INTRODUCTION
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Malaria is one of the oldest recorded disease in the world in 18th century. Italy people associated malaria with "bad air"- Mal-aria. Even though it has a world wide distribution, yet it is one of the main cause of morbidity and mortality in tropical countries.

In 1950's malaria was India's number one health problem. The Government launched national Malaria control programme in 1953 to reduce the incidence of malaria in the country. From 75 Million cases in 1952, the incidence of malaria had been brought down to 2 million in 1958. Encouraged by these results, the programme was upgraded to national malaria eradication programme in 1958.

With the successful implementation of N.M.E.P., the annual incidence of malaria further declined to an all time low of 5000 cases in 1961. These successes were short lived and soon hailed by set back due to resurgence of malaria.

Malaria in man caused by four distinct species of malaria parasite, viz. Plasmodium vivax, P. falciparum, P. malariae and P. ovale. Man is the intermediate host. In the life cycle of plasmodium, asexual reproduction occurs in humans and sexual reproduction occurs in the mosquito.

Malaria is transmitted by the bites of infected female anopheline mosquitoes or by inoculation of infected blood (e.g. transfusion malaria, congenital malaria). The infective stage, called

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sporozoites, are injected from the mosquito salivary glands into subcutaneous capillaries and circulate to the liver, where they invade hepatic parenchymal cells. Here the parasites multiply in stages called exoerythrocytic (Ei) forms and become hepatic schizonts. After 1-2 weeks of development, the hepatic schizonts rupture and each releases thousands of merozoites, which enter the circulation and invade erythrocytes. In *P. falciparum* and *P. malariae*, all Ei forms rupture more or less at the same time and none persists chronically in the liver. In contrast, EE forms in *P. vivax* and *P. ovale* exists in two types: the primary EE forms that develop and rupture within weeks after infection, and the latent Ei forms (also called hypnozoites) that may remain in the liver for months or years before they rupture, resulting in relapses of erythrocytic infection. Once the parasites enter the erythrocytic stage, they never reinvade the liver. Therefore, transfusion malaria never results in development of EE forms.

*P. vivax* as a rule causes uncomplicated malaria. *P. falciparum* causes the most serious form of the disease. Infection with this parasite is often fatal in the absence of prompt recognition and treatment and may include cerebral malaria, severe anaemia, renal failure, generalized convulsions, hypoglycaemia, fluid and electrolyte imbalance, pulmonary oedema, circulatory collapse and shock (algid malaria), spontaneous bleeding due to disseminated intravascular coagulation, hyper-pyrexia, hyperparasitaemia and malarial hemoglobinuria.
Renal function disturbances may be from mild-to-severe like oliguria (.5ml/-kg/-hour) anuria, proteinuria electrolyte imbalance etc. ARF was defined using WHO criteria - Urine output <400ml/24 hours in adult failing to improve after adequate hydration associated with serum creatinine of >3mg%.

Renal and renal-related disorders commonly occur in infection with plamodium falciparum, which can cause fluid and electrolyte disorders, glomerulonephritis, and acute renal failure (ARF). It appears that ARF and other life-threatening complications in falciparum malaria are not directly caused by the parasite itself but are the result of interaction of mechanical, immunological, and humoral components.

The pathophysiology of falciparum malaria is therefore the interaction of parasitized erythrocytes, cytokines, mediators, humoral factors and an acute-phase response.

Parasitized Erythrocytes:

P. falciparum in blood forms play a central role. Erythrocyte entry of merozoite occurs through the glycoprotien receptor on the RBC membranes. The knobs expressed on the surface of parasitized RBCs can adhere to the vascular endothelium, resulting in cytoadherence. The number of knobs increases as the parasite matures. The parasitized RBCs can also adhere to both parasitized and non parasitized erythrocytes, resulting in formation of rosettes. The endothelial cytofolds might enhance erythrocytes trapping. Tumor necrosis factor (TNF), a monocyte-
immunologic reactions. RBC debris and their free products can cause deleterious effects on the kidney. These include vasoconstriction, renal tubular toxicity, and activation of intravascular coagulation.

Parasite Antigens:

Circulating malarial antigens could trigger a cascade of immune reactions, including direct monocyte and complement activation and an HLA-restricted specific immune response. Massive monocyte activation is a crucial component of the syndrome. Endotoxin in malaria may be derived from the patient's gut. Vascular stasis in the gut in the failure of hepatic clearance of the absorbed endotoxin from the gastrointestinal tract may be the cause of endotoxemia. It is generally felt that malarial parasites have no endotoxin. However, it has recently been shown that glycosylphosphatidylinositol (GPI) moieties covalently linked to the surface antigens of malarial parasites act like endotoxin. GPI moieties are glycolipid substances that in free from or in association with protein can induce TNF and interleukin-1 production by microphages. GPI is capable of eliciting antibody production from primed B cells alone without requirement for cognate T-cell help.

Cytokines:

There is elevation of cytokines in malaria. A number of cytokines, especially TNF, IL-1, IL-6, IL-8 and IFN-\(\gamma\), play a very important role in the acute phase reaction, expression of adhesion molecules, and plasma leakage from the intravascular compartment. These
cytokines and vasoactive mediators have profound effects on systemic and renal hemodynamics, which is crucial in causing renal function changes. Positive correlation between the plasma levels of cytokines and the severity of malaria including renal failure has been observed because of the short half-life of cytokines, the time in release and the local biological effects at the site of production may not correlate with the severity of disease. The higher sCD14 level in parents with renal failure is also detected.

CD14 is a marker on human monocytes and serves as a receptor for GPI and endotoxin. sCD14 is spontaneously released by monocytes, macrophage and granulocytes. After release, sCD14 circulate in the blood steam. Elevated levels of sCD14 are another marker in the inflammatory response in complicated malaria.

**Humoral Factors:**

These include hypercatecholaminemia, increased levels of circulating plasma renin activity, inappropriate secretion of antiuretic hormone and hyperinsulinemia in quinine-treated patients.

Early renal vasconstriction is mediated through catecholamiine induced by sympathetic stimulation and stimulation of the adrenal gland by kinin. Besides the vasoconstriction effect, catecholamines, either alone or in combination with kinin increase vascular permeability, leading to hypovolemia, which further compromises the renal blood flow. *Plasma renin activity is increased*
in malaria ARF. A significant amount of nitric oxide produced in malaria. Despite its beneficial vasodilating and protective immune effects, its combination with superoxide generates peroxynitrite which causes renal damage.

**Acute-Phase Response and Nonspecific Factors:**

In response to infection, the liver releases, through TNF, IL-1 and IL-6 stimulation, a variety of proteins, including C-reactive protein, haptoglobin, protease inhibitors, fibrinogen and serum amyloid protein. The increased level of acute phase protein and fibrinogen in malaria cause increased plasma viscosity and rouleaux formation of erythrocytes. *Parasitized erythrocytes increased erythrocyte viscosity, blood viscosity is therefore increased.* By Poiseuille's law, the renal blood flow would be compromised.

Several non-specific features in malaria can either compromise in renal blood flow or cause renal injury. High fever can activate complements and cause free oxygen radical release, leading to renal injury. Intravascular hemolysis, intravascular coagulation and rhabdomyolysis can decrease renal blood flow. *Severe cholestatic jaundice in malaria can also compromise renal function.*

**Hemodynamics:**

Hemodynamics deterioration is the final result and in severe infection may be sufficient to lead to ARF. Although hemodynamic alterations and hormonal changes in falciparum malaria re-
semble those in sepsis, the role of cytoadherence and hemorrhheologic aberration in the later is less than in malaria. Renal hemodynamics would be less compromised in sepsis than in malaria.

Bundelkhand region is an endemic zone for malaria infection. So it is very important to study the clinical profile of this disease in this region which would help us to know the consequences of this disease and will also serve as a reference for further studies.