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MALARIA: EPIDEMIOLOGY, PATHOPHYSIOLOGY, DIAGNOSIS, MANAGEMENT AND PREVENTION - A COMPREHENSIVE REVIEW

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ABSTRACT

Malaria is a life-threatening mosquito-borne parasitic disease caused by Plasmodium species and transmitted primarily by infected female Anopheles mosquitoes. Despite considerable progress in malaria control, it remains a major public health concern, particularly in tropical and subtropical regions, contributing to significant morbidity and mortality worldwide. This review provides a comprehensive overview of malaria, including its epidemiology, etiology, transmission, life cycle, pathophysiology, clinical manifestations, diagnosis, management, and preventive strategies. The review highlights the role of different Plasmodium species and mosquito vectors in disease transmission and discusses the pathological mechanisms responsible for severe malaria. Conventional diagnostic methods such as microscopy and rapid diagnostic tests, along with advanced molecular techniques including polymerase chain reaction (PCR) and loop-mediated isothermal amplification (LAMP), are summarized. Current treatment strategies, particularly artemisinin-based combination therapies (ACTs), and emerging concerns regarding antimalarial drug resistance are also discussed. In addition, preventive measures such as insecticide-treated bed nets, indoor residual spraying, environmental management, malaria vaccination, larval control, and community awareness programmes are reviewed. Continued research, improved surveillance, integrated vector management, and equitable access to effective diagnosis, treatment, and preventive

interventions are essential for reducing the global malaria burden and achieving the long-term goal of malaria elimination.

KEYWORDS: Malaria, Plasmodium, Anopheles, Epidemiology, Pathophysiology, Diagnosis, Artemisinin-based combination therapy, Prevention, Malaria vaccine, Vector control.

INTRODUCTION

Malaria is a mosquito-borne protozoal disease caused by parasites of the genus *Plasmodium* and remains a major public health concern worldwide. The term "malaria" is derived from the Italian word *malaria*, meaning "bad air," reflecting the historical belief that the disease originated from marshy environments. In the late nineteenth century, Charles Louis Alphonse Laveran first identified the malaria parasite in the blood of infected patients, while Sir Ronald Ross subsequently demonstrated the role of *Anopheles* mosquitoes in malaria transmission.[1]

Malaria is widely distributed across tropical and subtropical regions, with the highest burden occurring in sub-Saharan Africa. Significant numbers of cases are also reported from countries such as India, Brazil, Afghanistan, Thailand, Indonesia, Vietnam, Cambodia, and China.[2] The disease is transmitted through the bite of an infected female *Anopheles* mosquito, which serves as the vector for *Plasmodium* parasites.[3]

Six *Plasmodium* species are known to infect humans: *Plasmodium falciparum*, *P. vivax*, *P. malariae*, *P. ovale curtisi*, *P. ovale wallikeri*, and *P. knowlesi*. Among these, *P. falciparum* is responsible for the majority of severe cases and malaria-related deaths. Clinical manifestations range from uncomplicated febrile illness to severe complications, including severe anaemia, cerebral malaria, acute kidney injury, respiratory distress, hypoglycaemia, and multi-organ failure. Despite substantial progress in prevention and control strategies, malaria continues to contribute significantly to global morbidity and mortality, particularly in low- and middle-income countries.[4,5]

Malaria Vectors

Malaria in India is transmitted primarily by mosquitoes of the genus *Anopheles*. Approximately 58 morphologically identified *Anopheles* species have been reported in the country, of which six species - *Anopheles culicifacies*, *Anopheles fluviatilis*, *Anopheles sundaicus*, *Anopheles stephensi*, *Anopheles baimaii*, and *Anopheles minimus* - are recognized

as primary malaria vectors. In addition, *Anopheles annularis*, *Anopheles subpictus*, *Anopheles philippinensis*, and *Anopheles jeyporiensis* serve as secondary vectors.[6]

Several primary malaria vectors exist as species complexes consisting of morphologically similar but genetically distinct sibling species that differ in their vectorial capacity and ecological characteristics. Among these, *Anopheles culicifacies*, responsible for approximately 65% of malaria transmission in India, comprises five sibling species (A–E). Species A is regarded as the most efficient malaria vector, whereas species B is considered a poor vector or non-vector.[7,8]

Similarly, *Anopheles fluviatilis*, which accounts for nearly 15% of malaria transmission, consists of three sibling species (S, T, and U), with evidence suggesting the presence of an additional form, provisionally designated as form X, in India (15,16). The *Anopheles minimus* species complex includes three sibling species (A, C, and E), of which species A, formally recognized as *Anopheles minimus* sensu stricto, is widely distributed in India.[9]

Understanding the distribution, biology, and vector competence of these *Anopheles* species complexes is essential for developing effective malaria surveillance and vector control strategies.

Epidemiology

Malaria remains a major global public health challenge, particularly in tropical and subtropical regions. According to the World Health Organization (WHO), an estimated 247 million malaria cases and 619,000 malaria-related deaths occurred worldwide in 2021 (19). The African Region accounted for approximately 94% of all reported cases (215 million cases), while the South-East Asia Region contributed about 3% of the global malaria burden.[10]

Children under five years of age are the most vulnerable group, accounting for nearly 67% of malaria-related deaths worldwide. Their increased susceptibility is largely attributed to underdeveloped immunity. In addition to mortality, recurrent malaria episodes can adversely affect growth and development through prolonged fever, poor appetite, reduced physical activity, and impaired social participation.[11]

The epidemiology of malaria in India is complex due to the country's diverse geographical, climatic, and ecological conditions. Malaria is predominantly caused by *Plasmodium*

falciparum and *Plasmodium vivax*, with approximately 57.3% of infections attributed to *P. falciparum* and 43% to *P. vivax*. Sporadic cases of *P. malariae* and *P. ovale* have also been reported from certain regions of the country. Transmission occurs through several *Anopheles* mosquito species, of which six are recognized as primary vectors.[12]

Approximately 95% of India's population resides in areas where malaria transmission is possible. High-burden states include Odisha, Chhattisgarh, Jharkhand, West Bengal, Maharashtra, and several states in the north-eastern region. Despite substantial progress in malaria control, the disease continues to pose a significant public health concern in the country.[13]

India contributes approximately 1.4% of the global malaria burden and 0.9% of malaria-related deaths worldwide, accounting for nearly 52% of malaria deaths reported outside sub-Saharan Africa. Furthermore, India bears approximately 46% of the global *P. vivax* malaria burden and contributes about 66% of malaria cases reported in the WHO South-East Asia Region. In recent years, the country has achieved notable success in malaria control and elimination efforts. Between 2021 and 2022, malaria incidence declined from 3.63 to 2.55 cases per 1,000 population at risk, while malaria-related mortality decreased from 0.006 to 0.001 deaths per 1,000 population at risk.[14]

Recent Global and Indian Malaria Trends

According to the World Health Organization (WHO) World Malaria Report 2025, an estimated 282 million malaria cases and 610,000 malaria-related deaths occurred globally in 2024, representing an increase of approximately 9 million cases compared with 2023. The WHO African Region continued to bear the greatest burden, accounting for approximately 94–95% of global malaria cases and deaths. Children younger than five years remained the most vulnerable population, accounting for nearly 75% of malaria deaths in the African Region. Despite substantial progress in malaria control since 2000, challenges such as antimalarial drug resistance, insecticide resistance, climate change, population displacement, humanitarian crises, and inadequate funding continue to impede malaria elimination efforts.[15,16]

India has made considerable progress in reducing malaria transmission over the past two decades through strengthened surveillance, vector control measures, improved diagnostics, and effective treatment strategies. However, malaria transmission remains concentrated in

specific high-burden states and tribal regions. Sustained implementation of the National Framework for Malaria Elimination and continued investment in prevention and control programmes are essential for achieving India's goal of malaria elimination by 2030.[17,18]

Etiology

Malaria is caused by intracellular protozoan parasites of the genus *Plasmodium*, which belong to the phylum Apicomplexa. More than 200 *Plasmodium* species have been identified, infecting a wide range of vertebrate hosts; however, only six species are known to cause malaria in humans.[19] These include *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium knowlesi*, and the two genetically distinct forms of *Plasmodium ovale* (*P. ovale curtisi* and *P. ovale wallikeri*).[20]

Among these species, *P. falciparum* is the most virulent and is responsible for the majority of severe malaria cases and malaria-related deaths worldwide, particularly in sub-Saharan Africa. *P. vivax* is the most geographically widespread species and is the predominant cause of malaria in many parts of Asia and Latin America. Unlike *P. falciparum*, *P. vivax* and *P. ovale* can form dormant liver stages (hypnozoites), which may reactivate and cause relapses months or even years after the initial infection.[21] *P. malariae* is associated with chronic low-grade infections, whereas *P. knowlesi*, a zoonotic malaria parasite naturally infecting macaques, has emerged as an important cause of human malaria in Southeast Asia.[22]

Malaria transmission occurs through the bite of an infected female *Anopheles* mosquito. More than 400 species of *Anopheles* mosquitoes have been identified worldwide, although only about 30–40 species are considered important vectors of human malaria. These mosquitoes typically bite between dusk and dawn, facilitating the transmission of *Plasmodium* parasites between human hosts.[23]

Life Cycle of *Plasmodium:*

The life cycle of *Plasmodium* is complex and involves two hosts: humans (intermediate host) and female *Anopheles* mosquitoes (definitive host). The parasite undergoes asexual reproduction in humans and sexual reproduction in mosquitoes. The life cycle can be divided into three major phases: pre-erythrocytic (hepatic) schizogony, erythrocytic schizogony, and sporogony in the mosquito vector.[24]

Pre-Erythrocytic (Hepatic) Schizogony

Human infection begins when an infected female *Anopheles* mosquito injects sporozoites into the bloodstream during a blood meal. The sporozoites rapidly migrate to the liver, where they invade hepatocytes and undergo asexual multiplication known as exo-erythrocytic schizogony. Each infected hepatocyte produces thousands of merozoites, which are subsequently released into the bloodstream. In *Plasmodium vivax* and *P. ovale* infections, some sporozoites remain dormant in the liver as hypnozoites and may reactivate months or years later, causing relapses. The duration of the hepatic stage varies among *Plasmodium* species and corresponds to the prepatent period of infection.[25,26]

Erythrocytic Schizogony:

Following release from the liver, merozoites invade red blood cells (RBCs) and initiate the erythrocytic stage of the life cycle. Within RBCs, the parasite develops sequentially through ring, trophozoite, and schizont stages. During the trophozoite stage, hemoglobin is degraded to provide nutrients for parasite growth, while toxic free heme is converted into insoluble hemozoin pigment. Mature schizonts rupture the infected RBCs, releasing new merozoites that invade additional erythrocytes and perpetuate the infection. This cyclic process occurs every 48 hours in *P. falciparum*, *P. vivax*, and *P. ovale* infections and every 72 hours in *P. malariae* infections.[27] The synchronized rupture of infected erythrocytes and release of parasitic products stimulate cytokine production, leading to the characteristic fever and other clinical manifestations of malaria.[28]

A proportion of intraerythrocytic parasites differentiate into male and female gametocytes, which circulate in the peripheral blood and are essential for transmission to mosquitoes.

Sexual Phase in Mosquito (Sporogony):

When a female *Anopheles* mosquito feeds on an infected individual, it ingests circulating gametocytes. Within the mosquito midgut, male and female gametocytes mature into gametes and fuse to form a zygote. The zygote develops into a motile ookinete, which penetrates the gut wall and forms an oocyst. Repeated divisions within the oocyst produce numerous sporozoites, which are released upon rupture of the oocyst and migrate to the mosquito salivary glands.[29,30] After an incubation period of approximately 10–18 days, the mosquito becomes infective and can transmit sporozoites to another human host during a subsequent blood meal, thereby completing the life cycle.[31]

Pathophysiology

The pathophysiology of malaria is primarily associated with the asexual erythrocytic stage of *Plasmodium* infection. Although *Plasmodium falciparum* is responsible for most severe manifestations, other species such as *P. vivax* and *P. knowlesi* can also cause severe disease and mortality. Following inoculation by an infected female *Anopheles* mosquito, sporozoites migrate to the liver, where they invade hepatocytes and undergo asexual multiplication. The resulting merozoites are released into the bloodstream and invade erythrocytes, initiating the erythrocytic phase of infection.[32]

During intraerythrocytic development, parasites digest hemoglobin and multiply within red blood cells (RBCs). Rupture of infected erythrocytes releases merozoites along with parasitic products such as glycosylphosphatidylinositol (GPI), parasite DNA, and hemozoin pigment. These products stimulate macrophages, monocytes, and endothelial cells to produce pro-inflammatory mediators including tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ), interleukin (IL)-1, IL-6, and IL-8. The resulting inflammatory response is responsible for many of the characteristic clinical manifestations of malaria, including fever, chills, headache, myalgia, malaise, vomiting, and gastrointestinal symptoms.[33]

Hemozoin and parasite-derived nucleic acids activate innate immune pathways, including Toll-like receptor signaling, leading to further cytokine release and fever generation. Persistent inflammation, together with repeated destruction of infected and uninfected erythrocytes and suppression of erythropoiesis, contributes significantly to the development of anemia.[34]

A hallmark of severe *P. falciparum* malaria is cytoadherence, whereby infected erythrocytes express parasite-derived proteins, particularly *Plasmodium falciparum* erythrocyte membrane protein-1 (PfEMP1), which mediate adhesion to vascular endothelial cells. This process results in sequestration of parasitized erythrocytes within the microvasculature of vital organs such as the brain, lungs, kidneys, liver, and placenta. Sequestration impairs microcirculatory blood flow, causing tissue hypoxia, metabolic disturbances, and local inflammatory responses.[35]

In addition, infected erythrocytes may adhere to uninfected erythrocytes, a phenomenon known as rosetting, which further increases vascular obstruction and reduces erythrocyte

deformability. The combined effects of hemolysis, inflammation, cytoadherence, sequestration, and microvascular obstruction contribute to the development of severe malaria complications, including cerebral malaria, severe anemia, acute kidney injury, metabolic acidosis, pulmonary edema, jaundice, and multi-organ dysfunction.[36]

Diagnosis of Malaria:

Malaria diagnosis is essential for prompt treatment, effective case management, and prevention of disease transmission. It involves the detection of *Plasmodium* parasites, parasite-derived antigens, nucleic acids, or metabolic products in the patient's blood. Accurate diagnosis can be influenced by several factors, including the infecting *Plasmodium* species, parasite density (parasitemia), developmental stage of the parasite, host immunity, endemicity of the region, previous antimalarial treatment, recurrent infections, mixed-species infections, and sequestration of parasites in deep tissues. These factors may affect the sensitivity and specificity of diagnostic tests and influence the interpretation of laboratory results. Therefore, selecting an appropriate diagnostic method is crucial for ensuring accurate diagnosis and timely initiation of treatment.[37]

Clinical Diagnosis of Malaria

Clinical diagnosis remains the first step in identifying malaria, particularly in resource-limited and highly endemic areas where laboratory facilities may not be readily available. It is inexpensive and relies on the patient's history, clinical symptoms, and physical examination. The most common clinical manifestations include fever, chills, headache, myalgia, generalized weakness, dizziness, nausea, vomiting, abdominal pain, diarrhoea, anorexia, and pruritus.[38] However, these symptoms are nonspecific and overlap with many other febrile illnesses such as viral infections, bacterial infections, dengue, and typhoid fever. Consequently, clinical diagnosis alone has low specificity and may lead to overdiagnosis, inappropriate use of antimalarial drugs, delayed diagnosis of other diseases, and increased risk of antimalarial drug resistance. Therefore, laboratory confirmation is recommended whenever possible before initiating treatment.[39]

Microscopic Examination of Peripheral Blood Smears:

Microscopic examination of Giemsa-, Wright's-, or Field's-stained thick and thin peripheral blood smears remains the gold standard for malaria diagnosis. Thick blood smears are more sensitive because they concentrate parasites and are useful for detecting low levels of parasitemia, whereas thin blood smears allow accurate identification of *Plasmodium* species

and estimation of parasite density. Microscopy is inexpensive and provides valuable information regarding parasite morphology and treatment response. However, its accuracy depends on the quality of blood smear preparation and the expertise of the microscopist, making it less reliable in settings with limited trained personnel.[40]

Quantitative Buffy Coat (QBC) Technique:

The Quantitative Buffy Coat (QBC) technique is a fluorescence-based diagnostic method developed to improve the rapid detection of malaria parasites. In this method, finger-prick blood is collected into capillary tubes containing acridine orange dye and anticoagulant, centrifuged, and examined using an epi-fluorescence microscope. The parasite nuclei fluoresce bright green, while the cytoplasm appears yellow-orange, allowing rapid visualization of infected erythrocytes. The QBC technique is highly sensitive and particularly effective for detecting *P. falciparum* infections and low parasite densities. However, it requires specialized fluorescence microscopy, is relatively expensive, has reduced sensitivity for non-*P. falciparum* species, and may show decreased specificity because leukocyte DNA also fluoresces.[41-43]

Rapid Diagnostic Tests (RDTs):

Rapid Diagnostic Tests (RDTs) are immunochromatographic assays that detect malaria-specific antigens in whole blood without requiring laboratory equipment or microscopy. Most commercially available RDTs detect histidine-rich protein-2 (HRP-2), parasite lactate dehydrogenase (pLDH), or aldolase. These tests provide results within 15–20 minutes and are particularly useful in remote and resource-limited settings where microscopy is unavailable. Several RDTs, including OptiMAL, ICT Malaria, ParaHIT-f, ParaScreen, SD Bioline, and Paracheck, are widely used for diagnosing malaria. Although RDTs are highly effective for detecting *P. falciparum*, some newer tests can also identify *P. vivax* and *P. knowlesi*. Their limitations include inability to quantify parasitemia, persistence of HRP-2 antigen after successful treatment, reduced sensitivity at low parasite densities, and false-negative results associated with HRP-2 gene deletions.[44]

Serological Tests:

Serological tests detect antibodies produced against *Plasmodium* parasites rather than the parasites themselves. The Indirect Immunofluorescence Antibody (IFA) test has long been considered a highly sensitive and specific method for detecting malaria antibodies. Since antibodies remain in circulation long after recovery, serological tests cannot distinguish

between current and past infections and are therefore not suitable for diagnosing acute malaria. Instead, they are primarily used for epidemiological surveys, blood donor screening, surveillance programs, and retrospective confirmation of previous exposure to malaria parasites.[45]

Polymerase Chain Reaction (PCR):

Polymerase Chain Reaction (PCR) is a highly sensitive molecular technique that detects and amplifies parasite DNA in blood samples. It is capable of identifying all human *Plasmodium* species, detecting mixed infections, and diagnosing malaria cases with very low parasitemia that may be missed by microscopy or RDTs. Because of its excellent sensitivity and specificity, PCR is widely regarded as the reference molecular diagnostic method. However, its routine use is limited by high cost, specialized laboratory infrastructure, skilled personnel requirements, and relatively long turnaround times, restricting its application mainly to reference laboratories and research settings.[46]

Loop-Mediated Isothermal Amplification (LAMP):

Loop-Mediated Isothermal Amplification (LAMP) is a simple and rapid molecular diagnostic technique that amplifies parasite DNA at a constant temperature without requiring a thermal cycler. It commonly targets the conserved 18S ribosomal RNA gene of *Plasmodium* species and has demonstrated high sensitivity and specificity for detecting *P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale*. Compared with PCR, LAMP is faster, less expensive, easier to perform, and more suitable for field laboratories, making it a promising tool for malaria diagnosis in resource-limited settings.[47]

Microarray Technology:

Microarray technology is an advanced molecular diagnostic method that simultaneously detects multiple pathogen-specific nucleic acid sequences through hybridization of labeled DNA or RNA to immobilized probes. This technology enables rapid identification of different *Plasmodium* species and mixed infections in a single assay. Although microarrays offer high diagnostic accuracy and multiplex capability, their high cost, sophisticated laboratory requirements, and technical complexity currently limit their routine clinical use. They remain primarily research tools with potential future application in point-of-care diagnostics.[48]

Flow Cytometry Assay (FCM):

Flow cytometry detects malaria infection by identifying hemozoin, the malaria pigment formed during digestion of hemoglobin by intraerythrocytic parasites. Hemozoin-containing leukocytes depolarize laser light as they pass through the flow cytometer, allowing automated detection of infected cells. Studies have reported sensitivities ranging from 49% to 98% and specificities between 82% and 97%. This method offers rapid and quantitative analysis but requires expensive equipment and trained personnel, limiting its availability to specialized laboratories.[49,50]

Automated Blood Cell Counters (ACC):

Modern automated hematology analyzers can assist in malaria diagnosis by detecting hemozoin-containing monocytes, analyzing depolarized laser light, or identifying characteristic changes in leukocyte volume, conductivity, and scatter (VCS). Studies have demonstrated sensitivities ranging from 72% to 98% and specificities from 88% to 96%, suggesting that these instruments can serve as useful adjunctive tools for malaria screening during routine hematological investigations. However, confirmatory testing with microscopy or molecular methods remains necessary.[51]

Laser Desorption Mass Spectrometry (LDMS):

Laser Desorption Mass Spectrometry (LDMS) is a novel diagnostic technique that detects parasite-derived hemozoin by identifying its heme component, which serves as a malaria-specific biomarker. The technique involves minimal sample preparation followed by ultraviolet laser desorption and mass spectrometric analysis of whole blood samples. LDMS is capable of detecting parasitemia as low as 10 parasites/µL and offers rapid, automated, and high-throughput diagnosis. Although highly promising, its high cost and limited availability currently restrict its use to research laboratories and specialized diagnostic centers.[52]

Management of Malaria:

The management of malaria involves both curative and preventive strategies aimed at reducing morbidity, mortality, and disease transmission. Early diagnosis followed by prompt initiation of effective antimalarial therapy is the cornerstone of malaria management, as untreated uncomplicated malaria can rapidly progress to severe disease with life-threatening complications. The choice of treatment depends on the infecting *Plasmodium* species, disease severity, drug susceptibility patterns, patient age, pregnancy status, and regional antimalarial resistance. To delay the emergence and spread of drug-resistant parasites, the World Health Organization (WHO) recommends the use of artemisinin-based combination therapies (ACTs)

for the treatment of uncomplicated *Plasmodium falciparum* malaria. Combination therapy employs at least two antimalarial drugs with different mechanisms of action, thereby enhancing treatment efficacy, reducing parasite survival, and minimizing the development of resistance.[53,54]

Pharmacological Treatment of Malaria:

Antimalarial drugs are broadly classified into quinoline derivatives, antifolate agents, and artemisinin derivatives based on their chemical structure and mechanism of action. Each drug class targets specific stages of the parasite's life cycle and is selected according to the infecting species, severity of infection, and local resistance patterns.

Quinoline Derivatives:

Quinoline derivatives include chloroquine, amodiaquine, quinine, quinidine, mefloquine, primaquine, lumefantrine, and halofantrine. Most of these agents are active against the erythrocytic stages of *Plasmodium* parasites, while primaquine is unique in its activity against dormant hepatic hypnozoites of *P. vivax* and *P. ovale* as well as mature gametocytes, thereby preventing relapse and reducing transmission (48,49). The primary mechanism of quinoline derivatives involves inhibition of hemozoin formation within the parasite's digestive vacuole. During hemoglobin digestion, toxic free heme is released, which the parasite normally converts into non-toxic hemozoin crystals. Quinoline drugs prevent this detoxification process by binding to free heme and inhibiting crystal formation, leading to accumulation of toxic heme and subsequent parasite death.[55]

Antifolate Agents:

Antifolate antimalarial drugs interfere with folate metabolism, which is essential for DNA synthesis and parasite replication. These drugs are classified into Class I and Class II antifolates according to their site of action. Class I agents, such as sulfadoxine, inhibit the enzyme dihydropteroate synthase (DHPS), thereby blocking the synthesis of dihydrofolic acid. Class II agents, including pyrimethamine and proguanil, inhibit dihydrofolate reductase (DHFR), preventing the conversion of dihydrofolate to tetrahydrofolate, an essential cofactor for nucleic acid and amino acid synthesis. These drugs exhibit schizonticidal activity against the asexual blood stages of the parasite and are commonly used in combination regimens to enhance efficacy and reduce resistance.[56]

Artemisinin Derivatives:

Artemisinin and its derivatives, including artesunate, artemether, arteether, and dihydroartemisinin, are currently the most effective antimalarial drugs against multidrug-resistant *P. falciparum*. These compounds are derived from the medicinal plant *Artemisia annua* and act rapidly against the asexual blood stages of the parasite. Their mechanism of action involves activation by intraparasitic heme released during hemoglobin digestion, resulting in cleavage of the endoperoxide bridge and generation of highly reactive oxygen-centered and carbon-centered free radicals. These free radicals alkylate and damage essential parasite proteins, membranes, and other cellular components, leading to rapid parasite death. Because of their rapid action and short half-life, artemisinin derivatives are always administered in combination with longer-acting partner drugs as artemisinin-based combination therapies (ACTs) to improve cure rates and delay resistance development.[57,58]

Preventive Measures for Malaria:

Effective malaria prevention combines vector control, personal protection, vaccination, environmental management, larval control, and community education. Integrated malaria control strategies have substantially reduced malaria incidence and mortality worldwide.

Insecticide-Treated Bed Nets (ITNs):

Insecticide-treated bed nets (ITNs) are among the most effective and cost-efficient malaria prevention measures. They provide both a physical barrier and an insecticidal effect against mosquitoes, significantly reducing human-vector contact during nighttime when *Anopheles* mosquitoes are most active. Long-lasting insecticidal nets (LLINs), which remain effective for up to three years without retreatment, are currently recommended by the WHO for widespread distribution, particularly among children under five years of age and pregnant women living in malaria-endemic regions. Numerous randomized controlled trials have demonstrated that ITNs significantly reduce malaria incidence, severe disease, and malaria-related mortality.[59-61]

Insect Repellents:

Personal protection using insect repellents provides an additional method of reducing mosquito bites. N,N-diethyl-meta-toluamide (DEET) remains the most effective and extensively studied topical insect repellent, offering prolonged protection against mosquito bites with an excellent safety profile when used appropriately. Plant-derived repellents such as citronella, neem, eucalyptus, and other essential oils provide shorter-lasting protection but are generally less effective than DEET. Permethrin, a synthetic pyrethroid insecticide, is

recommended for treating clothing, bed nets, tents, and other fabrics rather than direct application to the skin. The combined use of DEET-based repellents with permethrin-treated clothing provides nearly complete protection against mosquito bites in endemic areas.[62-64]

Malaria Vaccines:

Malaria vaccination has emerged as an important addition to existing malaria control strategies. The World Health Organization currently recommends the RTS,S/AS01 (Mosquirix) and R21/Matrix-M vaccines for the prevention of *Plasmodium falciparum* malaria in children residing in areas with moderate to high malaria transmission. Vaccination is initiated from five months of age and consists of a four-dose schedule, with an additional fifth dose recommended in areas of highly seasonal transmission. Although these vaccines do not provide complete protection, they significantly reduce the incidence of severe malaria, hospitalization, and malaria-related mortality when used alongside conventional vector control measures.[65-67]

Environmental Management

Environmental management aims to reduce mosquito breeding sites by modifying environmental conditions that support vector development. WHO defines environmental management as the planning and implementation of activities that modify or manipulate environmental factors to reduce malaria transmission. These measures include drainage of stagnant water, cleaning and maintenance of water channels, vegetation management, intermittent irrigation, riverbank modification to improve water flow, proper waste disposal, and elimination of temporary water collections around human settlements. Environmental interventions reduce mosquito breeding habitats and contribute to sustainable vector control with minimal environmental impact.[68-70]

Larval Control

Larval control targets the aquatic stages of mosquitoes before they develop into adults capable of transmitting malaria. Larviciding involves the periodic application of biological or chemical insecticides to water bodies, ponds, irrigation channels, and other mosquito breeding sites. One commonly used larvicide is pyriproxyfen, an insect growth regulator that disrupts larval development by interfering with metamorphosis and reproduction. As a result, larvae fail to develop into viable adult mosquitoes, thereby reducing vector populations and malaria transmission.[71]

Floating Larvicidal Tablets

Floating larvicidal tablets are slow-release formulations designed to remain on the surface of water bodies because of their low density. These formulations gradually release larvicidal agents over an extended period, maintaining effective insecticide concentrations while reducing the frequency of application. Floating tablets provide sustained mosquito larval control in ponds, reservoirs, and stagnant water bodies and have become an effective component of integrated vector management programs.[72]

Awareness and Community Education

Community awareness and health education are fundamental components of malaria prevention and control. Public health campaigns improve knowledge regarding malaria transmission, symptoms, preventive measures, early diagnosis, and treatment-seeking behavior. Educational programs encourage the consistent use of insecticide-treated bed nets, elimination of mosquito breeding sites, acceptance of vaccination, adherence to antimalarial treatment, and prompt healthcare consultation when fever develops. Community participation and intersectoral collaboration strengthen malaria control efforts and contribute significantly to reducing disease burden and sustaining elimination programs.[73]

CONCLUSION

Malaria remains a major global health problem, particularly in tropical and subtropical countries. Although significant progress has been made in reducing malaria cases and deaths through improved diagnosis, effective antimalarial treatment, vector control, and vaccination, the disease continues to pose serious challenges due to drug resistance, insecticide resistance, and changing environmental conditions. Early diagnosis, prompt treatment with effective antimalarial drugs, and preventive measures such as insecticide-treated bed nets, indoor residual spraying, environmental management, and public awareness are essential for controlling malaria transmission. Continued research, strong healthcare systems, and global collaboration are necessary to develop new diagnostic tools, effective vaccines, and novel antimalarial drugs. A comprehensive and integrated approach will be crucial to achieving the global goal of malaria elimination.

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