

Severe health effect of malaria and its treatment.

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ABSTRACT:-

Plasmodium falciparum hyperparasitemia (over or equal to 10%), isolated or associated with severity criteria, should be managed in paediatric intensive care unit according to the French paediatric guideline. The main objective of our study was to describe the management and course of these special cases. Malaria represents a medical emergency because it may rapidly progress to complication and death without prompt and appropriate treatment. Severe malaria is almost exclusively caused in human by five species of single celled eukaryotic plasmodium parasite (mainly *Plasmodium falciparum* and *Plasmodium vivax*) that are transmitted by the bite of *Anopheles* spp. mosquitoes. Malaria remains one of the most serious infectious diseases. The incidence of imported malaria is increasing and the case fatality rate remains high despite progress in intensive care and anti-malarial treatment. Clinical deterioration usually appears 3-7 days after onset of fever. Complications involve the nervous, respiratory, renal and hematopoietic systems. Metabolic acidosis and hypoglycaemia are common systemic complications. Intravenous quinine and quinidine are the most widely used drugs in the initial treatment of severe *falciparum* malaria, whereas artemisinin derivatives are correctly recommended for quinine resistant cases. As soon as the patient is clinically stable and able to swallow, oral treatment should be given. The intramuscular volume should be maintained at the lowest level sufficient for adequate systemic perfusion to prevent development of acute respiratory distress syndrome. Renal replacement therapy should be initiated early. Exchange blood transfusion had been suggested for the treatment of patients with severe malaria and high parasitemia. For early diagnosis, it is paramount to consider malaria in every febrile patient with a history of travel in an area endemic for malaria.

KEYWORDS: *Plasmodium falciparum*, severe malaria, treatment.

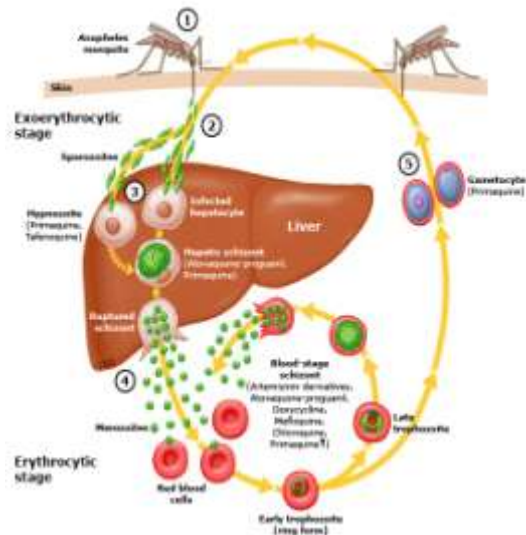
contact malaria each year, resulting in 1.5-2.7M deaths annually. Because of the increasing global travel to and immigration of people from areas endemic for malaria, the incidence of imported cases of malaria in developed countries has risen. Approximately 10,000-30,000 travellers from industrialized countries are expected to contact with malaria each year. Malaria is a life-threatening disease. The positive agent of malaria is a small protozoan belonging to the group of plasmodium species and it consists of several sub-species. The genus plasmodium is an amoeboid intracellular parasite which accumulates malarial pigment (an insoluble metabolite of haemoglobin). Parasites on different vertebrates; some in red blood cells, and some in tissue of the 172 of plasmodium species, 5 species can infect humans. These are:

- 1) *P. Malaria*
- 2) *P. Falciparum*
- 3) *P. vivax*
- 4) *P. ovale*
- 5) *P. Knowles*.

In South East Asia, zoonotic malaria *P. Knowles* is recorded. Other species rarely infect humans. All the mentioned plasmodium species caused the disease commonly known as malaria. Likewise, all species have similar morphology and biology. Plasmodium life cycle is very complex and takes place in two phases; sexual and asexual, the vector mosquito and vertebrate host. In the vector, mosquito, the sexual phase of the parasite life cycle occurs. The asexual phase of the life cycle occurs in humans, the intermediate host for malaria. Human malaria is transmitted only by female mosquitoes of the genus *Anopheles*. The parasite, in the form of sporozoite, after a bite by an infected female mosquito, enters the human blood and after half an hour of blood circulation, enters the hepatocytes. The first phase of plasmodium asexual development occurs in the hepatocytes, and then in the erythrocytes. All plasmodium species lead to the structure of erythrocytes. The most common species in the Americas and Europe are *P. vivax* and *P. malaria*, while in Africa it is *P. falciparum*.

I. INTRODUCTION:-

Malaria remains a devastating global health problem. Worldwide, and estimated 300-500M



The natural history of malaria involve cyclic infection of humans and females anopheles mosquitoes in humans. The parasites grow and multiply first in the liver and cell and then in the red cells of blood successive broods of parasites grow inside the red cells and destroy them, realising daughter parasites that continue the cycle by invading others red cells. The blood stage parasites are those that cause the symptoms of malaria. When certain forms of blood stage parasites (gametocytes, which occur in male and female forms) are ingested during blood feeding by a female anopheles mosquito, they made in the gut of the mosquito and begin a cycle of growth and multiplication in the mosquito. After 10 to 18 days forms of the parasite called a sporozoites migrates to the mosquito salivary glands. When the anopheles mosquito takes a blood meal on another human, anticoagulant saliva is injected together with the sporozoites, which migrate to the liver, there by the beginning of new cycle. Thus the infected mosquito carries the disease from one human to another (acting as a “vector”) while infected human transmit the parasite to the mosquito, in contrast to the human host, the mosquito vector does not suffer from the presence of parasites. The malaria parasite life cycle involve two host. During a blood mean, a malaria infected female anopheles mosquito inoculates sporozoites into the human host. Sporozoites infect liver cells and mature into schizonts, which rupture and release merozoites. (Of note, in *P. vivax* and *P. ovale* a dormant stage can persist in the liver and cause relapses by invading the bloodstream weeks, or even years later.) After this initial replications in the liver (exo-erythrocytic schizogony) the parasites undergo

asexual multiplication in the erythrocytes (erythrocyte schizogony). Merozoites infect red blood cells. The ring stage trophozoites mature into schizonts, which rupture releasing merozoites. Some parasites differentiate into sexual erythrocytic stages (gametocytes). Blood stage parasites are responsible for the clinical manifestations of the disease. The gametocytes, male and female are ingested by an anopheles mosquito during a blood meal. The parasites’ multiplication in the mosquito is known as the sporogonic cycle. While in the mosquito stomach, the microgametes penetrate the macrogametes generating zygotes. The zygotes turn become motile and elongated which invade the midgut wall of the mosquito where they develop into oocytes. The oocytes grow, rupture, and release sporozoites, which make their way to the mosquito salivary glands. Inoculation of the sporozoites into a new human host perpetuates the malaria life cycle. The malaria parasite develops both in humans and in the female anopheles mosquitoes. The side and genetic complexity of parasite mean that is infection presents thousands of antigens (proteins) to the human immune system. The parasites also changes through several life stage even while in the human host, presenting different antigens at different stages of its life cycle. Understanding which of these can be useful target for vaccine development has been complicated. In addition, the parasite has develop a series of strategies that allow it to confuse, hide, and misdirect the human immune system.

PRE-PATIENT AND INCUBATION PERIODS:- In non-immune individuals with *P. falciparum* infection, the median pre-patient period is 10 days (range 5-10 days), and the median incubation periods (time from sporozoites inoculation to development of systems) is 11 days (range 6-14 days). Non falciparum malaria the incubation periods is usually longer (median 15-16 days), and both *P. vivax* and *P. ovale* malaria may relapse month or year after exposure due to the presence of hypnozoites in the liver. The longest reported incubation period for *P. vivax* is 30 years.

SIGN AND SYMPTOMS OF MALARIA:- The symptom of disease may occur within 1 to 3 weeks after being infected. There 4 species of the plasmodium parasite that can infect the female anopheles mosquito and cause malaria in humans. A malaria patient is likely to suffer from many, if not all, of the symptoms mentioned below:

- Abdominal pain
- Chills and sweats
- Diarrhea, vomiting

- Headache
- High fever
- Low blood pressure
- Muscle aches
- Jaundice
- Dry cough
- Fatigue

In patient infected with the *P. falciparum* parasite, the following symptoms may also occurs:

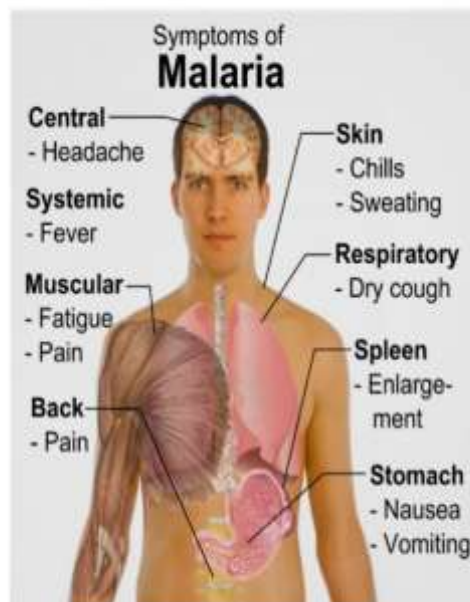
- Anaemia caused by the destruction of infected red blood cells.
- Kidney failure
- Anaemia
- Muscle pain

SEVERE MALARIA: - Almost all severe forms and deaths from malaria are caused by *Falciparum*. Rarely, *P.vivax* or *P. falciparum* produce serious complication, debilitating relapses, and even death. In 1990, the world health organization established criteria for severe malaria in order to assist future clinical and epidemiology studies. In 2000, the WHO revised these criteria for severe to include other clinical manifestation and laboratory values that portend a poor prognosis based on clinical experience in semi-immune patient. The major complication of severe malaria include cerebral malaria, abnormal behaviour, and impairment of consciousness, seizures, coma, or other neurologic abnormalities.

in various studies risk factor for severe malaria and death include age greater than 65 years, female sex, non-immune status, coexisting medical condition, no anti-malarial prophylaxis, delay in treatment, and severity of the illness at admission. In tropical countries with a high transmission of malaria, severe malaria is predominantly a disease of young children (1 month to 5 years of age). In industrialized countries, most life-threatening complication occur in non-immune travels returning from endemic.

Severe malaria accounts for approximately 5% of imported malaria cases. The cases fatality rate in returning travellers with *falciparum* malaria varies from 0.65% to 3.8%.

SING AND SYMPTOMS OF MALARIA.



COMPLICATION IN PATIENT WITH SEVERE MALARIA:-

patient with severe malaria should be treated in an ICU. Should clinical deterioration to severe malaria occurs, it usually develops 3-7 days after fever onset, although there have been rare reports of non-immune patient dying within 24 hours of developing symptoms. Severe malaria may develop even after initial treatment response and complete clearance of parasitemia due to delay cytokine release. In many patient several of these complication exist together or evolve in rapid succession within a few hours. In clinical practice, patient must be assessed for any of these signs or symptoms that suggest an increased risk for developing and complication and must be treated immediately. In various studies risk factor for severe malaria and death include age greater than 65 years, female sex non-immune status, coexisting medical condition, no antimalarial prophylaxis, delay in treatment, and severity of illness at admission. All cases of malaria are potentially severe and life threatening, especially when managed inappropriately. A major reason for progression from mild through complicated to severe disease is the parenteral administration of adequate, safe doses of an appropriate antimalarial, in the setting of the highest possible level of clinical care. Supportive management of complication such as coma, convulsion, metabolic acidosis, the most recent advance in antimalarial chemotherapy has been the use of artemisinin derivatives especially intravenous articulate, which may well revolutionize the

management of severe disease. Outside antimalarial therapy, mechanical ventilation and renal replacement have also played an important role in reducing mortality of this life-threatening condition.

DIAGNOSIS OF MALARIA:-light microscopy of thick and thin stained blood smears remains the Standard method for diagnosis malaria. Thick smears are 20-40 times more sensitive than thin smears for screening of plasmodium parasite, with a detection limit of 10-50 trophozoites. Thin smears allow one to identify malaria species, quantify parasitemia, and asses for the presence of schizont, gametocytes, and malarial pigment in ne-trophies and monocytes. The diagnosis accuracy relies on the quality of the blood smear and experience of laboratory personnel. Before reporting a negative result, at least 200 oil immersion visual field at a magnification of 1000x should be examined on both thick and thin smears, which has a sensitivity of 90%. The level of parasitemia may be expressed either as a percentage of parasitized erythrocytes or as the number of parasite per microliter of blood. In



ANTIMALARIAL TREATMENT OF SEVERE MALARIA:-non-immune patient with P. falciparum malaria should be treat as a medical emergency and be considered for hospital admission, regardless of disease severity at presentation. All patient with severe malaria and and those who are unable to tolerate drug orally should initially receive parenteral treatment immediately and be admitted to the ICU

In these patients, gastrointestinal intolerance and erratic intestinal absorption make the oral route of administration unreliable. To prevent medication error it is important to check where the recommended dose relates to a base or salt. Patient to check whether patient with severe malaria should always receive a full treatment dose,

no falciparum malaria, parasitemia rarely exceeds 2%, where as it can be considerably higher in falciparum malaria. In non-immune individual, hyperparasitemia generally associated with several disease.

ALTERNATIVE DIAGNOSIS METHOD:-although examination of the thick and thin blood smears is the gold standard for diagnosis malaria, important advances have been made in diagnostic testing, include fluorescence microscopy of parasite nuclei stained with acridine orange, rapid dipstick immunoassay, and polymerase chain reaction assays. Sensitivity and specificity of some of these methods approach or even excess those of the thin and thick smears. Rapid dipstick immunoassay detect species circulating parasite antigen targeting either the histidine rich. Although the dipstick test may enhance diagnostic speed, microscopic examination remains mandatory in patient with suspected malaria, because occasionally these dipstick test are negative in patient with high parasitemia, and their sensivity below 100 parasite is low.

including those with breakthrough malaria and those who received some prior antimalarial medication...

MONITORING TREATMENT RESPOSE:-when reailable and malaria is suspected on clinical grounds, empiric treatment for falciparum malaria should be administered without delay. Treatment response should be assessed by parasite count daily until clearance of all trophozoites is achieved parasitemia may rise during the first 12to14 hours, because available drugs do not inhibit schizont rupture and release of merozoits . rising parasitemia beyond 36to48 hours after the start of antimalarial treatment indicates treatment failure, usuallybecause of high level drug resistance .because non-immune hosts may exhibit a high pre-treatment total parasites burden it may take up to 6 days to achieve complete elimination of P. falciparum prophozoites from the blood, even with fast acting antimalarial agent (quinine artemisinin derivatives) a rising gametocyte count does not indicate treatment failure.

DRUG USED IN TREATMENT:-

- 1) Chloroquine.
- 2) Amodiaquine:
- 3) Quinine.
- 4) Mefloquine.
- 5) Prinaquine.
- 6) Pyrimethamine-Sulfonamide/Depose Combinations.
- 7) Proguanil (Chloroguanide).

8) Atovaquone

II. CONCLUSION

Recent Research Studies indicate that the disease malaria has hazardous and life threatening effect on human body as well as human brain it can be treated very well with the use of various drugs like Chloquine, Quinine, Mefloquine, Primaquine, Pyrimethamine –Dapsone, Proguanil, Atovaquone ,etc. and sometimes this used in combination of antibiotics to give boost effect .

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