Malaria in children: current approaches to treatment and prevention

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Abstract

Malaria remains a global healthcare challenge, especially in children under the age of five, who continue to be disproportionately affected. Clinical presentation of malaria is non-specific, ranging from flu-like symptoms in mild cases to multi-organ failure in severe cases. Prompt diagnosis and treatment determine case outcomes. Patient and caregiver education about malaria prevention is the cornerstone of malaria management and requires an individualised approach. As the seasonal transmission of malaria in South Africa starts waning towards May and rising again in October, it is essential that healthcare workers be informed about the latest prevention and treatment strategies.

Keywords: malaria, paediatrics, treatment, prevention, chemoprophylaxis

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Introduction

Malaria is a global preventable infectious disease that continues to be a major cause of illness and death.[1,2] According to the World Health Organization (WHO), there were approximately 249 million cases and 613 000 deaths in 2022.[3] Progress against the disease has largely been halted by the COVID-19 pandemic, with an increase of approximately 5 million cases and 55 000 deaths compared to 2021.[3] In sub-Saharan Africa (SSA), children under the age of five years old contribute to more than two-thirds of all malaria-related deaths.[3–5] This roughly translates to one death occurring every minute.[5]

Malaria transmission: South Africa

Malaria transmission in South Africa primarily occurs along the border regions of Mozambique, Zimbabwe, and Botswana. Some provinces (such as Limpopo, Mpumalanga, and KwaZulu-Natal) are endemic for malaria, posing a risk to approximately 4.9 million individuals, which is equivalent to 10% of the population.[6–8] Malaria transmission follows a seasonal pattern, with cases increasing in October, reaching a peak in January and February, and gradually declining towards May.[6] The majority of South Africans, including those living in regions with seasonal exposure, lack immunity to malaria, placing them at increased risk of developing severe malaria.[7]

Life cycle and aetiology of malaria

Malaria is caused by the protozoan parasite *Plasmodium,* which is transmitted to humans through the bite of an infected female *Anopheles* mosquito. When these mosquitoes feed, they inject sporozoites, the motile and infectious form of the parasite, that initiate malarial infection.[1,9–11] Sporozoites infect the liver cells first, and they undergo an asymptomatic replication cycle lasting seven days.[12] Merozoites are formed and eventually released from the liver cells, subsequently infecting red blood cells (RBCs). During this stage, daughter merozoites undergo a cycle of growth, replication, release, and invasion, while other blood-stage parasites differentiate into male and female gametocytes. This erythrocytic phase leads to symptomatic disease, such as anaemia and splenomegaly, which is mediated by extensive haemolysis.[1,12,13]

For the infection to spread, the female *Anopheles* mosquito must ingest male and female gametocytes. These gametocytes undergo sexual reproduction and maturation inside the mosquito. Mature sporozoites migrate to the salivary gland of the mosquito, where they may infect humans upon their next meal and continue the cycle.[1,13]

In South Africa, the infectious protozoans include *Plasmodium vivax, P. ovale, P. malariae, P. knowlesi,* and *P. falciparum*, with *P. falciparum* being responsible for 95% of malaria cases.[2,3,11]

Incubation period

The interval between being bitten by an infected mosquito and the onset of clinical symptoms varies depending on the *Plasmodium* species causing the infection. In *P. falciparum*, it is usually 10 to 14 days, ranging from as little as seven days to as long as 30 days.[13–15] *P. malariae* can persist at low levels for extended periods, potentially lasting for years. *P. vivax* and *P. ovale* can form dormant stages in the liver (hypnozoites) that persist for months or years after the initial infection. These hypnozoites can eventually reactivate to cause a relapse of symptomatic malaria.[9,10,13]

Symptom manifestation might also be delayed due to incomplete chemoprophylaxis or in patients with partial immunity.[13]

Pathogenesis

The pathogenesis of *Plasmodium* infection can be categorised into three categories: inflammation, anaemia, and end-organ damage.[13]

Inflammation

Inflammation is triggered by parasite metabolism, RBC rupture, and sequestration of infected cells.[13] Hemozoin (a toxic by-product) is produced when heme from haemoglobin is digested by the parasite. Subsequently, macrophages and monocytes release inflammatory cytokines after ingesting hemozoin. This triggers a systemic inflammatory response syndrome, oedema, and increased adhesion of infected cells into small vessels.[13]

Anaemia

Malaria infection induces **anaemia** by causing haemolysis through the replication of parasites, splenic clearance of less flexible RBCs, and the inflammatory suppression of compensatory RBC production. In *P. falciparum* infection, infected RBCs additionally adhere to the blood vessel walls in the spleen, causing a more severe clinical presentation.[13]

End-organ damage

End-organ damage occurs due to cytoadherence of infected RBCs (sequestration) in small blood vessels. Infected RBCs express proteins that cause adhesion to vessel walls and other cells. This cytoadherence, along with clumping of uninfected cells and inflammatory cells, obstructs microcirculation and injures endothelium, causing inflammation and tissue damage. Sequestration can occur in any organ, and, moreover, it prevents parasites from undergoing splenic clearance, thus causing persistent infection.[13]

Box 1: Common malaria symptoms & signs[7,8,14]

Common malaria symptoms & signs include:

- Fever, chills, perspiration, rigours (cold/ hot sweats)
- Headache
- Muscle/joint pain
- Malaise
- Lethargy, fatigue
- Loss of appetite (older children & adults), poor feeding (young children)
- Gastrointestinal symptoms (abdominal pain, diarrhoea, nausea, and vomiting)
- Cough (young children)

Clinical presentation and diagnosis

Malaria symptoms are typically non-specific; thus, the range of potential diagnoses is broad.[2,13,14] No set of signs or symptoms reliably distinguishes malaria from other causes of fever.[2,7] Relying solely on clinical features for diagnosis often leads to overtreatment.[2]

Clinical presentation depends on the causative species.[1] For example, *P. falciparum* is more prone to cause severe infection compared to the other species.[2,3,16–19] However, *P. vivax* can also sometimes cause severe infection due to its ability to cause repeated infections, leading to chronic anaemia.[13]

Uncomplicated malaria

Children often initially present with flu-like symptoms and/ or gastrointestinal symptoms (Box 1). [1,7,9,10,13,19] They frequently develop hepatosplenomegaly and severe anaemia but are less likely to have major organ dysfunction compared to adults.[9,10,19]

Since disease progression can rapidly occur in non-immune patients, high-risk patients (such as children) should be monitored for the first 24 hours of treatment.[7]

Table I: Clinical and laboratory manifestations of severe malaria in children[2,7,9,13,14,18,20]

Signs and symptoms	Definition
Altered consciousness	Blantyre coma score < 3 or altered mental state ranging from irritability, lethargy to coma, stiff neck or bulging fontanelle
Prostration	Generalised weakness causing inability to sit, stand or walk without assistance
Multiple convulsions/seizures	More than 2 episodes in 24 hours
Acidosis	A base deficit > 8 mEq/L or plasma bicarbonate level < 15 mmol/L or venous plasma lactate ≥ 5 mmol/L. Physical manifestations may include respiratory distress (rapid, deep, laboured breaths).
Hypoglycaemia	Blood or plasma glucose < 2.2 mmol/L
Severe anaemia	Haemoglobin level ≤ 5g/dL or haematocrit ≤ 15% in children under 12 years of age
Severe thrombocytopenia	Platelets < 50 x10^9/L
Renal dysfunction	High serum creatinine level for patient's age
Jaundice	Plasma or serum bilirubin > 50 µmol/L or visible yellowing of skin, eyes, etc.
Pulmonary oedema	Radiographic findings and high respiratory rate for patient's age
Significant bleeding	Bleeding from multiple sites such as nose, gums, drip-site, as well as blood in stool, vomit or in urine.
Shock	**Compensated shock:** capillary refill ≥ 3 seconds or temperature gradient on leg, but no hypotension. **Decompensated shock:** systolic blood pressure < 70 mmHg in children, with evidence of impaired perfusion, such as cool extremities or prolonged capillary refill time.
Hyper-parasitaemia	Plasmodium falciparum parasitaemia > 4% or > 3+

Complicated/ severe malaria

Mortality rates in patients who suffer from severe malaria (especially cerebral malaria) approaches 100% if untreated.[3] The severity of malaria infection depends on the level of acquired immunity in children. Immunity develops through ongoing parasite exposure. In endemic areas, children acquire immunity early in life while in non-endemic areas with seasonal transmission, immunity develops incompletely at a later age, resulting in more severe infections in both children and adults.[9] Table I illustrates the clinical and laboratory manifestations of severe malaria in children.

These clinical manifestations may occur together or alone.[13]

Cerebral malaria (CM)

Cerebral malaria (CM) is one of the most concerning clinical complications of malaria, usually attributed to *P. falciparum* parasitaemia.[12,16,18] CM is defined as otherwise unexplained coma or altered mental status (Table I) and/or with seizures in patients infected with malaria.[13,16,18]

Although the exact pathogenesis of CM is controversial, it has been observed that in *P. falciparum* malaria, sequestration of parasites in the small blood vessels of the brain appears to be common. As a result, complications such as cerebral oedema and death occur.[12,13,16,17]

Retinal whitening, vessel discolouring, and white-centred haemorrhages are frequently reported in children with CM and occurs in approximately two-thirds of cases.[16,17,21] CM may cause neurocognitive impairment in 25% of children that last at least two years after exposure. Retrospective trials indicate that these neurologic sequelae may last up to eight years and can include behavioural issues, mental health concerns and the onset of epilepsy.[21]

Diagnostic investigations

Rapid diagnostic tests (RDTs) to detect malaria are available in South Africa, and usually produce a result within 20 minutes.[7,20] A histidine-rich-protein II (HRP2)-based RDT is preferred to detect *P. falciparum*, as > 90% of malaria infections in South Africa are due to this organism.[1,7,13,20,22]

RDTs are highly sensitive, although false negative results are also possible.[9] Reasons such as low parasitaemia, symptom manifestations before parasite multiplication (common in non-immune infants or young children), improper storage or expiry of tests, the prozone effect (saturation of test binding receptors) or parasite genetic variability can cause this phenomenon.[7,9] However, it should be noted that patients can also have positive results up to 30 days after recovery, thus RDTs should not be used for follow-up monitoring.[7,9,20]

Microscopic visualisation of blood smears to identify parasites is the mainstay of diagnosing malaria.[1,9,19] Both thin and thick smears are recommended to confirm malaria diagnosis.[7,9,13,19] If initial RDT or blood smears return a negative result, despite the patient exhibiting symptoms consistent with malaria, and no other cause is identified, tests should be repeated every 6–12 hours until a definitive diagnosis is established.[7] Blood tests for parasites should be conducted regardless of the time of year or whether the patient has taken chemoprophylaxis or travelled to a malaria endemic area.[7]

Polymerase chain reaction (PCR) tests are highly sensitive and specific, however not recommended for routine use due to unpracticality. However, it is useful for identification of species, mixed-infections, and low-level infections.[7,19]

All malaria cases should be reported promptly, as malaria is a notifiable medical condition in South Africa.[7,23]

Prevention strategies

A variety of factors contribute to the risk of travellers acquiring malaria, including patient characteristics, travel activities and the geographic destination.[15,24] A risk assessment is recommended 4–6 weeks before departure, along with education about the consequences of malaria and the importance of preventative measures.[15,24]

Box 2: The "ABC" of malaria prevention:[8,10]

A: **A**wareness and **A**ssessment of malaria risk
B: Avoidance of mosquito **B**ites
C: **C**ompliance with **C**hemoprophylaxis (when indicated)
D: Early **D**etection of malaria disease
E: **E**ffective treatment

Adapted from the South African National Guidelines for Prevention of Malaria

Avoiding mosquito bites

Personal protective measures to avoid mosquito bites should form part of all travellers' prevention strategy, as chemoprophylaxis is not 100% effective.[8,25] Several steps can be taken to prevent mosquito bites, such as remaining inside between dusk and dawn when possible, wearing long, loose, light-coloured clothing, and topical insect repellants.[8]

Topical repellents range from synthetic chemicals to plant-derived products.[15,25,26] The most common are diethyltoluamide (DEET), picaridin, p-menthane-3,8-diol (PMD) and a range of botanical products (e.g. melaleuca, eucalyptus, citronella oils).[25,26] The American Academy of Paediatrics (AAP) recommends topical repellents containing DEET with a concentration of 10–30%.[8,26,27] DEET-containing topical repellents can be applied to uncovered skin during outdoor activities but should not be used on infants under two months old.[8,27,28]

Topical repellents should be reapplied every 4–6 hours, or according to manufacturer instructions. Alternatives such as citronella oils are less potent and shorter acting compared to DEET products.[8,25]

Insecticide-treated nets (ITNs) are an effective and often underutilised prevention measure that is safe for children and pregnant women.[15,25,26,29] Patients should be educated on the effective use of ITNs, such as making sure there are no holes or trapped mosquitos in the net, and that the nets are placed over the bed with edges tucked in.[8,9,15,30] Common insecticides used include permethrin or deltamethrin.[2,10]

Chemoprophylaxis

Antimalarial chemoprophylaxis works by eliminating certain *Plasmodium* parasite life stages in the human host, including liver schizonts, blood schizonts, or dormant hypnozoites.[24]

Table II: Summary of recommended malaria chemoprophylaxis for children:[8–10,15,24,25]

	Mefloquine	Doxycycline	Atovaquone-proguanil
Trade names	Lariam® tabs, Mefliam® tabs	Doxycycline Biotech ®, Cyclidox® caps, Doxycyl® caps	Malanil® tabs, NuMal®, tabs, Malateq®, Mozitec® tabs
Dosing interval	Weekly	Daily	Daily
Paediatric dose	1 tablet = 250 mg mefloquine **Weight: Dose** 5–20 kg: ¼ tablet 21–30 kg: ½ tablet 31–45 kg: ¾ tablet > 45 kg: Adult dose (1 tablet)	2 mg/kg of body weight daily (max 100 mg daily). Children > 15 or > 45 kg should use adult dose of 100 mg daily.	1 paediatric tablet = 62.5 mg atovaquone/25 mg proguanil **Weight: Dose** 11–20 kg: 1 paediatric tablet 21–30 kg: 2 paediatric tablets 31–40 kg: 3 paediatric tablets > 40 kg: 1 adult tablet (250 mg atovaquone/100 mg proguanil)
When to start	Start 1–2 weeks before entering area.	Start 1–2 days before entering area.	Start 1–2 days before entering area.
Duration	Use for 4 weeks after leaving area.	Use for 4 weeks after leaving area.	Use for 7 days after leaving area.
Side effects	Neuropsychiatric side effects: seizures, psychosis, vivid dreams, insomnia. **Other:** gastrointestinal upset, and headaches. Persistent dizziness is rare.	Gastrointestinal side effects, pill esophagitis, photosensitivity, and candida overgrowth.	Typically well tolerated. Gastrointestinal side effects, headaches and transaminitis.
Prophylactic efficacy	Effective against *P. falciparum* but resistance has emerged in parts of Southeast Asia. Effective against *P. vivax*. Limited data on other species.	Effective against chloroquine resistant *P. falciparum*. Limited protection against *P. vivax*.	Effective against chloroquine resistant *P. falciparum*. Effective against *P. vivax, P. ovale* and *P. malariae*.
Special precautions	May cause dizziness and lack of fine co-ordination. Do not use if going for underwater diving, etc.	Use with high SPF sunscreen due to photosensitivity. Patients should avoid milk and dairy products for at least 1 hour before and 2 hours after taking doxycycline. Supplements or antacids containing calcium, bismuth, aluminium, and magnesium should be taken at least 4–6 hours before taking doxycycline.	Take with food/milk for improved absorption. More expensive compared to other regimens, but longer half-life is more forgiving for missed doses.
Population considerations			
Young children	Use only if > 3 months old and > 5 kg. Typically, well tolerated in paediatrics.	Use only in children > 8 years due to risk of permanent teeth discolouration and inhibiting bone growth.	Use only in children > 11 kg.
Epilepsy	Contraindicated. May interact with valproic acid.	May interact with anticonvulsants, possibly resulting in ineffective prophylaxis of malaria.	Can be used.
Long-term use	May be used up to three years.	May be used up to two years.	May be used up to one year.
Diabetics	Insufficient data, use with caution and monitor blood glucose levels.	May cause hypoglycaemia with insulin, monitor blood glucose levels.	No known problems.
Cardiotoxicity or concomitant cardiac medications	May cause conduction abnormalities. Use with caution in patients on beta-blockers, calcium antagonists and quinidine.	Safe to use.	Safe to use.
Renal impairment	Caution (lack of data).	Safe to use.	Contraindicated in creatinine clearance < 30 ml/min.
Hepatic impairment	Contraindicated in severe impairment	Use with caution.	Safe to use in moderate hepatic impairment, but no data on severe impairment.
Psychiatric conditions	Contraindicated, even if only history of depression.	Can be used.	Can be used.

Adapted from South African National Guidelines for Prevention of Malaria and other resources. Refer to National guidelines for safety in pregnancy.

Table III: Dosage of artemether-lumefantrine according to weight bands:[2,7]

Artemether-lumefantrine (Coartem®) 20/120 mg tablets (oral)		
Weight band	**Dosage**	**Total amount for course**
5 to < 15 kg	One tablet immediately, then one tablet after eight hours, then one tablet twice daily for two days	Six tablets
15 to < 25 kg	Two tablets immediately, then two tablets after eight hours, then two tablets twice daily for two days.	12 tablets
25 to < 35 kg	Three tablets immediately, then three tablets after eight hours, then three twice daily for two days.	18 tablets
35 to < 65 kg	Four tablets immediately, then four tablets after eight hours, then four twice daily for two days.	24 tablets
> 65 kg	As for 35 kg, however close monitoring for inadequate response recommended.	24 tablets
> 85 kg	Off-label recommendation is to extend treatment course to five days, administering four tablets per dose for a total of 10 doses.	

Special precautions:
Tablets should be administered with food/milk containing a minimum of 1.2 g fat (e.g. ~100 ml of milk) to ensure adequate absorption.
*The WHO states that it can be safely used in children < 5 kg, but with close observation, however clindamycin + quinine is an effective alternative.[14]
Tablets may be crushed and mixed with a small amount of water (5–10 ml) for immediate consumption for patients unable to swallow tablets whole.

The choice of chemoprophylaxis should be based on patient characteristics, in addition to non-pharmacological prevention strategies.[8] In South Africa, three chemoprophylaxis medications are available, which include atovaquone-proguanil, doxycycline, and mefloquine.[8,24]

It is important to educate travellers that children can still acquire infection while on prophylaxis due to issues such as having trouble taking medications properly, inconsistent adherence and resistance.[9,13]

Medications such as chloroquine and primaquine are no longer recommended due to widespread medication resistance.[2,8,10]

Management of missed doses

If a patient misses a weekly dose of chemoprophylaxis, they should be instructed to take it as soon as they remember and then continue to take it on the normal scheduled day of the week. If more than two days are missed of a weekly regimen, serum levels may be subtherapeutic. However, the patient should still take the dose as soon as possible, with the next dose seven days later and then continue with the weekly regimen thereafter.[24]

Timing is important in daily dosing chemoprophylaxis; thus, doses should be taken at the same time every day. If a dose is missed by 1–2 days, serum levels are unlikely to remain therapeutic. Missed doses should be taken as soon as it is remembered, and the patient should continue with subsequent doses at the same time every day.[24]

Management strategies

The primary goals of malaria treatment include eradicating the parasitic infection, halting its transmission, reducing morbidity, and preventing progression to severe malaria and death. Public health goals include controlling the rise and spread of medication resistance.[2,7]

Uncomplicated malaria

Monotherapy is not recommended for treatment of malaria and contribute to medication resistance.[10]

Artemisinin-based combination therapies (ACTs), such as artemether-lumefantrine (Coartem®), are recommended by the WHO to treat uncomplicated malaria.[2,7] ACTs provide quick clinical response, increased cure rates, decreased malaria transmission and is less susceptible to medication resistance.[2,7] Artemether-lumefantrine boasts with advantages such as short treatment course (six doses over three days) and it is well tolerated.[2,7,31] However, it is only indicated for uncomplicated malaria, as there is no data on its effectiveness in severe disease.[7]

Medication interactions with Coartem®

Lumefantrine levels may decrease in young children (< 3 years), pregnant women, large adults and patients taking mefloquine, rifampicin or efavirenz and in smokers. Closer monitoring of these populations is recommended.[2] Manufacturing recommendations suggest avoiding concomitant use with drugs that prolong the QT interval or are metabolised by CYP2D6 and have cardiac effects.[7]

Alternative treatment options

For children < 5 kg with uncomplicated malaria, the preferred treatment is quinine plus clindamycin, as artemether-lumefantrine use in this population is considered off-label.[7]

Box 3: Dosing of quinine and clindamycin for uncomplicated malaria:

Quinine dose (oral): 10 mg salt/kg body weight every eight hours for seven to ten days.
Clindamycin (oral): 10 mg/kg twice a day for one week.

Quinine syrup is unavailable in South Africa, thus, administering it to children can pose a challenge. One alternative is to crush tablets and mix them with mashed bananas, chocolate syrup, or jam to enhance palatability, although the impact of food on bioavailability has not been investigated.[7]

Children who are unable to tolerate oral medications or have severe vomiting should be given intravenous (IV) artesunate or quinine.[2,7] In cases of *P. vivax* or *P. ovale* infection, primaquine should be given for two weeks to prevent relapse caused by their dormant liver stages.[13,14] To avoid haemolytic anaemia, screening for G6PD-deficiency should be performed.[13,14]

Table IV: Artesunate dosage and administration:[7,14]	
Artesunate (IV)	
Weight	**Dosage**
< 20 kg	3 mg/kg at 0, 12, and 24 hours then daily until able to tolerate oral treatment.
> 20 kg	2.4 mg/kg at 0, 12 and 24 hours, then daily until able to tolerate oral treatment.
Administration	
Dissolve 60 mg artesunate powder in 1 ml 5% sodium bicarbonate solution (supplied with the artesunate powder). Add 5 ml 5% dextrose (or 0.9% sodium chloride) to give a solution of 10 mg/ml for injecting as a **bolus into an IV cannula**. Once reconstituted, artesunate solution is not stable and should be administered within 30 minutes; solution not administered within 30 minutes should be discarded.	

Severe malaria

Severe infection warrants prompt parental treatment as death can occur within hours of presentation.[13]

Artesunate

Globally, IV artesunate is strongly recommended as evidence shows improved mortality rates compared to quinine.[7,10]

Artesunate is safe and is tolerated well. Common adverse effects such as gastrointestinal upset and dizziness have been reported. Rare side effects include blood dyscrasias (neutropenia, decreased reticulocyte counts, anaemia, and eosinophilia), elevated aspartate transaminase (AST), and transient electrocardiogram (ECG) abnormalities.[7] Cases of haemolytic anaemia, occurring more than one week after treatment with artesunate, have been documented in African children with high parasite counts and non-immune European travellers.[2,7] Due to this phenomenon, patients with high parasitaemia should be monitored closely to detect late-onset anaemia.[2,7]

Quinine

Quinine is recommended if artesunate is not available.[7]

Quinine should always be administered **via slow, rate controlled IV infusion** and never through bolus. A loading dose should be given, followed by maintenance dose eight hours after starting the loading dose. After which, maintenance therapy should be given every eight hours until the patient can use oral treatment.[7] Absorption in obese patients may be erratic, and ideal body weight should be used to calculate doses.[7]

General measures

General measures in managing severe malaria in young children include assessing and stabilising airway, breathing, and circulation (ABC). Hypoglycaemia, cerebral malaria, anaemia, and metabolic acidosis are important complications and should be monitored for. Agitation and respiratory distress due to metabolic acidosis signal poor prognosis. Fluid replacement via crystalloids is recommended, while boluses should be avoided. Children have an increased risk for dehydration. Third generation cephalosporins should be administered to children with severe malaria as secondary bacterial infections or sepsis are common. Seizures may be subtle in children, and underlying causes could be hypoglycaemia, CM, or fever.[2,7,9,14]

Box 2: Quinine dosage:[7]
Quinine loading dose: 20 mg/kg quinine dihydrochloride salt, diluted in 5–10 ml/kg 5% dextrose and given IVI over four hours.
Quinine maintenance dose: 10 mg/kg quinine dihydrochloride salt, diluted in 5–10 ml/kg 5% dextrose and given IVI over two to four hours.

Note: Do not confuse doses of salt and base. Doses are usually prescribed as salt (10 mg salt = 8.3 mg base).[7]

Future directions

Recently, vaccination has become a part of the armamentarium used to prevent malaria.[2,16] The RTS,S/AS01 malaria vaccine is recommended by the WHO for the prevention of *P. falciparum* malaria in children living in moderate to high-risk endemic areas.[2,3,32] However, it is currently not yet available in South Africa.

In a large phase three randomised controlled trial in over 15 000 children in SSA, the vaccine was deemed efficacious, however several safety concerns emerged. Severe adverse events and deaths occurred at similar rates in control and intervention groups. Febrile seizures were slightly more common in the 2–3 days after the RTS,S/AS01-vaccinated children but not infants. Meningitis and CM occurred more frequently among vaccinated girls compared to control groups. While these findings may have been attributed to chance given the large sample size of the study, their severity warrants further investigation in real-life pilot programmes to establish risk-benefit ratios.[32]

In contrast, a recent qualitative study found that caregivers had positive perceptions about the malaria vaccine for children, with fewer admissions to hospital and cost benefits. Healthcare workers played a crucial role in vaccine uptake. Fear of unknown side effects were identified as possible barriers to recommending the vaccine to other caregivers.[33]

A second vaccine, R21/Matrix-M (R21), is recommended by WHO since October 2023 for children living in high-risk areas.[3]

Conclusion

Worldwide efforts against malaria have recently hit a standstill, and continued interventions are needed to get countries back on track.[3] South Africa has shifted from malaria control towards malaria elimination, however majority of cases in the country is

now imported, and often present late to facilities in malaria-free regions.[7,23]

Healthcare professionals in South Africa, regardless of whether they work in malaria-endemic regions, should be knowledgeable about malaria prevention and treatment for travellers.[7,8,24]

Educating travellers to malaria-endemic countries about preventative steps is the best way to encourage adherence and preventing transmission. If malaria infection does occur, a high index of suspicion, rapid diagnosis and urgent treatment is vital to prevent severe illness and death, especially in children.[7,10,16]

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