

## A Review of Malaria in Pediatrics

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### Abstract

**Background:** As a tropical disease, malaria, which causes one death per minutes globally, is still common in both tropical and subtropical regions around the world. From millions of reported cases, one million cases would end in death each year.

**Methods:** Different databases, including PubMed and Google Scholar, were investigated to collect the required data for the completion of the present review article. The following keywords were used for searching in these databases: Malaria in Children, Plasmodium Falciparum in Children, Malaria in Paediatrics, and Plasmodium Falciparum in Paediatrics.

**Results:** Children under five years of age make the majority of death reports; i.e. 90% of the whole death statistics. Although malaria is mostly common in sub-Saharan Africa, it still occurs in other tropical and subtropical countries. In other regions, malaria is the result of both immigration and travel; regardless of the sources of the disease, it can be potentially severe and, sometimes, fatal.

**Conclusions:** It would be important to become familiar with the clinical presentation of malaria among pedestrians and find approaches to prompt diagnosis, appropriate treatment and sufficient prevention methods against it.

**Key Words:** Malaria, Paediatrics, Plasmodium Falciparum, Severe Malaria, Treatment.

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## 1- INTRODUCTION

Malaria is considered as a one the most infectious diseases in the world; every country encounters malaria cases, some due to travel and immigration and some as a result of epidemic situations (1). According to various reports and estimates, 2.48 million malaria cases occur annually in South Asia (2). According to WHO report on 2011 of Switzerland the total number of confirmed cases was 3031, among whom 1847 were locally acquired and 1184 were imported cases, in 2010 (3). Almost half of the world's population lives in regions where malaria is epidemic (4). Although malaria can be prevented, it should be treated as soon as it happens. The most common symptoms include fever, weariness, chills, headache, sweats and myalgia. Children more suffer by Vomiting and nausea than in adults. More than 90 percent of cases getting infected in sub-Saharan are children under age 5; because children are considered as the main vulnerable group who are immunologically weak for malaria parasite, the most potent of which is *Plasmodium falciparum* (1, 5). Young children in remote areas mainly succumb to death, mainly because of the lack of proper health services.

Cerebral malaria involves the most severe neurological complication of infections with *plasmodium falciparum*. It can change mental status; even coma can be resulted from. Malaria is an acute and vast disease which can affect any organ. If the person with malaria is not treated timely, it could be fatal in 1 - 3 days (6). This paper is aimed to declare the basic understanding of the epidemiology of malaria and approaches to diagnosis, treatment and prevention of it in children.

There is a strong relationship between poverty and challenges imposed on the vulnerable and impoverished communities. Malaria imposes heavy costs, such as more than 12 billion \$ annually in Africa, on the

economy of regions. Studies in regions such as Africa have shown that the spread of malaria among children does have direct and indirect impacts on poor communities (6-8). Damages associated with severe and chronic episodes of malaria disease have impact on children's social and cognitive developments and they would stop children from normal education circumstances. (9, 10)

Unnecessary treatments of malaria would be considerably reduced through developing rapid and cost-effective antigen tests. Prior to the inauguration of any treatment for malaria, all required efforts should be given to diagnose it as soon and correctly as possible. Whatever, when a malaria patient gets complicated and worsen the additional treatment should have started even before diagnostic tests. In developed countries, the possibility of malaria, regardless of other signs or symptoms, should be checked out in any potential traveler moved on from endemic areas.

*Plasmodium falciparum* which is responsible for the incidence of malaria, is mostly common in Africa, Eastern Asia, Middle East, Oceania, and countries in the region of Amazon. *Plasmodium vivax* rarely kills, but it is the most common form of malaria and can cause recurring and debilitating infections. *Plasmodium vivax* and *plasmodium ovale* can be gathered in liver and cause relapse of symptoms several months later. *Plasmodium falciparum* is more common among communities. The present study aimed to overview different types of malaria, their clinical symptoms and diagnosis in relation with children.

## 2- EVIDENCE ACQUISITION

Different databases, including PubMed and Google Scholar, were investigated to collect the required data for the completion of the present review article. The following keywords were used for search

in these databases: *Malaria in Children, Plasmodium Falciparum in Children, Malaria in Paediatrics, and Plasmodium Falciparum in Paediatrics*. 41 articles were found, and included, in the present review study. All selected articles were published after 1990. Qualitative data is presented in this review.

### 3- RESULTS

#### 3-1. Clinical Presentation of Malaria

The symptoms of malaria, fever, chills, headache, and myalgia in muscles, are similar to the flu. In primary episodes, periodic fevers are not so common, unless the illness isn't treated for several days. Gastrointestinal and reparatory symptoms can be observed in children with *p. falciparum* malaria. These symptoms can be mistaken with malaria symptoms in patients with acute gastroenteritis (11). Hypoglycemia has been observed frequently among children with *p. falciparum* malaria (12).

Infections in patients with *plasmodium vivax* and *plasmodium ovale* are not fatal and parasitemia levels are below 2%; however, fevers can be high. Patients with chronic or recurrent disease caused by *plasmodium vivax* show anaemia and splenomegaly symptoms; these patients may have different responses to treatment (13). Chronic infection with *plasmodium* malaria associated with nephrotic syndrome can't be improved with treatments such as chemotherapy (14).

Since *Plasmodium falciparum* shows a high capacity for attacking red blood cells, there would be a high tendency of amplification for *plasmodium falciparum*. Red blood cells infected with *plasmodium falciparum* would sequester in the capillaries and venules. The critical organs, like kidneys and brain, will destroy with insufficient oxygen and nutrient feeding (15).

#### 3-2. Severe Malaria

Accrued and complicated *plasmodium falciparum* result in severe malaria and after that serious organ failures or abnormalities will occur. It can usually be observed in endemic area's young children. *Plasmodium falciparum* virulence depends on several factors, such as multiplicative Capacity of *P. falciparum*, which give it the ability to attack various human populations. This ability comes from different surface antigens, including *plasmodium falciparum* erythrocyte membrane Protein-I (PfEMP I), that can bind into CD36 and thrombospondin specifically. Other factors, such as Parasitized RBCs Membrane Modification, cyto-adherence, sequestration of parasitized erythrocytes, Rosetting and Agglutination, and RBC Deformability contribute to the severity of *plasmodium falciparum*. The genes coding polymorphism in this infection in adhesion molecules of human, endothelial selectin, intercellular adhesion molecule, and CD36 are also important variables in propensity to severe malaria.

#### 3-3. Cerebral Malaria

Cerebral malaria is a common complication of *plasmodium falciparum*'s infection among children. It comes with neurological complications, ranging from soft depression in sensorium to extreme coma; decerebrate and opisthotonic posturing are also possible in cases with cerebral malaria. Depending on treatment, resources, and supportive cares, the mortality rate can raise from 7 to 50 percent (16-18).

Cerebral malaria is one of the most serious complications known by abnormal behaviour, decrease in consciousness, seizures, coma or other metabolic acidosis and neurological abnormalities in form of respiratory complication or severe anaemia. Pediatric groups suffer with seizure more than adults (19, 20).

Neurological complications and the way of presentation are different and can lead to die soon due to brain death. Renal failure and pulmonary edema are rarely seen in African children (21). Other symptoms include severe hypoglycaemia, metabolic acidosis, shock, and electrolyte disturbances. Inability to stand or sit in children is also seen in very severe malaria. (**Table 1**).

In order to accurately identify and assess the condition of patients, accurate knowledge of cerebral malaria is very important. In medicine, cerebral malaria is often referred to as any CNS disorder in a patient with malaria. Symptoms include clinical manifestations of systemic malaria falciparum disease and a range of mood disorders to coma.(21). Hence, cerebral malaria is an acute brain disease associated with fever.

We can classify older children with malaria as adults. For the young children, mostly less than 10 years old, the Coma Blantyre scale, a related diagnostic tool, can be used to assess the responses. (22, 23) (**Table 2**). There is a lot of disagreement between researchers and doctors about scale evaluation. However, it does not eliminate the scale of disability in children with severe disease, which many studies use a score of 2 summaries to define CNS malaria. (22). The Blantyre scoring system is very similar to the Glasgow coma scale, but it also has components to measure the baby's alertness (24).

Unlike other species, Plasmodium falciparum can be caused from large numbers of infected red blood cells, which is responsible for a large proportion of deaths and global complications. The overall mortality rate is between 1 and 5 percent, but in patients with severe or complex malaria falciparum, it can reach more than 20 percent (25). Severe manifestations of falciparum disease are the result of several factors, including red

blood cell lysis, cytokine production, and microvascular sequestration. (26). Severe *Plasmodium falciparum* shows it's led, most likely, as cerebral malaria in children, with seizures or a reduction of consciousness, severe anaemia or acidosis. Respiratory distress has been recognized as a common symptom or indicator of severe disease in infants and children; however, there is no symptom of acute respiratory distress syndrome, which is seen in adults (27).

### **3-4. Diagnostic Tests**

Currently, although microscopic examination remains as the most used clinical test, thick blood smear has provided higher accuracy and sensitivity. The highest smears belong to the Giemsa stain. Giemsa stain's smears have the disadvantage of taking considerable time. Thick smears may take between 6 to 8 hours and thin smears take just 30 minutes (28). Field stain provides less sensitivity but more pace in its application. Use of blood smear suffers from inaccuracies, inappropriate use of antimalarial occurs commonly, and nonspecific symptoms of Paediatric malaria. Non-microscopic methods, such as enzyme-linked immunoassays (ELISAs), antigen-capture, polymerase chain reaction (PCR), and quantitative buffy coat (QBC) techniques have been developed for the diagnosis of malaria (29, 30). The most practical method for diagnosis is the rapid antigen tests. Rapid antigen test is inexpensive and it detects lactate dehydrogenase isoenzymes and histidine-rich protein 2 (HRP-2), as the water-soluble antigen specific for *plasmodium falciparum* (28, 31, 32).

### **3-5. Management of Malaria in Children**

Oral quinine, atovaquone-proguanil and coartem can all be used for the treatment of uncomplicated malaria in children. Oral quinine is usually tolerated by infants and

can be a good drug to treat malaria falciparum without complications in children. While there are concerns about increasing the failure rate of anti-folate drugs, pyrimamine-sulfadoxine appears to be effective when combined with quinine with low recurrence rates in infants and children, and it is more difficult to use alternative drugs such as doxycycline or tetracyclines in children compared to

adults. For children under 12 years of age, Tetracyclines should not be prescribed because of the risk of discoloration of teeth and dental hypoplasia. Clindamycin, in the form of liquid, is not readily available, but it can be used in the form of swallowing capsules. There is limited experience regarding the use of coartem and atovaquone-proguanil in a non-endemic paediatric population.

**Table-1:** Severe or complicated malaria in children

Decreased Level of conscious or epilepsy
acidosis (pH < 7.3) (Metabolic or Respiration)
Low level of Glucose
Severe anaemia (< 8 g/dL)
Severe weakness
More than 2% red blood cells parasitized

**Table-2:** Blantyre and Glasgow Coma Scales

Blantyre coma Scale	Glasgow Coma scale
Verbal	Verbal Response
2. Appropriate cry 1. Inappropriate cry or moan 0. No cry	5. Oriented 4. Confused 3. Inappropriate 2. Incomprehensible 1. None
Motor (Responses to pain)	Motor Response
2. Localizing 1. Withdraws 0. Non-specific or no response	6. Obeys 5. Localizes pain 4. Withdraws 3. Flexion 2. Extension 1. None
Eye Movement	Eye Opening
1. Directed 0. Not directed	4. Spontaneous 3. To voice 2. To pain 1. None

To check and manage the disease in children in a timely manner, ABC measures should be taken urgently, including establishing a safe airway and ensuring adequate blood supply. (33). Children with severe malaria must be

hospitalized and treated in well-equipped centers for children. (34).

Hypoglycaemia as a sign of severe malaria should be evaluated. Serial blood sugar estimation should be performed and blood

glucose should be corrected using 5-10% glucose in the preservative fluid (35). Because septic shock or meningitis is often difficult to isolate or differentiate from severe malaria at the same time, broad-spectrum antibiotics should be given to children with severe malaria to ensure complete elimination of bacterial infection (36, 37). Management of seizures should be followed by means of any evidence-based guidelines. Although blood transfusions may be required for severe anaemia, it has been found that routine transfusion would not reduce mortality and it would rather cause more adverse effects (38).

There was a report of spreading malaria throughout the country in India. Since 1978, directorate of National Vector Borne Diseases Control Program has been monitoring the response of antimalarial drugs with falciparum malaria according to the new WHO Protocol on "Therapeutic efficacy of antimalarial drugs in uncomplicated *plasmodium falciparum* malaria (39). There were reports of resistance against Sulfadoxine-Pyrimethamine (SP) at various levels in some districts of India (40). Five therapeutic efficacy studies with SP were undertaken in four districts of India and three of them had reported treatment failure in more than 10% of cases (40, 41).

#### 4- CONCLUSION

Malaria still affects children's health around the world. In different regions, such as sub-Saharan Africa, the mortality rate is still high and it does have an effect on the economy of such countries. There is a demand for an effective, developed, and widespread distributed vaccine. By establishing appropriate treatments, diagnosis methods, preventive strategies and treatments in pregnant women and infants, the risk of malaria disease would be controlled.

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