
A Review Report on Epidemiology, Etiology and Prophylaxis of Malaria and the Life cycle of Plasmodium

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Abstract

Malaria is a parasite disease transmitted by mosquitoes that can be fatal. Malaria affects around 40% of the world's population, mostly those living in the world's poorest nations (undeveloped and developing). There are also alarming signs that malaria is spreading to new parts of the globe and resurfacing in previously eradicated locations. This review article brings awareness about its various aspects in terms of its epidemiology, symptoms, causes, diagnosis and treatment. The information related to the life cycle of the parasite, sources of infection, mechanism behind the disease are well discussed to have a clear understanding of the disease and the parasite. Preliminary symptoms to identify the disease and various diagnostic protocols to confirm the infection are explained. By highlighting the statistics of the disease, its prevalence and spread has been described and importance of preventing the infection is focused. Malaria can be lethal if the causative protozoa infect and destroy red blood cells (anemia) or clog the capillaries that supplies blood (cerebral malaria) or other essential organs. Malaria must be identified early in order to treat the patient in a timely manner and to prevent the transmission of infection further in the community via mosquitoes.

Keywords: Malaria, Female Anopheles, Life cycle of Plasmodium, Mosquito transmission

Introduction

The word 'Malaria' is derived from Italian language which means "Mal: Bad", "aria: air" meaning Bad air. In 1880, researchers identified the actual cause of malaria: plasmodium, a single-celled parasite. They eventually determined that the parasite is passed from person to person via a female Anopheles mosquito bite. The female anopheles mosquito is its prime vector. The outbreak started in mid-18th century in Africa, where it has co evolved with the hosts like mosquitoes and other primates. The disease was thought to have spread to humans from Gorillas. The discovery of malaria occurred at a military hospital in Constantine (Algeria) in 1880, when Laveran discovered the malaria parasite [15]. This disease is prevalent in tropical and subtropical regions. It evolved over millennia with its victims expanding along the Neolithic dwellers, Chinese, early Greeks, princess and paupers[20].

Vital Statistics of Malaria

Malaria is now found throughout the world's tropical and sub-tropical regions, contributing around 300-500 million acute infections and at least one million fatalities each year. Malaria kills 90% of individuals in Africa south of the Sahara, especially kids under the age of five.

A public survey reveals that worldwide victims of malaria accounts for approximately 198 million every year. The population of the world being 7.2 billion, 3.2 billion among them are at a risk of malarial infection. On an average scale, the death rate due to malarial infection is about 584,000 per year, Africa being the hotspot for the onset and spread of this infection [5].

According to the reports of WHO, 228 million cases of malaria were reported worldwide for the year 2018 [1]. The number of malarial deaths recorded was 405000 globally for the year 2018. The most sensitive group being affected by the parasite is children under the age of 5. Africa shares the highest percentage of infected individuals i.e. 93% of the malarial cases reported worldwide.

Causes of Malaria

The major organism causing malaria stated is the protozoan plasmodium. However the spread of malaria and its outbreak is caused by its host- the Mosquito. A total of 5 species of Plasmodium are detected to be disease causing

in Humans, among them the 2 important species having a major impact are *vivax* and *Plasmodium falciparum* [18]. The infection spreads from one to other due to the bites of a mosquito causing transfer of the protozoan from its oral cavity to the human blood stream. The eggs of the parasites are carried from the infected human by female anopheles mosquito wherein the eggs get nurtured from the blood sucked from the humans.

Though the plasmodium and mosquito are the direct causes of malaria, there are several factors which may act as indirect causes of this disease. Maintenance of improper and unhygienic environment is one of the major causes of malaria spread in the country. This interconnection of malaria with hygiene is because of the active vector involved in the disease, the mosquito [16]. These mosquitoes breed on stagnant and dirty water where the eggs are laid. These eggs would develop into adult mosquito which would later act as a vector for malarial parasite and start spreading malaria with its bite. Thus unhygienic environment is a major cause for the spread of malaria.

Peculiar nature of malaria for Individuals with Sickle Cell

Sickle Cell is a condition in the humans where in the genetic makeup is altered leading to a modified shape of RBCs [11]. The regular shape is biconcave in nature whereas the damaged cells show sickle shape. This shape causes a disturbance to the oxygen carrying capacity in the cells. Researchers have revealed that the individuals affected with sickle develop a natural resistance towards malarial parasite. This is due to the in efficiency of the parasite to divide and develop inside the sickle cells.

Symptoms of Malaria

Malarial patient experiences different symptoms in the condition which may be person specific or generalized. Some of the commonly reported symptoms are: Fever, Cold, Cough, body pains, Chills and shivers [10]. Several cases also show loss of appetite, Nausea, fatigue, tiredness, dry cough, sweating, diarrhea, unbearable-high intensity head ache etc. These symptoms may start being detected after 7 days of the infection by the parasite. However the incubation of parasite and onset of initial symptoms completely depends on the species of plasmodium involved in infection. In some worst cases the symptoms may be developed after one year of the infection. The malarial symptoms are mild and often confused with common flu and may even remain non-recognized. In some kind of species infection symptoms arise in 48hr cyclic intervals [3]. This cyclic effect is due to the bursting of the cells and release of mature parasites into the body. This causes a feeling of cold followed by shivering. It is often associated with unbearable headache.

Malaria Strain

Parasitic disease caused by Plasmodium species, that are parasitic microorganisms. A diversity of species could become infected by parasite Plasmodium. Involving mammals, birds, and reptiles. There are roughly 100 species of Plasmodium long been known to infect humans in the wild. Humans are infected by the following species: *P. falciparum*, which is widespread globally in tropical and subtropical regions, and particularly in Africa. Because replicates fast in the blood, it can cause severe malaria and substantial blood loss (anemia). Moreover, infected parasites have the ability to obstruct tiny blood arteries. When this happens in the brain, cerebral malaria develops, which is a potentially lethal complication.

- *P. vivax*, is most prevalent in Asia, Latin America, and portions of Africa. It is the most common human malaria parasite, especially in Asia, due to high population concentrations. *P. vivax* (and *P. ovale*) have latent liver stages ("hypnozoites") that can reactivate and penetrate the bloodstream months or years after the infectious mosquito bite ("relapse").
- *P. ovale* is usually found in Africa (particularly West Africa) and the western Pacific islands. It resembles *P. vivax* physiologically and morphologically. In contrast to *P. vivax*, it may infect people who do not have the Duffy blood type, which is the situation for many people in Sub-Saharan Africa. This explains why *P. ovale* (rather than *P. vivax*) is more common throughout much of Africa.
- *P. malariae* is the only human malaria parasite species with a quartan cycle, and it's found all over the world (three-day cycle). (The other three species have a two-day tertian cycle.) *P. malariae* produces a long-term, chronic infection that can last a lifetime if left untreated. *P. malariae* can cause major consequences in certain persistently infected people, such as nephrotic syndrome. *P. knowlesi* is a natural pathogen of long-tailed and pig-tailed macaques prevalent across Southeast Asia. It has lately been discovered to be a major source of zoonotic malaria in that region, especially in Malaysia. As *P. knowlesi* has a 24-hour reproduction cycle, an infection can quickly escalate from mild to severe; fatal instances have been observed.

Mechanism of Infection

The malarial parasites are introduced into the host body by the bite of a female anopheles mosquito carrying the parasite. [17] After entering the host, the parasite goes straight to the liver to develop. The parasite is completely formed when it reaches the bloodstream and begins infecting RBCs [14] The parasite begins to multiply inside the RBSs, and the RBCs break open within 48 to 72 hours. With other RBCS, the infection is repeated. The cycle continues indefinitely. This is the cause of the patient's state fluctuating periodically throughout infection.

Life cycle of malaria parasite:

The malarial parasite needs two hosts to complete its life cycle. The female anopheles mosquito is the first, followed by humans..

- 1) Initially the malaria parasite in its sporozoite stage enters the blood stream of a human by a mosquito bite from an infected insect .
- 2) The parasite then passes into the liver from the blood stream.
- 3) The sporozoites proliferate asexually in the liver cells for 7 to 10 days. This stage is asymptomatic.After multiplication the parasites bust open the liver cells and are released out in the form of merozoites.
- 4) They pass from the liver to the heart and then to the lungs. Later the vesicles disintegrate releasing the merozoites into the blood phase.
- 5) Here in the blood stream the merozoites enter into the RBCs and start multiplying until the cells burst and release out the parasite. This is the reason for intermitten chills and fever [13].
- 6) When the infected human is bitten by a mosquito the parasite enters the mosquito. This stage is the gametophyte stage. Inside the mosquito, the gametophytes mature into mature cells known as gametes..
- 7) The female gametes mature into Ookinetes, which are living organisms [8]. These ookinetes live deep within the mosquito's midgut. On the external surface, they create oocysts.Within the oocyst, sporozoites develop actively which are released out upon maturity as sporozoites and enter the salivary gland of mosquito [6].
- 8) This cycle repeats upon the invasion of mosquito to an infected individual [7].

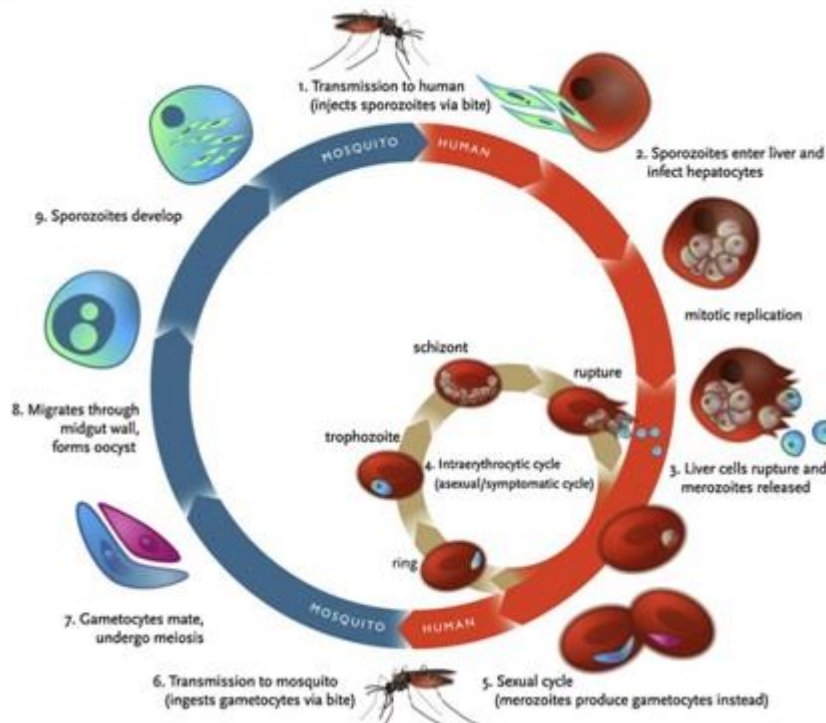


Fig 1: Life Cycle of the Malaria Parasite

[Picture Courtesy: E.Y.Klein(4)]

Diagnosis

Malaria infection may be diagnosed accurately and quickly, increasing the chances of a successful recovery and lowering the disease's mortality rate [2]. Malaria diagnosis involves the identification of either the malarial parasite or its antibodies or products in the cells.

- 1) The most important and accurate test in order to confirm of malarial infection is the identification of malarial parasite in the blood sample of patient using microscopy. A special staining protocol is employed to identify the parasite under the microscope. The peripheral blood samples are stained with Giemsa, Wright's or Field's stains and observed under the microscope [9].
- 2) **Rapid diagnostic test:** This test is abbreviated as RDT. This approach is used in case of absence of blood smears. The sample collected in this case is a drop of blood with needle prick.[12] The sample is placed on a diagnostic strip, which changes color depending on whether or not the malarial parasite is present.. However the major drawback of the protocol is its inefficiency in identifying the type of parasite/ species of plasmodium causing the infection [19].
- 3) **Antibody test:** Here the test is based on the presence of the malarial antibodies in the blood that would react with the antigen and indicate the antigen antibody specificity and presence of the infection.
- 4) **Drug resistance test:** This is based on the resistivity of the malarial parasites to specific known drugs. This is an indirect approach for the diagnosis.
- 5) **Blood test:** This is an advanced test that not only diagnoses the presence of infection but also reveals the presence of any other opportunistic infections or the side effects of infection like anemia or kidney failure. Here the venal blood is drawn and tested for all the parameters like cell count and its cyto-chemistry [21].

Treatment and Prophylaxis

Currently four different medicine groups are proposed to treat malaria. These include quinoline-related compounds, artemisinin derivatives, antifolates and antimicrobials. In view of the different species of parasite involved in the onset of infection, no common treatment is proposed yet. Thus instead of single drug a combination of drugs is suggested in the treatment. The treatment not only depends on the type of parasite involved in the infection but also the geographical location of the infected individual.

The World Health Organization has proposed an ABC mechanism to prevent malaria and stop its spread.

The mechanism is described hereunder:

A: **Awareness** of risk: The risk depends upon the place and the time of the year.

B: How to avoid mosquito **Bite:** Maintenance of proper hygiene.

C: Prevention is better than **Cure**

Conclusion

From the review five important species of human malaria causing protozoa could be identified *viz vivax, P. malariae, P. ovale, P. knowlesi* and *P. vivax* and are the most common causing deadly type of malaria infection. *falciparum* malaria is most common in Africa, south of the Sahara and Asia accounting in large part for the extremely high mortality in this region. Typically, Fever, headaches, diarrhea, vomiting, and other flu-like symptoms are common signs of malaria. When an infected Anopheles mosquito feeds on the blood of a human, the malaria parasite is transmitted. As part of its intricate life-cycle inside the human host, the parasite goes through a variety of changes. Plasmodium may elude the immune system, infect the liver and red blood cells, and eventually evolve into a form that can infect a mosquito again when it bites an infected person via its many phases. The parasite grows within the mosquito until it reaches the sexual stage, at which point it can infect a human host again when the mosquito takes their next blood meal 2 to 4 days later. Symptoms of malaria usually develop 9 to 14 days after the infective mosquito bite, however this might vary depending on the plasmodium type. If medications aren't accessible or the Parasites have developed resistance to them. The infection has the potential to rapidly develop into a life-threatening situation.

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