated with signs of meningeal irritation (neck stiffness, photophobia, or Kernig's sign).
 - White blood cell count for other infections and chest x-ray for bronchopneumonia.
 - Rt-PCR for Covid-19, or antigen-sensitive ICT for Covid-19

Monitor considering the following 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 edema.
- **3.** Vital signs: Monitor vital signs every 6 hours to detect complications of severe malaria. If pulmonary edema develops (rapid respiratory rate and deep labored 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.

The patient and relatives should be educated about compliance with a full course of treatment, home prevention of malaria, and the sequelae of severe malaria. Wait for the patient of severe malaria to recover before counselling.

3.4 Pre-referral treatment at peripheral units

In many rural settings in Sudan, it is usual to see patients with severe malaria seeking care at primary healthcare units. The health personnel in these units should refer the

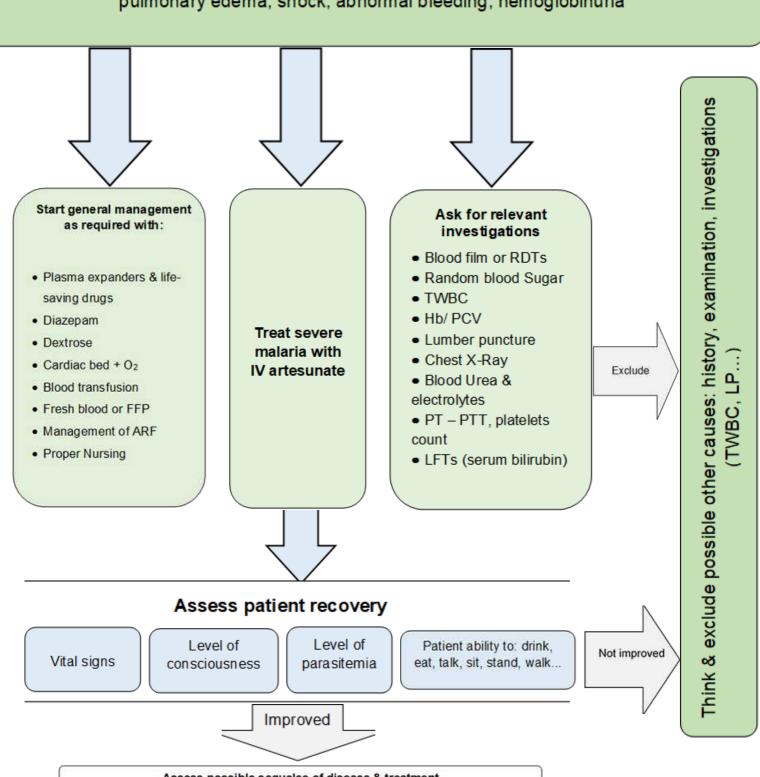
patients to the nearest hospital. Pre-referral treatment, if available, should be given. The choice is IV artesunate. If IV artesunate is not available, rectal artesunate should be used for children less than 6 years of age. The dosage is as follows:

- For IV artesunate see section 3.2
- Artesunate suppositories: Artesunate should be given rectally at 10 mg/kg once the diagnosis of malaria is made. If the rectal capsule is expelled within 30 minutes of insertion, another rectal capsule should be inserted and the buttocks held together for 10 minutes to ensure retention. Artesunate rectal capsules are recommended only for children under six years.

If after 24 hours the patient has not been referred to a hospital and is still unable to take oral medication, a second dose should be administered.

Suspect severe malaria if the patient presents with one or more of the following clinical features

Prostration, impaired consciousness, multiple convulsions, jaundice, respiratory distress, pulmonary edema, shock, abnormal bleeding, hemoglobinuria



Assess possible sequelae of disease & treatment

Perform neurological examination

Assess vision & hearing

Repeat BFFM on Day 7, Day 14& 1 month later

Repeat Hematocrit on Day 7, Day 14 & 1 month later

UNIT 4: MALARIA IN PREGNANCY

Malaria in pregnancy (MIP) is common in Sudan. It causes high morbidity and mortality to the mother and her fetus. The infection contributes to maternal anemia, fetal loss, premature delivery, intrauterine growth retardation and low birthweight.

4.1 Diagnosis and treatment of uncomplicated MIP

4.1.1 Diagnosis of uncomplicated MIP

- The symptoms of MIP may be confused with early pregnancy features such as morning sickness.
- For the diagnosis of MIP, the same steps outlined in Unit 1 should be followed.
- In addition to parasitological testing, CBC is mandatory (for hemoglobin and platelet count).

4.1.2 Treatment of uncomplicated MIP

The first line of treatment in all trimesters is artemetherlumefantrine (AL).

The second line of treatment in the 2nd and 3rd trimesters is dihydroartemisinin-piperaquine (DHAP) (For more information on AL and DHAP regimens, see Unit 2).

4.2 Diagnosis and management of severe MIP

The diagnosis, management and anti-malarial drugs of choice for severe malaria in pregnancy are the same as outlined in Unit 3: Management of Severe Malaria.

When managing severe malaria in pregnancy special concern must be paid to anemia, hypoglycemia and pulmonary edema as these are more likely to present in pregnant patients.

4.3 Treatment of P. vivax and P. ovale in pregnancy

The 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.

4.4 Intermittent preventive treatment of malaria in

pregnancy (IPTp)

Intermittent preventive treatment of malaria in

pregnancy is the administration of a course of an

antimalarial medicine at predetermined intervals,

regardless of whether the pregnant woman is infected

with malaria.

IPTp improves a wide range of outcomes, including

maternal and placental infection, maternal anaemia and

low birthweight.

IPTp is recommended for pregnant women in high

transmission settings in Sudan. These include the states

of Gedarif, Blue Nile, South and West Kordofan, East,

Central, South and West Darfur, in addition to refugee

camps and nomad settlements all over the country.

Drug of choice: Sulfadoxine-pyrimethamine (SP) is the

44

drug of choice for IPTp.

Dosage: IPTp-SP should be administered as directly observed therapy (DOT) with three tablets of SP (each tablet containing 500 mg/25 mg SP), for the total required dosage of 1500 mg/75 mg SP.

Regimen: IPTp-SP should be started in the second trimester and doses should be given at each scheduled ANC contact until the time of delivery, provided that doses are at least one month apart. At least three doses of IPTp-SP should be received during pregnancy.

Contraindications:

- Pregnant women before week 13 of pregnancy
- Pregnant women with allergy to any of the components of SP.
- Patients receiving co-trimoxazole.

UNIT 5: MALARIA IN CHILDREN

Children under 5 years of age are the most vulnerable group to malaria. A major cause of ill-health in children, malaria can contribute to death in young children in three principal ways:

- Low birthweight frequently the consequence of malaria infection in pregnant women - is a major risk factor for death in the first month of life.
- 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 anemia, which substantially increases the risk of death.

5.1 Uncomplicated malaria in children

5.1.1 Diagnosis of uncomplicated malaria in children

Healthcare providers should suspect uncomplicated malaria in:

- Any child with fever
- 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 quality-assured microscopy or RDTs is mandatory (see Unit 1: Malaria Diagnosis).

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 considered.

5.1.2 Treatment of uncomplicated malaria in children

The recommended treatment for uncomplicated malaria in children is the same as outlined in Unit 2: Management of Uncomplicated Malaria.

As young children are more likely to vomit or regurgitate

treatment than older children or adults, mothers should be advised on the technique of drug administration and the importance of administering the drug again if it is regurgitated within one hour of administration.

5.2 Severe malaria in children

The diagnostic criteria and management steps of severe malaria in children are as described in Unit 3: Management of Severe Malaria.

5.3 Treatment of P. vivax and P. ovale

The eradication of P. vivax or P. ovale hypnozoites using primaquine is contraindicated in children under 6 months.

5.4 Congenital malaria

Congenital malaria is defined as the presence of asexual forms of the Plasmodium parasite in the peripheral blood within the first 7 days of life. Clinical features of congenital malaria include fever, anaemia and splenomegaly. Less common features include

hepatosplenomegaly, jaundice, regurgitation, loose stools, and poor feeding.

The treatment of choice for congenital malaria is IV artesunate.

It should be noted that fever during the first 3 weeks of life is mostly due to bacterial infection, but congenital malaria should be considered as a differential diagnosis.

UNIT 6: MALARIA PREVENTION AND PROPHYLAXIS

6.1 Insecticide-treated nets

Healthcare workers play an important role as health promoters. All malaria patients should be counselled on the importance of ITN utilization to prevent future infections. Additionally, ITN counselling should be provided during antenatal and pediatric primary healthcare visits.

Usage: ITNs can be used both indoors and outdoors, wherever they can be suitably hung. However, hanging nets in direct sunlight should be avoided, as sunlight can affect insecticidal activity.

6.2 Preventive chemotherapy for travelers

For travelers from malaria-free areas, the recommended

prophylactic regimen is mefloquine. For adults, the dose is 250 mg (one tab) every 7 day, starting at least one week (preferably 2-3 weeks) before entering the area, once weekly while in the area, and once weekly for 4 weeks after leaving the area. For children the dose is 5 mg/Kg with the same interval as for adults.

Atovaquone-proguanil (Malarone®) offers an alternative for chemoprophylaxis in individuals who cannot take mefloquine. The prophylactic dose for adults is 250 mg of atovaquone plus 100 mg of proguanil (one tablet) daily beginning one day before entering the malaria-endemic area and for seven days after leaving. For children, the dose is 62.5 mg atovaquone + 25 mg proguanil.

REFERENCES

Adeel, A. A., Elnour, F. A., Elmardi, K. A., Abd-Elmajid, M. B., Elhelo, M. M., Ali, M. S., Adam, M. A., Atta, H., et al. (2016) 'High efficacy of artemether-lumefantrine and declining efficacy of artesunate + sulfadoxine-pyrimethamine against Plasmodium falciparum in Sudan (2010-2015): Evidence from in vivo and molecular marker studies', Malaria Journal, 15(1). doi:10.1186/s12936-016-1339-x.

Federal Ministry of Health (2017a) Sudan malaria indicator survey 2016. Khartoum.

Federal Ministry of Health (2017b) Sudan malaria treatment protocol 2017. Khartoum.

Federal Ministry of Health (2020) Sudan malaria strategic plan 2021-2025. Khartoum.

Federal Ministry of Health (2022) Annual statistical report 2021. Available at: http://sho.gov.sd/controller/knowledge_hub.php? sm id=132&mid=110&lid=1.

Mohamed, A. O., Abdel Hamid, M. M., Mohamed, O. S., Elkando, N. S., Suliman, A., Adam, M. A., Elnour, F. A. A., and Malik, E. M. (2017) 'Efficacies of DHA-PPQ and AS/SP in patients with uncomplicated Plasmodium falciparum malaria in an area of an unstable seasonal transmission in Sudan', Malaria Journal, 16(1). doi:10.1186/s12936-017-1817-9.

World Health Organization (2015) 'Global technical strategy for malaria 2016-2030'. Available at: https://www.who.int/docs/default-source/documents/global-technical-strategy-for-malaria-2016-2030.pdf.

World Health Organization (2022a) Incidence estimation using routine data and adjustments 2017-2021, fig.

World Health Organization (2022b) 'WHO guidelines for malaria 25 November 2022'. Available at:

https://www.who.int/publications/i/item/guidelines-for-malaria.

World Health Organization (2022c) World malaria report. Available at: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2022.