Clinical Manifestations of Complicated Malaria –
An Overview

Dharmeshkumar N Patel*, P Pradeep**, MM Surti*, SB Agarwal***

Abstract

Malaria remains today as it has been for centuries – a heavy burden on tropical countries like India. Resistance of mosquitoes to insecticide and increasing prevalence of chloroquine resistance has led to an increase in complicated malaria in different parts of India. Malaria, especially falciparum malaria, can cause various complications involving various systems of the body. Cerebral malaria, acute renal failure, black water fever, hypoglycaemia, adult respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), hypotension and shock are among the common manifestations of complicated malaria. Complicated malaria in pregnant women and in patients with HIV co-infection has increased morbidity and mortality. Peripheral blood smear (PBS) still remains the gold standard for the diagnosis of malaria. Antimalarial chemotherapy alongwith general supportive measures including meticulous fluid-electrolyte balance and exchange transfusion helps to decrease the morbidity and the mortality of complicated malaria.

Key words: Complicated malaria, Cerebral malaria, Peripheral blood smear.

Introduction

Malaria is one of the most important parasitic diseases of humans, affecting more than 1 billion people worldwide, causing more than 1 to 3 million deaths every year with prevalence in 103 countries. Four species of plasmodium cause nearly all malarial infections in man, being transmitted by the bite of female anopheles mosquito. These are P. vivax, P. falciparum, P. ovale, and P. malariae. About 1% of the patients with P. falciparum infections develop more severe manifestations culminating in failure of various organ systems. This is rare with P. vivax, P. ovale, and P. malariae. In areas of intense P. falciparum transmission, severe malaria never occurs in adults but is confined to infants and children (6 month to 3 years).

Definition of severe malaria by the working group of World Health Organisation.

One or more of the following criteria + the presence of asexual parasitaemia defines severe malaria.

Cerebral malaria/unarousable coma: Not attributable to any other cause in a patient with falciparum malaria. Coma should persist for at least 30 minutes after a generalised convulsion.

Severe anaemia: Normocytic normochromic anaemia with haematocrit < 15% or haemoglobin < 5 gm/dl in the presence of parasitaemia > 1,000/microl. If anaemia is microcytic/hypochromic – iron deficiency, thalassaemia, and haemoglobinopathy should be ruled out.

Renal failure: Urine output of < 400 ml/24 hrs in adults and < 12 ml/kg body weight in children.

No improvement with rehydration and a serum creatinine level > 3 mg/dl.

Pulmonary oedema/adult respiratory distress syndrome (ARDS)

Hypoglycaemia: Plasma glucose level of < 40 mg/dl (2.2 mmol / l).

Hypotension/shock: Systolic B.P. < 50 mmHg in children aged 1-5 years or < 80 mmHg in adults, with cold, clammy skin, or core/skin temperature difference of ≥ 10°C.

Bleeding/disseminated intravascular coagulation (DIC): Significant bleeding from gums, nose, and GIT and evidence of DIC.

Convulsion: Repeated generalised convulsions > 2 within 24 hrs, despite cooling.

Acidosis/acidaemia: Arterial pH < 7.25 or plasma bicarbonate level of < 15 mmol/l. Venous lactate level of > 15 mol/l.

* Senior Resident, ** Resident, *** Head, Department of Medicine, and Director, PG Studies and Research, B.J. Medical College and New Civil Hospital, Ahmedabad-16.
Manifests as laboured, deep breathing.

**Macrosopic haemoglobinuria** : Black, brown, or red urine not associated with effect of oxidant drugs and red blood cell enzyme defects (such as G6PD deficiency).

**Postmortem confirmation of diagnosis** : In fatal cases, a diagnosis of severe falciparum malaria can be confirmed by histological examination of needle necropsy of brain. In the grey matter, venules and capillaries are packed with RBCs containing mature schizonts and trophozoites.

**Other manifestations of severe malaria, which do not by themselves define the condition.**

**Impairment of consciousness** less marked than unarousable coma.

**Prostration and weakness** – Patient cannot sit or walk with no obvious neurological explanation.

**Hyperparasitaemia** : Parasitaemia > 10% indicates potentially dangerous infections irrespective of other features. > 5% parasitaemia is dangerous in non-immune individuals but well tolerated in semi-immune children.

**Jaundice** : Detected clinically/S. bilirubin concentration > 3 mg/dl.

**Hyperpyrexia** : Rectal temperature above 40° C (104° F) in adults and children.

**Pathology, pathophysiology, and clinical features of complicated malaria**

A. Cerebral malaria

**Pathology** 1,3,4

The brain is slightly swollen with petechial haemorrhages throughout the white matter; haemorrhages are unusual in the grey matter. Large haemorrhages, infarcts, and herniations are rare. Large amount of intra - and extra - erythrocytic pigments are also seen. There is no evidence of thrombosis or vasculitis. Accumulation of glial cells surrounding haemorrhagic foci in white matter is called Durck’s granuloma.

**Pathophysiology**

It is exactly not known, but proposed hypotheses are as following:

1. **Permeability hypothesis (Maegraith and Fletcher):** It suggests that a toxic substance released by the parasites increases the permeability of the blood brain barrier (BBB) resulting in cerebral edema, coma, and death.

   This hypothesis is less favoured because adults with cerebral malaria have normal CSF pressure and blood brain barrier shows normal permeability to albumin and no response to corticosteroid therapy. Imaging studies have also failed to show oedema. In severe malaria, there is a mild generalised increase in systemic vascular permeability. But increased intracranial tension (ICT) in cerebral malaria in children probably arises from increase in blood volume independent of permeability.

2. **Toxic/cytokine hypothesis** : A glycolipid material similar to bacterial endotoxin (not a toxin in the strict sense) is released on merozoite rupture. These products induce cytokine cascade from macrophage monocyte series and possibly endothelium, initially IL-1 and TNF alpha which then in turn induces IL-6 and IL-8. These are responsible for many of the signs and symptoms including paroxysms. There is positive correlation between cytokine levels and prognosis. TNF alpha conc. > 100 pg/ml of serum is highly associated with cerebral involvement and death.

3. **Mechanical hypothesis** : Apparent obstruction to the blood flow in the brain caused by parasitised erythrocytes might be the cause of coma and death in cerebral malaria.

The processes involved are:

**Sequestration** : This is central to pathophysiology of *falciparum* malaria. It is a process by which RBCs containing mature parasites adhere to microvascularule (cytoadherence) and disappear from the circulation. This occurs predominantly in the venules of vital organs, being greatest in brain – particularly in the white matter.

**Cytoadherence** : It is mediated by parasite derived protein called *Plasmodium falciparum* erythrocyte membrane protein I (PFEMP-I). This is anchored to the
surface of RBC through the membrane to the submembranous parasite derived histidine-rich protein (HRP), producing humps or knobs on the surface. These are the points of attachment to the vascular endothelium. In vivo cytoadherence may be modulated by spleen. Cytoadherence begins in the middle of the asexual life cycle. Pf EMP-I undergoes antigenic variation. Highly variable genes called “var” genes encode PfEMP-I.

Vascular endothelial ligands*: Most important is CD36. Binding is increased at low pH and high calcium concentration. ICAM1, thrombospondin, VCAM, ELAM, and E selectin are other ligands. ICAM1 is the major ligand in brain and CD36 in other organs. ICAM1 and E selectin are inducible, but only in brain. Chondroitin sulphate A expressed on placenta is responsible for infection in pregnant women.

Rosetting*: Binding of two or more uninfected RBCs to an infected RBC is called rosetting. Rosetting occurs in the middle of asexual life cycle. It is trypsin sensitive and inhibited by calcium chelators and certain heparin subfractions. All fresh isolates of P. falciparum cytoadhere but do not rosette. Species which do not sequester, do rosette. The force required to separate rosette is approximately 5 times greater than that required to separate cytoadherence. Rosetting is associated with cerebral malaria and cytoadherence with other vital organ dysfunctions. Rosetting encourages adherence. Rosetting ability is greater for blood groups A and B than blood group O. Rosetting may be inhibited by drugs like artemisinins and quinine (Artemisinin > Quinine).

Deformability*: As the parasite matures inside the RBC it becomes progressively more spherical and rigid.

Pathogenesis of coma
There is increase in cerebral anaerobic glycolysis. Cerebral blood flow is inappropriately low for arterial oxygen content and increase in CSF lactate concentration. These interfere with neurotransmission. Nitric Oxide is a potent inhibitor of neurotransmission. Raised ICT is not the cause for coma.

Clinical features*:
It is a symmetric encephalopathy characterised by unarousable coma of > 30 minutes with a Glasgow coma scale (GCS) < 7/15 or in children Blantyre coma scale < 2/5, with evidence of acute falciparum infection (asexual form in peripheral blood smear).

Onset of coma may be sudden following a seizure, or it could be gradual – with drowsiness, confusion, disorientation, delirium, or agitation. A seizure could be generalised or focal. Length of prodrome is several days in adults and in children it could be as short as 6-12 hrs. The average duration of coma in adults is 2-3 days. Sinus tachycardia, low normal B.P., and intermittent goose pimples are common. Anaemia, jaundice, and bleeding (< 5%) can occur. Sustained hyperventilation indicates either metabolic acidosis, pulmonary oedema, or pneumonia. Focal signs are unusual. Decorticate/decerebrate rigidity and opisthotonus are possible. Cranial nerve abnormalities are rare. Gaze is usually normal or divergent with the pupils mid-size and reacting. There is no evidence of extra-ocular muscle paralysis. Tone and deep tendon reflexes (DTR) are normal, increased, or decreased. Corneal reflex is preserved, except in deep coma. Abdominal reflexes are invariably absent. Cremasteric reflex is often preserved. Extensor plantar response occurs in half of the patients. Bruxism, brisk jaw jerk, and pout reflex can be there. Other release signs are unusual. Some passive resistance to head flexion may be detected, but signs of meningeal irritation are lacking. Papilloedema occurs in < 1% and flame shaped retinal haemorrhages occurs in < 15%.

Liver and spleen are enlarged and soft. Untreated cerebral malaria is uniformly fatal.

Sequelae
Complete recovery occurs in 50% cases, partial recovery occurs in 25%, and no recovery in 25%.

Rarely, adults (< 3%) and children (> 10%) suffer from sequelae. Psychosis (paranoid, mania, hallucination, and delusion) was the commonest sequelae in some series. Hemiplegia, cerebral palsy, cortical blindness/deafness, impaired cognition and learning have been reported. Hemiparesis due to P. vivax has been reported. Rare cases of Gullain-Barre syndrome (GBS) and cerebellar ataxia have also been observed.
Extra-pyramidal symptoms (chorea, athetosis, tremors, and rigidity), trismus, peripheral neuropathy, isolated 6th nerve palsy, and foot drop have been reported. Occasionally other cranial nerve palsies occurs.

Ocular bobbing, nystagmus (vertical and horizontal), and sudden blindness due to vitreous haemorrhage have been observed.

Subarachnoid haemorrhage due to DIC and myelitedes – resembling amyotrophic lateral sclerosis (ALS) and tabes dorsalis like syndrome, and combined disseminated encephalomyelitis have also been reported.

**Post-malaria neurological syndrome (PMNS)**

Criteria: Recent symptomatic malarial infection with parasites cleared off from blood and development of neurological and psychiatric symptoms within 2 months after acute illness. Clinical features include generalised convulsion, delayed cerebellar ataxia, psychosis, and tremors.

**Eye changes**

Involvement of almost every part of eye and its adnexa which includes keratitis, uveitis, retinitis pigmentosa, optic neuritis, ocular muscle paresis, subconjunctival haemorrhage, papilloedema, retinal oedema, retinal haemorrhage, etc., have been described in patients of malaria.

**B. Acute renal failure (ARF)**

The kidneys are often slightly swollen. Tubular abnormalities consistent with acute tubular necrosis (ATN) are seen. Sequestration in glomerular capillaries, mesangial endothelial cell proliferation, and immunoglobulin deposits may be seen. Cortical necrosis never occurs. When there is fulminant presentation of ARF with oliguria, there is high incidence of hepatic dysfunction (jaundice and bleeding tendency), metabolic acidosis, and pulmonary edema. Blood pressure is usually normal. Mild proteinuria may be there but urinary sediments are unremarkable.

In subacute presentation with oligura/polyuria, serum creatinine rises over a period of days producing uraemic complications requiring dialysis or there is a gradual resolution. In survivors, urine flow resumes in 4 days. Creatinine returns to normal in 7 days. In certain studies, 30% of ARF was due to malaria. Renal failure may be associated with haemoglobinurina (Black water fever). Nephrotic syndrome can occur with *P. falciparum*.

**C. Black water fever**

It was previously described as a disease to “blanch the cheek of the bravest”. Earlier, mortality was high (20% to 30%). Presently, mortality is much lower. Passage of black or dark brown or red urine is often not associated with significant renal impairment. It is usually transient, and resolves without complications. In severe cases ATN develops from massive haemolysis. Transfused blood is also rapidly haemolysed where plasma may also be red. The patient often has a slate grey appearance. Patients with G6PD deficiency may develop haemoglobinuria precipitated by primaquine. In high transmission areas, ARF is very rare.

**D. Metabolic acidosis**

This may result form renal failure, but more commonly there is a primary lactic acidosis (Type B). Arterial, venous, capillary, and CSF concentration of lactate increases in proportion to the severity. Lactic acidosis results from:

1. Anaerobic glycolysis due to microvascular obstruction.
2. Failure of hepatic and renal lactate clearance.
3. Production of lactate by the parasite.

Lactate levels rise after generalised convulsions. There is accompanying hyperalanninaemia due to impairment of gluconeogenesis. Triglyceride and fatty acid levels also rise. Ketone bodies increase due to decreased food intake.

Hyperventilation (Kussmaul breathing) with a clear chest on auscultation suggests metabolic acidosis. It is a sign of poor prognosis, often followed by respiratory and circulatory failure and respiratory arrest.
Venous lactate concentration at 4 hours after admission to hospital is the BEST PROGNOSTIC INDICATOR in severe malaria.

**E. Hypoglycaemia**

It is due to:

1. Increased peripheral requirement of glucose consequent upon anaerobic glycolysis.
2. Increased metabolic demands of febrile illness.
3. Obligatory demand of parasites.
4. Failure of hepatic gluconeogenesis and glycogenolysis (parasites consume up to 70 times as much glucose as uninfected cells).
5. Quinine stimulated insulin secretion from pancreatic beta cells. Hyperinsulinaemia is balanced by decreased tissue sensitivity.

Hypoglycaemia occurs in 8% of adults and 30% of children (particularly problematic in pregnant women and children). Usual signs of increased sympathetic activity like flushing and sweating are absent. Hypoglycaemia contributes to nervous system dysfunction.

‘Malaria induced hypoglycaemia’ is often present at admission and response to glucose is unimpressive, while ‘quinine induced hypoglycaemia’ usually develops 24 hours after treatment, and response to glucose administration is dramatic.

Hypoglycaemia is a sign of poor prognosis with a mortality rate as high as 40%.

**F. Pulmonary oedema/adult respiratory distress syndrome (ARDS)**

Despite intense sequestrations, the heart remains remarkably normal, though, in anaemic patients the heart may become dilated. Cardiac function is remarkably well preserved in severe malaria. Pulmonary oedema results from increase in pulmonary vascular permeability which is not reflected in other vascular beds. Cause of increased permeability is not known.

Pulmonary oedema/ARDS can develop at any time in falciparum malaria, even after several days of antimalarial treatment, and even in otherwise uncomplicated vivax malaria. It is particularly common in pregnant women, but rare in children. It may be difficult to distinguish from aspiration pneumonia. Heart sounds, pulmonary capillary wedge pressure (PCWP), and central venous pressure (CVP) are usually normal. The chest X-ray shows increased interstitial shadowing. It has a mortality rate of > 85%.

**G. Hypotension/shock**

Systolic BP < 50 mmHg in children and < 80 mmHg in adults defines hypotension/shock. Patient with severe malaria can develop sudden hypotension and become shocked. This is called “Algid Malaria”. The patient can have cold, clammy, cyanotic skin, peripheral vasoconstriction, and rapid feeble pulse with core/skin temperature difference of ≥ 10° C. In some cases there is septicaemia. In the majority, blood cultures are negative.

Hypotension usually responds to saline infusions and inotropes, but these therapeutic measures could provoke pulmonary oedema. The overall mortality is high. Circulatory collapse can also be seen in patients with pulmonary oedema, metabolic acidosis, GI haemorrhage, and ruptured spleen. Dehydration and hypovolaemia could also contribute to hypotension/shock.

**H. Anaemia**

**Pathology**

**Bone marrow**: Dyserythropoietic changes are prominent. Macrophages contain pigment and erythrophagocytosis may be seen. Iron is usually in plenty. Platelets and WBCs are usually normal.

**Spleen**: Often dark from malarial pigment, enlarged, soft and friable. There is reticular hyperplasia. Recurrent malaria is associated with hard, fibrous splenic enlargement.

**Pathogenesis**: It is multifactorial:

1. Obligatory destruction of RBCs containing parasites at merogony.
2. Accelerated destruction of non-parasitised RBCs,
parallels disease severity.


4. Lowered threshold for splenic clearance of abnormal erythrocytes. Red blood cell survival is decreased.

5. Decreased concentrations of IL-10 and increased concentration of TNF alpha. IL-10 has inhibitory effect on TNF alpha which contribute to bone marrow suppression and RBCs destruction.

The role of antibodies (Coomb's positive) in anaemia is unresolved.

The degree of anaemia and the rate at which it develops vary enormously. Haemoglobin may fall upto 2 gm/dl every day. It is a serious problem in children in whom sudden death can occur particularly at Hb < 4 gm/dl.

Haptoglobin is a marker of haemolysis. Haptoglobinaemia may be considered as a useful indicator of falciparum malaria.

I. Coagulopathy and thrombocytopenia

Severe haemorrhage is seen in 5% of severe malaria.

There is accelerated coagulation cascade activity with accelerated fibrinogen turnover, consumption of antithrombin III, and increased concentration of fibrinogen degradation products (FDP). RBCs containing parasites and released cytokines are procoagulant. Prothrombin time (PT) and activated partial prothrombin time are prolonged.

Thrombocytopenia is caused by increased splenic clearance. Platelet turnover is increased. Role of platelet bound antibody is controversial.

The patient may develop bleeding gums, epistaxis, petechiae, subconjunctival haemorrhages. Significant bleeding, malena, and haemetemesis occurs in < 10% cases. This is more common in non-immune individuals in the temperate zone.

J. Jaundice

Pathology

Liver is enlarged and black due to malarial pigment. There is congestion of centrilobular capillaries with sinusoidal dilatation and Kupffer cell hyperplasia. Sometimes centrizonal necrosis is seen.

Pathophysiology

Hyperbilirubinaemia results from the following factors:

1. Intravascular haemolysis of parasitised erythrocytes.
2. Hepatic dysfunction.
3. Microangiopathic haemolysis associated with DIC.
4. Liver function impairment due to associated septicaemia.
5. Concomitant viral hepatitis.

Jaundice appears to have haemolytic, cholestatic, and hepatic components. Cholestatic component may persist well into the recovery period. Fulminant liver failure is unusual. But death due to hepatic coma and serum bilirubin levels upto 25 mg/dl have been observed more common in adults than children. Jaundice and hepatic dysfunction are important determinants of mortality in cerebral malaria.

K. Hyperpyrexia

It is defined as rectal temperature > 40° C (104° F) in adults and children. High fever (39-40° C) is especially common in children and may contribute to convulsion and altered consciousness. There is evidence that high body temperature in pregnant women contributes to foetal distress. Sustained, very high body temperature of 42° C and above, which may cause permanent severe neurological sequelae, are rarely seen in malaria. The expectation that P. falciparum malaria should have a tertian fever pattern may lead to the diagnosis of malaria being missed.

L. Hyperparasitaemia

It is defined as a parasitaemia of > 5% (> 250,000 parasites/microl) in peripheral blood smear in non-immune individuals. A parasitaemia of > 10%
indicates potentially dangerous infection, irrespective of other factors. But in endemic areas, partially immune children can tolerate high degree of parasitaemia up to 20% - 30% without clinical symptoms.

M. Other acute complications

1. Fluid and electrolyte changes.
   Total body water and extra-cellular fluid (ECF) volume are usually normal. Renin – aldosterone – ADH concentrations increase to maintain adequate circulatory volume in presence of generalised vasodilatation and falling haematocrit.

2. Gastrointestinal dysfunction
   Minor stress ulcerations of stomach and duodenum are common. There is decreased splanchnic perfusion resulting from both, gut sequestration and visceral venoconstriction. There may be increased gut permeability and decreased local defences.

3. Endocrine change
   Pituitary thyroid axis abnormalities results in the sick euthyroid syndrome. Parathyroid dysfunction can occur. Mild hypocalcaemia is common. Pituitary adrenal axis appears normal.

4. Bacterial infections
   Patients are prone to bacterial infections particularly of lungs and urinary tract. Post-partum sepsis and spontaneous gram-neg fishemia, Salmonella bacteraemia, and aspiration pneumonia following convulsions can occur.

Poor prognostic indicators

1. Clinical
   Age < 3 years
   Deep coma
   Witnessed or reported convulsions
   Absent corneal reflexes
   Decerebrate/decorticate rigidity or opisthotonus
   Clinical signs of organ dysfunction (e.g., renal failure, pulmonary oedema)

   Respiratory distress (acidosis)
   Circulatory collapse
   Papilloedema and/or retinal oedema

II. Laboratory indicators

   Hyperparasitaemia (> 250,000/microl or > 5%)
   Peripheral schizontaenemia
   Polymorphonuclear leukocytosis
   Mature pigmented parasites (> 20% of parasites)
   Peripheral blood polymorphonuclear leukocytes with visible malarial pigment (> 5%)
   Haemoglobin < 5 gm%
   Packed cell volume (PCV) < 15%
   Blood glucose < 40 mg/dl (2.2 mmol/l)
   Blood urea > 60 mg/dl
   Serum creatinine > 3 mg/dl
   High CSF lactic acid (> 6 mmol/l) and low CSF glucose
   Raised venous lactic acid (> 5 mmol/l)
   More than 3-fold elevations of serum enzymes (Aminotransferases)
   Increased plasma 5' nucleotidases
   Low antithrombin III level
   Very high TNF alpha level

Chronic complications of malaria

A. Hyperreactive malarial splenomegaly (Tropical splenomegaly)

   It occurs when transmission is intense and has been reported throughout tropics. Genetic factors undoubtedly play a role.

Pathology

Gross splenomegaly with normal architecture. This leads to hypersplenism. There is polyclonal hypergammaglobulinaemia with high serum IgM. High titres of malarial antibodies and auto-antibodies are also usually present.

Clinical features

Abdominal swelling and dragging sensation in the abdomen is usually found. The huge spleen is vulnerable
to trauma. Pain due to splenic infarction can occur. Liver is also enlarged. There is pancytopenia and increased susceptibility to infection. Peripheral smear is usually negative for parasites.

**Treatment**

Size of spleen and liver regresses with antimalarial treatment. Treatment is required for the period of malarial exposure. Splenectomy is recommended in severe hypersplenism and treatment failure, i.e., when treatment has been given for 6 months.

**B. Quartan nephropathy:**

Nephrotic syndrome with albuminuria, hypoalbuminaemia, and variable renal impairment is common in tropics. Repeated or continuous *P. malariae* infection is associated with childhood nephrotic syndrome. Evidence of other species of malaria causing glomerulonephritis is less convincing.

**Pathology**

It is a chronic immune-complex nephropathy, focal or segmental. Thickening of the subendothelial aspect of the basement membrane giving rise to a double contour of argyrophilic fibrils. Capillary lumen becomes narrowed and obliterated.

Immunofluorescence study shows IgG, M, and C3 (in 2/3rd cases). Coarse granular pattern of IgG3 is more common than fine granular or linear staining of IgG1.

Severity of nephropathy is graded from I to III:
- Grade I – < 30% glomeruli involved.
- Grade II – 30-70% glomeruli involved with tubular atrophy.
- Grade III – >75% of glomeruli involved with extensive tubular pathology.

**Clinical features**

The pattern varies from asymptomatic proteinuria to full blown nephrotic syndrome:
- Fever, anaemia, hepatosplenomegaly are common.
- Haematuria and red cell casts are rare.
- It usually progresses inexorably to renal failure over 3 to 5 years.
- Spontaneous remission is rare. Some cases respond to cytotoxics, but antimalarials and corticosteroids do not prevent progression.

**C. Burkitt’s lymphoma**

There is a strong association between Burkitt’s lymphoma and malaria. Progression of EBV (Epstein-Barr virus) infection in B lymphocytes is controlled by virus specific cytotoxic T cells. This response is significantly decreased during malarial infection. This may predispose to malignant transformation.

**Malaria in special situations**

1. **Pregnancy**

Pregnant women in 2nd and 3rd trimester are likely to develop severe malaria, complicated by pulmonary oedema and hypoglycaemia. There is probably suppression of systemic and placental cell-mediated immune response. Sequestration of infected RBCs in placenta leads to maternal anaemia and placental insufficiency, leading to retarded foetal growth and still birth.

**Pathology**

Placenta may be black with trophoblastic thickening, macrophage infiltration, and perivillous fibrin deposition.

**Clinical features**

Premature labour and foetal death are common. Severe malaria can also present immediately following delivery. Postpartum bacterial infection is a common complication. Falciparum malaria can cause severe mid-trimester haemolysis. Congenital malaria occurs in < 5% of newborns and is related directly to parasite density in maternal blood and placenta.

2. **HIV**

There are different thoughts regarding the relationship between malaria and HIV. There are even reports that HIV 1 viral burden is higher in patients with *P. falciparum* malaria than in controls and this viral burden can, in some patients, be partly reduced with antimalarial therapy. Studies in Uganda showed that
HIV 1 infection is associated with an increased frequency of clinical malaria and parasitaemia. Lower CD4+ counts were associated with higher parasite densities.

Maternal HIV infection predisposes pregnant women to a higher prevalence of malaria and parasite density and predisposes their newborn to congenital malarial infection and low birth weight. It is found that placental malarial infection and maternal HIV infection increase post-neonatal mortality beyond the independent risk associated with exposure to either of them.

Conclusion

Complicated malaria is more commonly caused by *P. falciparum* and it is rarely caused by other malarial parasites. Timely clinical and laboratory diagnosis with meticulous treatment including supportive measures and specific antimalarial chemotherapy helps to lessen immediate mortality and long term morbidity.

References