

Malaria - The Formidable Enemy of Humanity

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Keywords: Malaria, Plasmodium, clinical manifestations, economy

ABSTRACT. Malaria, a disease caused by protozoan parasite of the genus *Plasmodium*, is an ancient enemy of the human race. Despite enormous efforts to control, it is still a main cause of morbidity and mortality in many endemic countries of the world, particularly Africa, South of Sahara. Malaria seems to be unstoppable due to lack of an effective vaccine, acquisition of drug-resistance by malaria parasite, and insecticide resistance by *Anopheles* mosquitoes. In this scenario, along with search for novel preventive approaches, adequate health facilities, health literacy and awareness among people are required to control and eliminate this formidable disease from society.

1. HISTORICAL PERSPECTIVE

Malaria is one of the most life-threatening ancient parasitic diseases, causing great morbidity and mortality in many developing countries. It is probably one of the oldest diseases and supposedly had its origins in the jungles of Africa, where it is still very much rampant. Man and malaria seem to have evolved together. References of this disease can be found in the ancient Chinese, Indian and Egyptian manuscripts. The history of malaria dates back to the prehistoric times and the documented history began as early as in 1600 B.C. in ancient Egypt. Hippocrates in 400 B.C. was the first to classify intermittent fever along with other characters of the disease. Previously, malaria was known by various names like jungle fever, intermittent and remittent fever and marsh fever etc. The disease was named malaria by Macculloch in 1827 on the idea that it was caused by filthy air of marshy regions [1].

Alfonse Laveran, a French army medical officer in Algeria in 1880, first of all discovered the malarial parasite in an unstained preparation of wet blood smear of a patient [2]. In 1892, a German doctor, Richard Pfeiffer proposed the role of some sanguivorous insect in malaria transmission. Sir Patrick Manson (1894) was the first to suggest the role of mosquitoes in spreading of malaria [3]. Sir Ronald Ross (1898) discovered the complete sporogony of *Plasmodium relictum*, a blood malaria parasite in *Culex pipiens fatigans* [4]. The sporogony of *Plasmodium falciparum* [5], *Plasmodium vivax* and *Plasmodium malariae* [6] was also recognized in *Anopheles* mosquito. Exoerythrocytic schizogony of *Plasmodium elongatum* in tissue cells was described by Raffaele (1934) [7]. Shortt and Garnham (1948) reported the pre-erythrocytic cycle of *Plasmodium cyanomolgi* [8] and *P. vivax*; whereas, that of *P. falciparum* was discovered by Shortt *et al.* (1951) [9].

2. CURRENT STATUS

Malaria is still a major global health problem despite the extensive research in the development of novel antimalarial drugs, vaccines and insecticides. It is responsible for nearly 250 million new clinical cases resulting about 1.2 million deaths annually, the majority of which are caused by *P. falciparum* [10]. In 2012, out of the 104 endemic countries, seventy-nine are classified as being in the malaria control phase, ten are in the pre-elimination phase, and 10 are in elimination phase. Besides this, five countries are in the prevention of re-introduction phase as these are without ongoing transmission. Approximately 3.3 billion people were at risk of malaria in 2011 worldwide;

mostly those living in sub-Saharan Africa are at highest risk. The WHO African Region is severely affected, as nearly 80% of malaria cases and 90% of deaths are likely to occur here. Children below the age of five years and gravid women are most harshly affected. It has been estimated that about 50 million women of pregnancy age are at the risk of malaria each year. Pregnant women are more susceptible as compared to non-pregnant women, particularly in first and second pregnancy [11].

It is intriguing to note that malaria was recognized as the third reason of HIV-related morbidity in Africa [12]. Any kind of interaction between HIV infection and malaria may have potentially important public health implications [13]. However, because of a enormous scale-up in malaria control programs by the WHO, as part of the Millennium Development Goals, the estimated incidence of malaria globally has reduced by 17% and malaria-specific mortality rates by 26% between 2000 and 2010 [14]. Out of 43 countries with ongoing malaria transmission in the African Region, 8 countries namely Algeria, Botswana, Cape Verde, Namibia, Rwanda, Sao Tome and Principe, South Africa and Swaziland and the island of Zanzibar, have achieved decrease in malaria admission rates by 75% [11].

3. HUMAN MALARIA PARASITES

Malaria in humans is caused by an apicomplexan protozoan parasite of genus, *Plasmodium*. Five species of *Plasmodium* that infect humans are *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae* and *Plasmodium knowlesi*. Of these, *P. falciparum* and *P. vivax* are the most prevalent species found in most endemic areas; whereas, *P. malariae* and *P. ovale* infections have sparse and restricted distribution [15,16]. *P. knowlesi*, a natural parasite of macaques, causes acute illness and deaths also in persons living in proximity to the monkeys [17,18]. Among these species, *P. falciparum* causes malignant malaria and is accountable for most malaria morbidity and almost all malaria mortality. However, in tropical and subtropical areas, *P. vivax* can equal *P. falciparum* as a source of community-wide morbidity [19]. *P. vivax* is the most widespread species outside Africa in Asia and South America; whereas, illness with *P. malariae* and *P. ovale* are usually minor [20,21].

Until recently, it was thought that the malaria caused by *P. vivax* was clinically less severe than that associated with *P. falciparum* and rarely lethal, but various studies in Southeast Asia have shown that about 25% of patients with severe malaria have mono-infection and multi-drug resistant *vivax* has been identified as causative agent [19,22]. Long-lasting infections are caused by *P. malariae*, which can persist asymptotically for years and even for a lifetime, if untreated [23]. Various species of *Plasmodium* differ morphologically, immunologically, in geographical distribution, relapse pattern and drug resistance etc. The biology of *P. falciparum* differs from *P. vivax* in relapse pattern, severity and less preference of reticulocytes for invasion [24]. The life-cycles of most of the malaria parasites are basically the same despite various differences affecting appearance and pathogenicity among various species [25].

4. MALARIA TRANSMISSION

Malaria is a vector-borne disease, which spreads by the female mosquitoes of genus *Anopheles*. Out of the 460 recognized species of *Anopheles*, 100 species can transmit malaria in humans [26]. Sometimes, it is transmitted by transfused blood from infected to healthy individuals, sharing infected needles, or from an infected gravid woman to her fetus. A number of factors, including the spread of drug-resistant parasites, the emergence of insecticide-resistant mosquito vectors and the absence of an efficient vaccine are responsible for the persistence of malaria. Along with these global warming, changing agricultural practices, and human migration are also major contributors [27,28]. Persons in Refugee camps exposed to malaria and other infectious diseases in their country of origin, after immigration to developed nations may act as important reservoirs and further accelerate the spread of malaria [29]

5. CLINICAL MANIFESTATIONS OF MALARIA

Upon rupturing of infected erythrocytes, an unknown toxin is discharged in blood stream, resulting in production of cytokine response, responsible for clinical manifestations. The clinical manifestations in malaria infected persons include fever, anemia, malaise and splenomegaly, and are due to the asexual multiplication of merozoites in RBCs [30,31]. Disease produces a strain of repeated paroxysms, each having three stages—chills, followed by temperature and then sweating. Besides these, the patient may have severe headache, nausea and vomiting. Within duration of an hour or two, the fever increases and then, as the fever falls, a wetting sweat initiates and the patient feels very weak, exhausted and sleepy. The malaria symptoms appear after 10 to 16 days of infection and coincide with the rupturing of infected RBCs. The spectrum of severe pathology is broad during *P. falciparum* infection, and includes metabolic acidosis, cerebral malaria (CM), and severe malarial anemia (SMA), and it is usually accompanied by hypoglycemia, hypoxia and lactic acidosis due in part to the increased metabolic demands of the parasite and occasionally multi-organ system failure may result in coma and death [30,31]. Therefore, new approaches, such as proper diagnosis, vaccine development and discovery of novel therapeutic agents, are urgently needed to combat the disease.

6. MALARIA AND ECONOMY

Malaria is directly linked to socio-economic development and referred as both a disease of poverty and a cause of poverty. It exerts a huge economic load on endemic countries [27,32]. It is a well-known fact that annual economic growth in malaria endemic countries has historically been lower than in malaria free countries. According to economists, the malaria is responsible for a growth penalty of upto 1.3% per year in some African countries. Malaria destroys the capacities of individuals and hence the economic development of their countries. Mocumbi (2004) reported that the disease delays the development of sub-Saharan African countries at a cost of at least US\$ 12,000 million per year [33]. Poverty and childhood mortality cannot be reduced in these countries without adequate malaria control measures. But, the problem of malaria control in these countries is strengthened by perilous socioeconomic conditions and insufficient health-care infrastructures. Population growth, fertility, saving and investment, worker productivity, absence, premature mortality and medical costs are different channels by which malaria affects development [27].

Acknowledgements

Authors acknowledge the financial assistance provided by the University Grants Commission (UGC), New Delhi as RFSMS under UGC-CAS programme to Anil Pawar.

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