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Recent Advances in Prevention, Treatment and Medication of Malaria

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Abstract

Malaria imposes great socio-economic burden on humanity.Moreover, in India, the government health sector, which provides free or highly subsidized health care, caters to the needs of 20% of the population, mainly in rural areas, whereas the rest of the population seeks health care in the private sector as their first point of contact, where the bulk of malaria is generally treated empirical. Malaria parasites have the capability of multiplying into thousands every few days after they enter the bloodstream and hence, the disease can quickly turn into an epidemic. Therefore, a little caution, correct diagnosis and timely treatment can help save you a lot of trouble. Malaria is spread by the bite of the female Anopheles mosquitoes, which are most active between dusk and dawn. In most people, the symptoms begin showing 10 days to four weeks after infection. Malaria is widespread in many parts of India throughout the year. However, the colder regions of northern India usually have lesser cases of the disease as mosquitoes do not thrive in low temperature areas. Malaria may be treated using the drugs. The treatment of the malaria is very complicated because different types of malaria require different types of drugs. Quinine is a classic type of treatment used for the malaria. Quinine is effective for particular types of malaria, but other parasites developed resistance to the quinine. These drugs are clindamycin, tetracycline, mefloquine, or sulfadoxine/ pyrimethamine. Chloroquine is advanced type of quinine.

Key words: Quinine, anopheles mosquitoe, chloroquinine.

Introduction

Malaria is parasitic disease transmitted due to mosquitoes from one person to another. Some times this disease is life threatening. When the mosquito (infectious) bites, malaria parasites transmits to that person and person becomes ill. Other mosquitoes bite to the infected person and pick up the parasite and then transmit to other persons. Fever, headache and aching are the primary malaria symptoms. The malaria symptoms are same as that of other diseases and therefore they are confusing. If proper treatment is not given then malaria leads to organ damage, severe anemia, coma, convulsions and death. The people living in poorest area in the world can suffer from the malaria and they are approximately 40 percent. This is wide spreading disease, but in some of the some of the countries it is eliminated completely during 20th century by maintaining the temperature. Now days malaria is found in tropical and non-tropical areas of the world and occurs acute illness of 300 million and annual death near about 1 million.Malaria is transferred by female mosquitoes because male mosquitoes don't transmit the infection because they are not developed for biting and can not cut the skin. Four species of malaria parasites are present. A parasite is one of the organism which lives in another organism. From these four species of the malaria, three species are found in India. Following are 4 species of malaria: Plasmodium Vivax that may cause relapsing malaria but seldom death (50-55% of total reported cases) , P. Malariae that may cause severe malaria (small numbers found in foothills in Orissa) ,P. Falciparum that causes malignant malaria and may lead to death (48-52% of total cases) and P. Ovale (not found in India) Generally 0.5 percent to 2 percent of P. Falciparum cases can create severe malaria with the complications. Rate of death in these cases are near about 30 percent or more than that if the proper treatment is not given. In India, malaria mortality is only because of P. Falciparum. In the rainy season, the chances of malaria are more because populations of mosquitoes are highest. You can only get malaria if you're bitten by an infected mosquito, or receive infected blood from someone during a blood transfusion. Malaria can be transmitted from mother to child during pregancy. The mosquitoes that carry *Plasmodium* parasite get it from biting a person or animal that's already been infected. The parasite then goes through various changes that enable it to infect the next creature the mosquito bites. Once it's in you, it multiplies in the liver and changes again, getting ready to infect the next mosquito that bites you. It then enters the bloodstream and invades red blood cells. Eventually, the infected red blood cells burst. This sends the parasites throughout the body and causes malaria symptoms. The deadliest form of malaria can be caused because of speedily spreading resistance of P. Falciparum parasites. For existence, different drugs are used such as artemisinin combination. Do not treat malaria own because some of the times it becomes life threatening. For the correct treatment and correct medications, past medical history and identification of particular kind of parasite are very important. A person contracts malaria when the parasites are transmitted from the mosquito's saliva into the person's bloodstream. Therefore, malaria cannot spread from direct contact with a person infected with malaria. Additionally, a person can be afflicted with malaria if he is receives infected blood during blood transfusion. This type is also used. Special treatment or hospitalizations are required for the patient in case of serious malaria.

Current scenario of malaria in India

In India, nine Anopheline vectors are involved in transmitting malaria in diverse geo-ecological paradigms. About 2 million confirmed malaria cases and 1,000 deaths are reported

annually, although 15 million cases and 20,000 deaths are estimated by WHO South East Asia Regional Office. India contributes 77% of the total malaria in Southeast Asia. Multi-organ involvement/dysfunction is reported in both *Plasmodium falciparum* and *P. vivax* cases. Most of the malaria burden is borne by economically productive ages. The states inhabited by ethnic tribes are entrenched with stable malaria, particularly *P. falciparum* with growing drug resistance. The profound impact of complicated malaria in pregnancy includes anemia, abortions, low birth weight in neonates, still births, and maternal mortality. Retrospective analyses of burden of malaria showed that disability adjusted life years lost due to malaria were 1.86 million years. Cost–benefit analysis suggests that each Rupee invested by the National Malaria Control Program pays a rich dividend of 19.7 Rupees. Most of the point prevalence studies in India have been carried out for outbreak/epidemic investigations. There is very limited information on age- and sex-specific seasonal prevalence of malaria in different paradigms in the country. In the available studies, age and sex classification used is arbitrary. The burden is generally higher in men than women in all age groups. Children in the states of Assam, Arunachal Pradesh, and Rajasthan had a higher incidence of malaria than adults, whereas in the indo-gangatic plains, the situation was reversed. It is well known that pregnant women constitute an important risk group for malaria infection, particularly in hyper- and holoendemic situations. The well-known effects include effectiveness of placental barrier, parasite sequestration in placenta, suboptimal nutrition of the fetus, congenital malaria, intrauterine growth retardation, low birth weight, premature interruption of pregnancy, infant mortality, and maternal death. It may be the cause of cerebral malaria and severe anemia. In low transmission areas, maternal mortality is ~1%, whereas in Africa it could be between 84 and 2,000 per 100,000 live births (0.00084–2%). In the 1950s and early 1960s, a major global initiative of WHO to eradicate malaria also brought malaria under firm control in India and almost on the verge of eradication, but a reverse followed in the mid-1960s until the mid-1970s; the disease staged a comeback with vengeance. In the 1980s, new malaria ecotypes developed from environmental and developmental impact and were followed by outbreaks and epidemics in the 1990s.There are vast lands inhabited by ethnic tribes in Madhya Pradesh, Chattisgarh, Jharkhand, Orissa, and the entire northeastern region, where malaria has remained deeply entrenched, *P. falciparum* preponderance is persistent, and asymptomatic burden in these areas is not known. The emergence of resistance to chloroquine in *P. fal-ciparum* in many pockets of the country and reports of reducing sensitivity in *P. vivax* are major causes of concern. In some areas in the northeastern region, even foci of multi-drug–resistant *P. falciparum* have been found. Alternate therapies such as mefloquine and artemisnin derivatives or combination therapies are expensive, and since they have been selectively introduced in the control program, would require constant monitoring for their judicious use and to observe emergence of resistance against them. Some of the changes in the national vector-borne disease control programme's new National Drug Policy on Malaria (2008) are particularly worrisome. Artemesinin, an expensive drug of last resort, will be given as first-line treatment for all proven falciparum malaria cases in certain states – even when chloroquine might be the best choice. All studies on the malaria parasite's sensitivity to various drugs such as chloroquine and sulphadoxine-pyrimethamine will be stopped. Expensive rapid diagnostic tests are promoted in place of microscopy. Pregnant women will no longer receive preventive drugs, taking away whatever little protection they used to receive from this important cause of maternal mortality. Finally, the changed treatment protocols, as well as new guidelines for treating complications in severe malaria, are to be implemented by a health system that doesn't have the necessary infrastructure, personnel or other facilities. The

World Health Organisation estimates 15 million cases in India annually, with 20,000 deaths every year. According to another estimate, based on the consumption of the anti-malarial drug chloroquine, there are anywhere from 30 million to 40 million cases of malaria a year. Malaria is well known for its debilitating, demoralizing, and impoverishing consequences, and therefore, estimation of its true burden and control is central to addressing these issues, with the final aim of lifting the human resource above the poverty line. The poor may find it hard to deal with persistent malaria problem, as coping with the disease is economically disastrous for the communities living on the edge. The estimated 20-fold returns on expenditure makes a strong case for adequate investment in malaria control in India. A good investment in malaria control not only makes public health sense but also economic sense in the present era of economic liberalization in India. Firm malaria control is imperative for human resource development, which in turn is imperative for equitable and sustained economic growth.

Types of Malaria

There are three types of malarial fever that may be classified depending on symptoms or caused by the parasite. The leading symptoms are mainly same but their occurrence and duration do vary. They are:

1.Tertian Fever: The attacks surface on alternate days.

2. Quartan Fever: In this fever the attack of fever occurs after an interval of two days, i.e. if first attack of fever occurs on the first, another attack will occur on the 4th day, then 7th, 9th and so on.

3. Malignant Tertian: It is a variety of severe type of malarial fever when malignancy sets in and is, thus, the most severe and most alarming type of malarial fever.

Causes of Malaria

The main cause of malaria is female mosquitoes. It carries plasmodium parasite in the body that transmit the malaria. When mosquito bites to human, it inserts small amount of saliva in blood stream of the human. The parasites are contained in the saliva that moves from person's blood stream to the liver. Reproduction of parasite takes place there. Again they leave the liver and moves back to the blood stream. In blood stream they starts to cause the malaria symptoms. Malaria can not directly transmit from person to person but it transfers through the mosquitoes. A mosquito bites to one infected person with the malaria parasite. When it takes some blood, it also takes some parasites. If same mosquito bites to another uninfected person, then it transfers to that person. Because of blood transfusion, malaria may also transfer. If blood is donated by the infected person, then it contains the parasites. The incubation period of the malaria is different for different persons. Incubation period means the time between the bite of mosquito and time for displaying the malaria symptoms. The incubation period also depends on the amount of parasite involved.

Symptoms

The following malaria symptoms are experiences in the persons who are suffering from malaria: First stage (Cold stage): This is characterized by immediate onset of fever with strictness and sensation of the extreme cold. The patient desires to cover with the blankets. This uncontrollable condition lasts after some hours. Second stage (Hot stage): The temperature of the may rises to

the 41o C. The patient feels too burning hot and casts off the clothes. Headache is also very severe. This condition lasts after toe to six hours. Third stage (Sweating stage): With the profuse sweating, fever comes down. This condition lasts after the two to four hours. Other malaria symptoms may include fatigue, nausea, severe headache, and vomiting. After the third stage, the patient may falls sleeping from the tiredness. Above three stages are repeated with the particular periods and varied from the particular days such as, two days later or the every 3rd day or at some of later time. Latency periods last after several weeks or several months. In some of the cases, the classical symptoms which are mentioned above may not appear. Any type of infection leads to the fever, at the time of epidemics; it is good to test all types of fever under the microscope. This guaranteed that fever does not missed among fever cases and those cases in which malaria can found, take the proper malaria treatment.

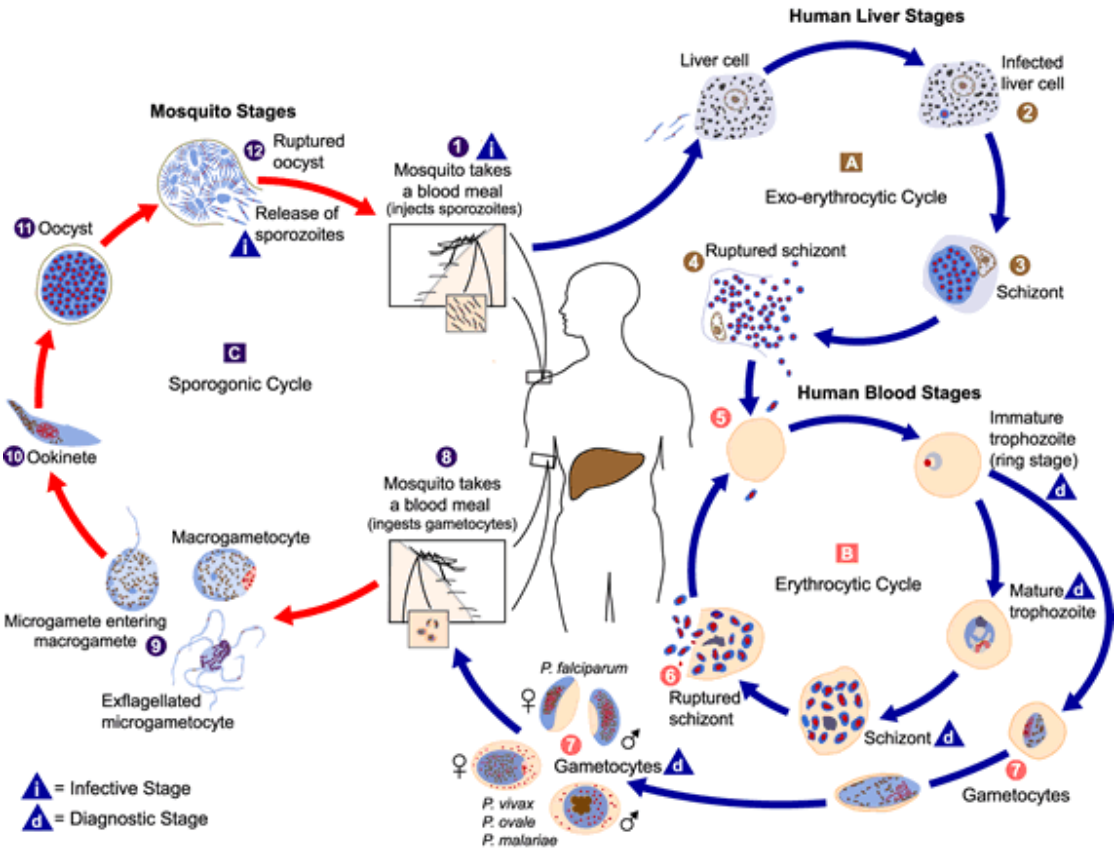

Figure-Life Cycle of Malaria

Diagnosis

Blood test is the useful test for diagnosing the malaria. For the confirmation of diagnosis, blood test is repeated after 72 hours. Above three stages are also responsible for diagnosing the disease. The person living in common area of malaria and who has fever, chills and very high temperature, those people should have to take immediate blood test. The classic and most used test is the blood smear on a microscope slide that is stained (Giemsa stain) to show the parasites inside red blood cells. Although this test is easily done, correct results are dependent on the technical skill of the lab technician who prepares and examines the slides with a microscope.

Other tests based on immunologic principles exist, including RDT's (rapid diagnostic tests) approved for use in the U.S. in 2007 and the polymerase chain reaction (PCR) tests. These are not yet widely available and are more expensive than the traditional Giemsa blood smear. Some investigators suggest such immunologic based tests be confirmed with a Giemsa blood smear

Treatment of Malaria

Three main factors determine treatments: the infecting species of *Plasmodium* parasite, the clinical situation of the patient (for example, adult, child, or pregnant female with either mild or severe malaria), and the drug susceptibility of the infecting parasites. Drug susceptibility is determined by the geographic area where the infection was acquired. Different areas of the world have malaria types that are resistant to certain medications. The correct drugs for each type of malaria must be prescribed by a doctor who is familiar with malaria treatment protocols. Since people infected with *P. falciparum* malaria can die (often because of delayed treatment), immediate treatment for *P. falciparum* malaria is necessary.Mild malaria can be treated with oral medication; severe malaria (one or more symptoms of either impaired consciousness/coma, severe anemia, renal failure, pulmonary edema, acute respiratory distress syndrome, shock, disseminated intravascular coagulation, spontaneous bleeding, acidosis, hemoglobinuria [hemoglobin in the urine], jaundice, repeated generalized convulsions, and/or parasitemia [parasites in the blood] of > 5%) requires intravenous (IV) drug treatment and fluids. Drug treatment of malaria is not always easy. Chloroquine phosphate is the drug of choice for all malarial parasites except for chloroquine-resistant *Plasmodium* strains. Although almost all strains of *P. malariae* are susceptible to chloroquine, *P. falciparum*, *P. vivax* and even some *P. ovale* strains have been reported as resistant to chloroquine. Unfortunately, resistance is usually noted by drug-treatment failure in the individual patient. There are, however, multiple drug-treatment protocols for treatment of drug resistant *Plasmodium* strains (for example, quinine sulfate plus doxycycline [Vibramycin, Oracea, Adoxa, Atridox] or tetracycline [Achromycin], or clindamycin [Cleocin], or atovaquone-proguanil [Malarone]). There are specialized labs that can test the patient's parasites for resistance, but this is not done frequently. Consequently, treatment is usually based on the majority of *Plasmodium* species diagnosed and its general drug-resistance pattern for the country or world region where the patient became infested. For example, *P. falciparum* acquired in the Middle East countries is usually susceptible to chloroquine, but if acquired in sub-Sahara African countries, is usually resistant to chloroquine. Anti-Malarial Drugs are :

1) Quinine (Therapy only)
2) Chloroquine (Therapy and prophylaxis; usefulness now reduced due to resistance)
3) Cotrifazid (Therapy and prophylaxis)
4) Doxycycline (Therapy and prophylaxis)
5) Mefloquine, trade name Lariam (Therapy and prophylaxis)
6) Primaquine (Therapy in *P. vivax* and *P. ovale* only; not for prophylaxis)
7) Proguanil (Prophylaxis only)
8) Sulfadoxine-pyrimethamine (Therapy; prophylaxis for semi-immune pregnant women in endemic countries as "Intermittent Preventive Treatment" - IPT)
9) Hydroxychloroquine, trade name Plaquenil (Therapy and prophylaxis)

Herbal and Home remedies

1) Lime and lemon play a vital role in the treatment of quartan type of malarial fever. About three grams of lime and a juice of 1 lemon should be dissolved in about 60 ml of water. This mixture can be taken before you suspect the attack to take place.
2) The herb *chirayata*, botanically known as Swertia chirata, is also beneficial in the treatment of intermittent type of malarial fevers. It helps in lowering the temperature. An infusion of the herb, prepared by immersing 15 gm of chirayata in 250 ml of hot water with aromatics like cloves and cinnamon, should be given in doses of 15 to 30 ml.
3) Alum is also useful in malaria - First take a small amount of alum and then roast it over a hot plate. Now powder it. Half a teaspoon of this powder 0should be taken about four hours before the expected attack and half a teaspoon every two hours after it. This may help you in giving relief.
4) The leaves of holy basil are also considered beneficial in the prevention of malaria. The juice of about eleven grams of leaves of holy basil mixed with three grams of powder of black pepper can be taken beneficially in the cold stage of the malarial fever. This will check the severity of the disease.

Conclusion

Malaria is a chronic disease. It affects the humans through mosquitoes. Malaria is caused by a parasite called Plasmodium. In the human body, the parasites multiply in the liver, and then infect red blood cells. It is prevalent mainly in tropical and sub-tropical regions. Many cases of malaria are considered today all over the world. Each year, there are approximately 515 million cases of malaria, killing between one and three million people, the majority of whom are young children.It is most common disease and an enormous public health problem. Malaria affects 40% of world's population. Medical treatment should be sought immediately. The effectiveness of antimalarial drugs differs with different species of the parasite and with different stages of the parasite's life cycle. The other strains such as Plasmodium vivax, ovale, or malariae can infect the liver and persist in a dormant state for months, or even years after exposure to the infection. Should a relapse develop it can be treated by restraining the acute symptoms with chloroquine and then overcome the liver infection with medication called primaquine.This medication is more toxic and has more side effects than chloroquine but is a very effective form of treatment. People with a deficiency of the blood enzyme G6PD are predisposed to reactions from primaquine treatment but such an enzyme blood deficiency is easy to ascertain with a simple blood test before treatment with primaquine is started. Prevention is better than curing the disease as the infection is becoming increasingly resistant to prescribed drugs. Various insecticides, which are used to spray areas favored by mosquitoes, are also no longer effective, and a constant struggle is under way to develop new anti-malarial drugs and insecticides, to keep the disease at bay.

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