

Malaria in South Sudan 2: clinical features and diagnosis

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The previous article, 'Introduction and patho-physiology', reviewed the mechanism of transmission of malaria, the types of parasite and the life cycle of the malarial parasite. In South Sudan, 90% of malaria is caused by *Plasmodium falciparum* (*P. falciparum*). This article focuses on the clinical features and diagnosis of *P. falciparum* but for completeness will also discuss the other main species of malarial parasites.

The incubation periods of the different types of malaria are shown below:

Type of malaria incubation period

- *P. falciparum* 12-14 days
- *P. vivax* 15 days
- *P. ovale* 15 days
- *P. malariae* 18 days

However, it must be remembered that *P. vivax* and *P. ovale* may present weeks or months after the initial illness due to reactivation of hypnozoites in the liver (1, 2). Furthermore, longer incubation periods may be likely in individuals who are semi-immune or in those taking ineffective anti-malarial prophylaxes. Thus asking about type of anti-malarial taken and compliance is extremely important.

Clinical features

Symptoms

The clinical features may be preceded by non-specific symptoms such as

- malaise
- arthralgia (joint pain)
- myalgia (muscle pain)
- diarrhoea and
- nausea.

The classical presentation of malaria is:

1. The 'cold stage' associated with rigors (shaking).
2. The 'hot stage' where the patient becomes febrile, often

exceeding 40°C associated with nausea and vomiting.

3. The 'sweating' stage where the temperature returns to normal (3).

The fever is referred to as a 'swinging fever' and the duration between fevers may point to a certain type of malaria:

- *P. ovale*/*P. vivax* 38-42 hours between fevers ('tertian fever')
- *P. malariae* 62-66 hours between fevers ('quartan fever') (3).

This clinical presentation is due to red blood cell rupture and subsequent merozoite release into the circulation. However in *P. falciparum* the timing of fevers tends to be less periodic. Other features include

- headache
- abdominal pain and on rare occasions may suggest an "acute abdomen",
- vomiting (3)
- a dry cough. If this occurs then typhoid must be considered in the differential diagnosis.

Signs

Signs of malaria include:

- conjunctival pallor (a sign of anaemia)
- mild jaundice which is caused by haemolysis. *P. falciparum* may be associated with severe jaundice and is caused by liver damage
- splenomegaly (the spleen is palpable). It takes only a few days for the spleen to enlarge in an acute attack of malaria. However, there are many causes of anaemia, jaundice and splenomegaly
- hepatomegaly (liver enlargement).

Other more general signs are those that may suggest sepsis; and may include tachycardia (fast heart rate) with a bounding pulse, and tachypnoea (fast breathing rate) especially in children.

Chronic malaria

The persistence of malaria in the blood, especially in people who live in subtropical regions, leads to 'chronic

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malaria.' Symptoms may include attacks of 'acute malaria' interspersed with anaemia, weight loss or other infections (e.g. gastroenteritis). Chronic malaria can improve with the patient developing some immunity to the parasite or there may be other complications such as:

- Hyper-reactive malarial splenomegaly. This takes the form of massive splenomegaly causing anaemia, pancytopenia (low levels of red blood cells, white blood cells and platelets), secondary infection, fever and jaundice.
- Quartan malarial nephropathy. This is caused by *P. malariae* infection and malarial antigens are found in the renal glomerular basement membranes. It presents as a nephrotic syndrome which is a triad of:
 - low albumin levels (hypoalbuminaemia) (>3.5g/day) secondary to protein leaking from the kidney into the urine
 - high fat levels (hyperlipidaemia)
 - oedema.

Complicated malaria

This is characterised by high levels of parasitaemia (≥ 5 to 10 percent of RBCs affected) (4) and is mostly due to *P. falciparum*, although patients with complicated infection due to *P. vivax* have been reported. Those at greatest risk of severe disease are:

- non-immune individuals
- immunocompromised individuals
- children 6 to 36 months old
- pregnant women (1).

The pathogenesis of complicated malaria is due to capillary infarcts, leakage and organ dysfunction. Organ dysfunction may appear as:

- altered consciousness with or without seizures
- respiratory distress or acute respiratory distress syndrome (ARDS)
- circulatory collapse
- metabolic acidosis
- renal failure
- haemoglobinuria (when haemoglobin escapes into the urine turning it dark brown and giving the name 'black water fever')
- hepatic (liver) failure
- coagulopathy (blood clotting abnormalities) with or

without disseminated intravascular coagulation

- severe anaemia or massive intravascular haemolysis
- hypoglycaemia.

Poor prognostic markers include:

- impaired consciousness (the deeper the coma the graver the prognosis)
- convulsions >3 in 24 hours
- respiratory distress
- substantial bleeding
- shock
- renal impairment (creat >265 $\mu\text{mol/L}$)
- acidosis (bicarbonate <15 mmol/L)
- jaundice
- raised lactate >5 mmol/L
- hypoglycaemia
- parasitaemia >500,000 parasites/ mm^3 or >10,000 mature trophozoites and schizonts/ mm^3
- >5% neutrophils contain malaria pigment.

The combination of renal failure and jaundice carries a particularly grave prognosis (5).

Symptoms of malaria in children

Symptoms of malaria present differently in children and they may display:

- convulsions
- confusion and neurological impairment progressing to coma
- hypoglycaemia
- metabolic acidosis
- severe anaemia.

Jaundice, renal failure and lung complications are less frequently observed than in adults.

Malaria during pregnancy

Pregnant women are a high-risk population. However previous exposure (which can give partial immunity) may mean that patients remain asymptomatic, despite high concentrations of parasites in the placental microcirculation. Pregnant women with no previous exposure are prone to severe infection and are vulnerable to the complications of malaria (6).

Malaria in primigravid (first pregnancy) and secundigravid (second pregnancy) women puts them at higher risk of:

- foetal distress, premature labour and stillbirth
- low birth weight (average reduction 170 g in *P. falciparum*) (6).

HIV co-infection reduces birth weight further and increases morbidity and mortality associated with the malaria infection. Mothers with HIV may be immunosuppressed and therefore have higher parasite densities and develop more severe clinical disease. Post-partum they are at higher risk of anaemia (7).

Differential diagnosis

Viral illnesses can present with a variety of features including malaise, headache, myalgia and abdominal discomfort. Tachypnoea may indicate an acute respiratory tract infection in a child. A severe dry cough should alert the clinician to the possibility of typhoid or respiratory tract infection especially bacterial pneumonia, tuberculosis (TB) and *Pneumocystis jirovecii* (PCP) (formerly called *P. carinii*). However, the cough of PCP and TB is likely to have a longer history than that of malaria or typhoid. The headache, fever and vomiting associated with malaria can be misdiagnosed as meningitis or even an atypical pneumonia. However meningism (photophobia - avoiding bright lights- and neck stiffness) is not seen in malaria. Malaria is not associated with a rash, unless disseminated

intravascular coagulation (DIC) ensues and anyone with a fever and a rash should have viral haemorrhagic fever or leptospirosis considered in their differential diagnosis.

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