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A brief summary of Malaria, its diagnosis, and contemporary treatment management

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ABSTRACT
One of the major parasitic diseases spread by mosquitoes in the world is malaria. Plasmodium protozoa are the culprits behind it. It is a newly discovered infectious disease that affects both tropical and non-tropical nations. Every year, over a million cases of malaria are reported, primarily affecting youngsters. The illness was once known as ague or marsh fever because of its connection to marshlands and wetlands. The word malaria is derived from the Medieval Italian word mala aria, which translates to 'bad air.'To treat and prevent malarial infections, doctors administer antimalarial drugs. Most antimalarial drugs act on the erythrocytic stage of the malaria infection, which is when symptoms first manifest. In 2020, India would account for over 80% of all deaths in the nation with 96% of all deaths and 955 instances of malaria. The pathogenesis, aetiology, medical management, diagnosis, life cycle, and symptoms and indicators of malaria are covered in this review article.

Keywords: *Malaria, Epidemiology, Etiology, Diagnosis, Medical Management.*

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I. INTRODUCTION

The parasite malaria, spread by the Anopheles mosquito, is extremely dangerous and a serious threat to world health. Humans contract it by being bitten by female Anopheles mosquitoes carrying the parasite, which introduces itself into the bloodstream. In areas where it is a major cause of illness and mortality, the disease is widespread. A serious threat to public health is malaria. Roughly two-thirds of malaria deaths occur in children under five, who are the most susceptible. Malaria frequently causes fever, chills, headaches, aches in the muscles, and exhaustion. Severe cases may result in organ failure, anaemia, or even death (1). Due to its association with marshlands and swamps, the disease was once known as ague or marsh fever. The term malaria comes from the Medieval Italian word mala aria, which means "bad air." Although it is no longer endemic, imported instances of malaria still happen in most of North America and Europe, where it was historically prevalent. Certain animals become infected with different species of Plasmodium. Different mammals, birds, and reptiles have different types of malaria. Throughout documented history, beginning in China about 2700 BC, references have been made to the distinct periodic fevers caused by malaria. Given how common malaria was in Rome, it was dubbed "Roman fever" and may have played a role in the fall of the Roman Empire (2). The pathophysiological, economic, and ecological difficulties associated with malaria are extremely complex. Reducing the breeding grounds for the vectors that cause morbidity and death from these diseases is a public health problem, even if some regions have no recorded history of malaria and many have not reported cases of the disease for 20 years or more. Approximately 40% of the world's population, or 2.5 billion people, live in malaria-risk zones today. One of these locations is susceptible to malaria transmission, and the regional (3). Despite significant global efforts over the past ten years to reduce the malaria burden, millions of children remain at risk, particularly in tropical regions. Malaria cases in India have also decreased significantly, from 2 million in 2000 to 1.1 million in 2015 (4). Plasmodium falciparum has the lowest incubation time (9–40 days), while Plasmodium malariae has the longest (40–60 days), during which the patient is asymptomatic. After that, a two- to three-day prodrome sets in with vague symptoms including headache, exhaustion, myalgia, arthralgia, and chest and abdomen pain that may be mistaken for any mild viral infection. Fever, the primary symptom of malaria, then starts to develop. Fever is frequently elevated, reaching as high as 40°C in non-immune people and children. An infection with Plasmodium vivax may be linked to severe rigors (5,6). The traditional malarial paroxysm is characterized by fever, chills, and rigors that come on periodically (48 hours for vivax and ovale, 72 hours for malariae). Other symptoms include nausea, vomiting, diarrhea, back pain, myalgia, pallor, and jaundice. It coincides with the plasmodium merozoites' release from the lysed red blood cells (7). A blood smear is a blood sample spread over a glass slide that has been

stained with a particular chemical. All blood smears were previously inspected by laboratory experts under a microscope. Digital automated devices can now be employed to assist in the examination of blood smears. Examining a blood smear is done to determine the quantity, size, and form of three different types of blood cells: White blood cells combat infection; platelets aid in blood clotting; and red blood cells transport oxygen from your lungs to the rest of your body. Other names for this product include blood smear analysis, manual differential, blood film, peripheral smear, peripheral blood film, smear, and blood cell morphology (8,9). This test aids in determining whether a blood sample contains malaria antigens. This test uses a testing strip that contains an anti-malarial antibody. When a drop of blood is added to the testing strip, the color of the strip changes to show a positive outcome. The result of an antigen-antibody response is this color shift. Nevertheless, it might not be possible to identify the precise Plasmodium species that is causing the infection with this test (10). Antimalarial medications are prescribed to treat and prevent malarial infections. The majority of antimalarial medications target the malaria infection's erythrocytic stage, which is when symptoms start to appear. Pre-erythrocytic activity for the majority of antimalarial drugs is not well understood. For all types of malaria, treatment of the acute blood stage infection is required. In addition, terminal prophylaxis with a medication that fights hypnozoites is necessary for infections caused by Plasmodium ovale or Plasmodium vivax (11).

TYPES OF MALARIA

Malaria originates in five different forms:

- ***Plasmodium vivax (P. vivax)***

Sickness in a milder form that is usually not deadly. Animals with the infection, however, still require medical attention since, if left untreated, they might develop a variety of health issues. Geographically speaking, this variety is found in the most places worldwide. P. vivax is responsible for around 60% of infections in India. This parasite may persist in the body for years without harming people and has a liver stage. If the patient is not given treatment, the liver stage may reactivate after months or even years without symptoms, resulting in malaria bouts known as relapses.

- ***Plasmodium ovale (P. ovale)***

Lesser variation of the illness that is usually not deadly. The afflicted person must still receive treatment, though, as the infection may worsen and result in a variety of health issues. This parasite may live in the body for years without harming it and has a liver stage. After months or even years without symptoms, the liver stage may reactivate and trigger relapses, or malaria episodes, if the patient is not treated.

- ***Plasmodium falciparum (P. faliparum)***

The disease's most dangerous variation. Africa is where it is most prevalent, particularly in sub-Saharan Africa. According to available data, incidents are now being documented in regions of the world where it was previously believed that this kind had been exterminated.

- ***Plasmodium knowlesi (P. knowlesi)***

Produces malaria in macaques and has the potential to infect people.

- ***Plasmodium malariae (P. malariae)***

Milder kind of the illness that is usually not lethal. Even yet, the diseased animal still requires medical attention because failing to do so might result in a number of other health issues. It has been reported that this kind of parasite can remain in some people's blood for several decades (2,12).

EPIDEMIOLOGY

Malaria is mostly a tropical and subtropical disease that is common in hot, humid areas of South and Central America, Asia, and Africa. More than 100 nations currently have an endemic malaria situation, and 40% of the global population resides in a region where infection is possible. There are differences in the rate of malaria transmission between nations, regions, and even within individual countries. In addition to having warm temperatures and enough of rainfall that are ideal for mosquito reproduction, endemic areas also include coexisting populations of malaria parasites and human hosts. Seasonal maps that show where epidemics are likely to develop and when transmission will be at its peak can be created due to the necessary climate conditions**.** These seasonal data should aid in the creation of malaria control schedules and enable health services target their control efforts-drug acquisition and anti-vector measures, for example-appropriately. The map displays regions of the world with varying degrees of endemicity, or the intensity of transmission (13,14). Sub-Saharan Africa, along with other tropical and sub-tropical locations like Asia, the Middle East, and Central and South America, are known to have high malaria rates. The mosquito vector and the geographic distribution of malaria are coordinated. Malaria is therefore typically not seen at high altitude locations. Despite the presence of Anopheles mosquitoes in the US, public health initiatives have halted the spread of parasites. Therefore, "imported malaria," or malaria contracted by a person visiting the country from an endemic zone, accounts for the majority of cases of malaria in the United States. There are two types of factors that can start a malaria epidemic: man-made (conflict and war, agricultural projects, dams, mining, forestry), and natural (climatic fluctuations, natural disasters). The majority of these elements alter the physical environment and boost mosquito potential to spread malaria. Massive population

movements caused by certain conditions also expose nonimmune people to malaria infection. Understanding which communities will be most at risk and designing control programs appropriately depends heavily on the epidemiology of malaria (13,15,16). According to the World Health Organization's malaria report, there were 241 million cases of malaria globally in 2020, with 627,000 deaths. This is approximately 14 million more cases and 69,000 more deaths than in 2019. Approximately 96% of all deaths and 955 cases of malaria will occur in India in 2020, accounting for roughly 80% of all deaths in the country. Twenty-four countries have reported malaria deaths to the WHO since 2015. Within Over the same period, the number of malaria cases decreased by 27.6%, 28.4% in 2019 from 390,000 to 444,600, while the 11 countries with the largest number of cases increased from 150 million in 2015 to 163 million in 2020. India is the only highly endemic nation whose percentage decreased by 17.6% in 2019 compared to 2018. In 2018, the Annual Parasitic Incidence (API) decreased by 27.6% from 2017 to 2018, and in 2019, it decreased by 28.4% from 2018 to 2019. Since 2015, India has had fewer than one API. Across 2015, initiatives to combat malaria were launched across the nation. Every year, mosquitoes infect almost 40 million individuals in India (1).

ETIOLOGY

Plasmodium parasites are the cause of malaria. A vertebrate host and an arthropod vector are involved in the heterotenous life cycle of Plasmodium species, which belong to the apicomplexa class. Humans, birds, rodents, monkeys, and reptiles are examples of vertebrate hosts. Each Plasmodium species will only infect a restricted spectrum of hosts and vectors, making them generally host and vector specific (17,18). Plasmodium falciparum, P. vivax, P. malariae, P. ovale, and P. knowlesi are the five species of Plasmodium known to infect people and cause malaria, a protozoan disease. The bite of an infected female anopheles mosquito is the most significant mode of transmission. using tainted needles and donating blood that has become contaminated. Through the placenta, from the sick mother to the fetus (4).

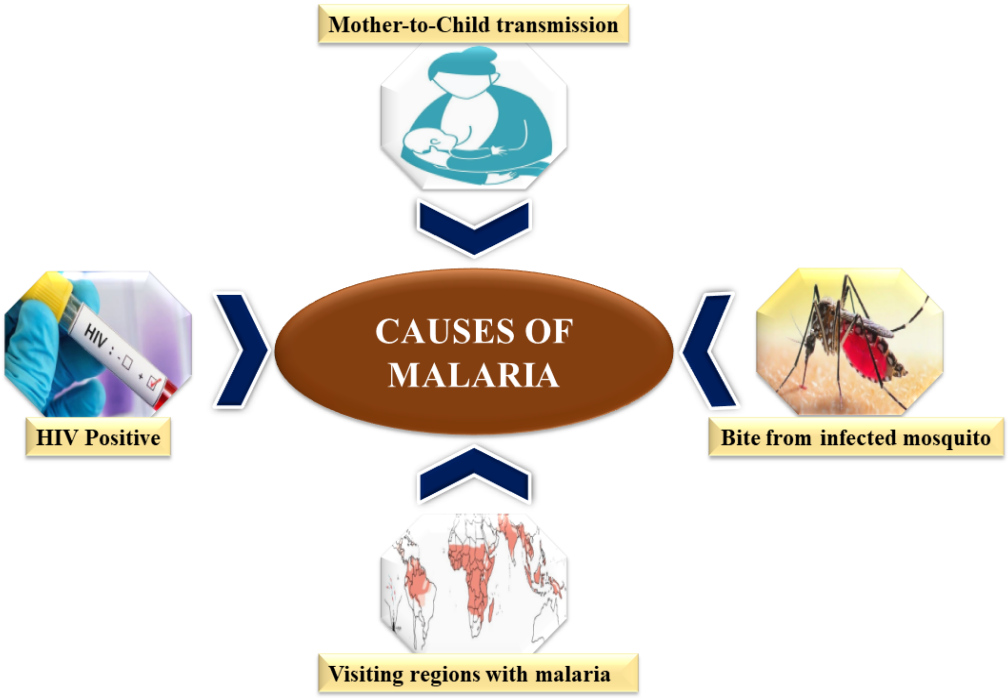

Fig.1: A few malaria causes.

SIGNS AND SYMPTOMS

Fever and associated symptoms are the hallmarks of malaria, a febrile sickness. But it's crucial to keep in mind that malaria is not just a simple illness characterized by a fever, chills, and rigors. In fact, malaria can appear with so many various and severe forms in a malarial environment that it may need to be ruled out as a differential diagnosis for nearly all clinical issues. Malaria is a cunning mimic, especially in regions where it is endemic. Anemia in the blood is the cause of all clinical manifestations of malaria. The 'malarial pigment' and hemolysis of the infected red cell are caused by the developing parasite gradually consuming and breaking down intracellular proteins, primarily hemoglobin. The red cell becomes less flexible and more spherical as a result, and this also modifies the red cell membrane's transport characteristics. Certain substances and poisons are released when merozoites break apart red blood cells (19,20). Malaria's clinical symptoms are caused by the parasite's blood stage phase of life cycle. Malaise, abdominal discomfort, anemia, splenomegaly, chills, fever, and non-

specific flu-like symptoms are among the signs and symptoms of malaria. Malaria fevers occur on a periodic basis and coincide with the asexual growth of parasites. However, because this recurrent fever is often not observed clinically, it is not always useful in differentiating malaria from other fever-causing conditions. For instance, fevers brought on by P. falciparum infections occur every 48 hours. This is the amount of time P. falciparum needs to get from the ring stage to rbc rupture and invasion of other rbcs, the point at which the parasite returns to the ring form as indicated by morphology. Splenogaly, vascular sequestration, and the rupture of infected erythrocytes all contribute to anemia. Severe anemia, respiratory distress, renal failure, cerebral malaria, and mortality are among the more severe malarial symptoms. Falciparum malaria may cause as much as 40% of deaths in non-immune people (21,22).

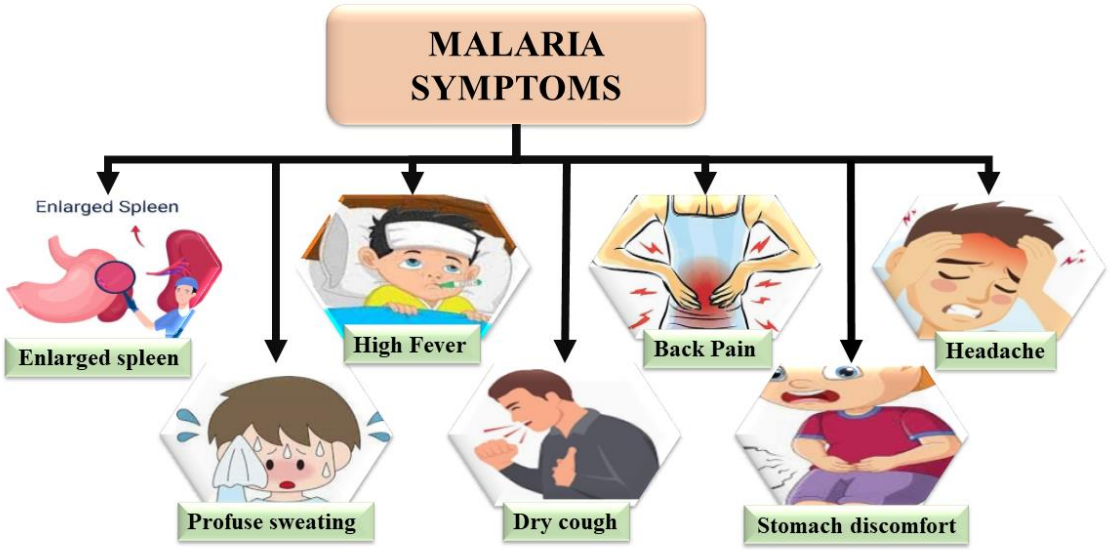

Fig.2: Malaria signs and symptoms.

LIFE CYCLE OF MALARIA PARASITES

The expression of particular proteins is necessary for the survival of the malaria parasite in both vertebrate and invertebrate hosts, due to its intricate life cycle. These proteins are necessary for numerous cell types to enter, for intracellular and extracellular survival, and to evade host immunological reactions. Sporophytes of Pseudomyces falciparum and malariae produce instant schizophrenia when injected into a human host; sporozoites of Pseudomyces ovale and vivax P. can cause delayed schizophrenia after passing through the aforementioned hypnozoite phase (23). Plasmodia go through several stages during their two-host life cycle, just like many other protozoa. Approximately 1 × 7 µm in size, the uninucleate, lancet-shaped sporozoite is the stage that is infectious to humans. In the midgut of vector anopheline mosquitoes, sexual reproduction produces sporozoites, which then go to the salivary gland. Upon biting a human, an infected Anopheles mosquito may inject saliva and sporozoites into tiny blood vessels. It is believed that 30 minutes after inoculation, sporozoites penetrate liver parenchymal cells. The parasite grows into a spherical, multinucleate liver-stage schizont within the liver cell, containing between 2,000 and 40,000 uninucleate merozoites. We refer to this massively amplified process as exoerythrocytic schizogony. The duration of the exoerythrocytic or liver phase of the illness typically ranges from 5 to 21 days, contingent upon the plasmodium species. On the other hand, liver-stage schizont maturation may be postponed for up to a year in cases of P vivax and P ovale infections. Hypnozoites are the name for these inactive liver-phase parasites. The adult schizonts finally burst, releasing thousands of uninucleate merozoites into the bloodstream, regardless of the amount of time needed for growth. One red blood cell can be infected by each merozoite. The merozoite evolves into a spherical or banana-shaped, uninucleate gametocyte or an erythrocytic-stage (blood-stage) schizont within the red cell through the process of erythrocytic schizogony. Upon rupture, the mature erythrocytic-stage schizont releases 8–36 merozoites, each measuring 5–10 µm in length, into the bloodstream. These merozoites then infect erythrocytes in a subsequent generation. The traditional periodicity of fever in malaria is caused by the length of time needed for erythrocytic schizogony, which establishes the interval between the release of consecutive generations of merozoites. This duration varies depending on the species of plasmodium. When ingested by mosquitoes while feeding, the plasmodium's gametocyte, or sexual stage, becomes infectious. Gametocytes within the mosquito grow into male and female gametes (macrogametes and microgametes, respectively). These gametes are fertilized, and after two to three weeks, they become sporozoites, which can infect humans. Because of the time lag between sporozoite maturation and mosquito infection, female mosquitoes need to survive for at least two to three weeks in order to spread malaria. In the fight against malaria, this information is crucial (12).

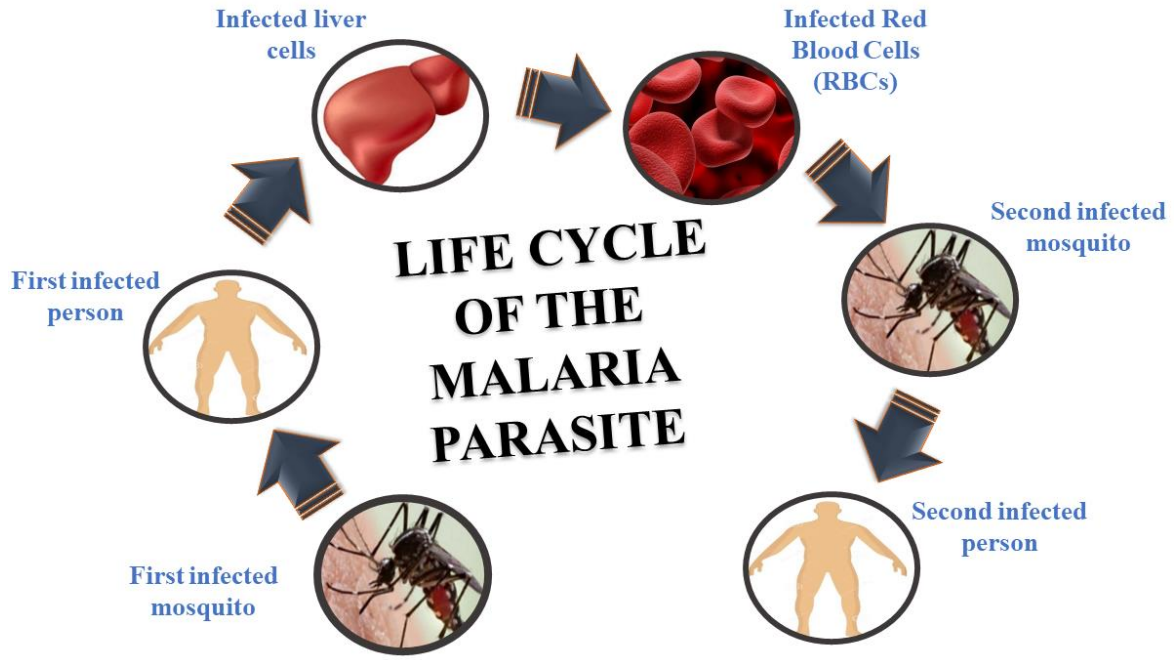

Fig.3: The Malaria Parasite's Life Cycle.

PATHOGENESIS

The life cycle of Plasmodium occurs in two separate hosts: Man is the vertebrate host of the asexual cycle (= schizogony), and the merozoite is the product of schizogony. Sporogony is a sexual disease that primarily affects the invertebrate host, Anopheles. The disease's product is known as a sporozoite. The infectious form of plasmodium known as sporozoites enters human hosts through the bite of a female Anopheles mosquito. Via the bloodstream, they enter the hepatocytes and multiply there to produce merozoites, or pre-erythrocytic schizogony. This is consistent with an incubation phase in which the patient is asymptomatic and non-infectious, and the peripheral blood is sterile. Merozoites are released from ruptured hepatocytes into the bloodstream, where they enter red blood cells to initiate erythrocytic schizogony. A small number either remain latent for a number of years to eventually trigger a relapse of malaria, or they re-enter the hepatocytes (only in the case of P. vivax and P. ovale) to carry out the exo-erythrocyticschizogony. A single merozoite changes into an early trophozoite (ring form), then a late trophozite, and finally goes through multiple mitotic divisions to create the schizont during erthrocytic schizogony within RBCs. This is in line with the prodromal symptoms period. The malarial paroxysm of fever with chills and rigors is caused by the release of many merozoites, which are transformed from the schizont. This occurs when the RBC ruptures. Next, these merozoites invade other RBCs. A small number develop into gametocytes, both male and female. The plasmodium life cycle is completed when female anopheles swallows the blood of an infected human. This is because the gametocytes are consumed by the mosquito and go through a sexual cycle to become sporozoites (4,24).

DIAGNOSIS

❖ **Laboratory Diagnosis**

Nowadays, a variety of laboratory methods are available to confirm and diagnose malaria, including molecular methods like polymerase chain reaction (PCR), rapid malaria diagnostic tests (RDTs), and conventional microscopy techniques. The World Health Organization (WHO) has certified the majority of these for more widespread everyday use. Overall, and as demonstrated by research conducted both domestically and internationally, laboratory- or parasite-based malaria diagnosis is more economical than clinical diagnosis since it guarantees optimal medicine use and, when used wisely, lowers the morbidity associated with malaria and other diseases. Like clinical diagnosis, laboratory diagnostic techniques have their own set of drawbacks, including: i) sensitivity; ii) specificity; iii) accuracy; iv) precision; v) time consumed; vi) cost-effectiveness; vii) labor-intensiveness; viii) the requirement for skilled microscopists; and ix) the issue of inexperienced health workers (both technicians and clinicians) (25–29).

▪ **Rapid Diagnostic Tests (RDTs)**

RDTs are now recognized by the World Health Organization (WHO) as a viable substitute for microscopy in the efficient and timely diagnosis of malaria. They are quick, easy, accurate, and affordable diagnostic tests for detecting the presence of malaria parasites. There are a lot of RDTs on the market right now, under brands including SD Bioline, OptiMAL, Para check, ICT, para-sight-F, and para-screen. Unlike the other microscopy

methods, RDTs are based on the same idea and do not require laboratory equipment to detect malaria antigen in blood flowing along a membrane that contains particular antimalarial antibodies. While some RDTs detect P. falciparum along with other Plasmodium proteins such aldolase or pan-malaria pLDH, the majority of RDTs now in use are protein specific to P. falciparum (either histidine rich protein II -HRP-II or lactase dehydrogenase-LDH). RDT performance has been reported to be excellent in several trials. RDTs are unquestionably improving the advantages of parasite-based malaria diagnosis, however not without issues or restrictions. According to recent reports from both locally and internationally, RDT shortcomings include variations in sensitivity, the inability to be utilized as a "stand-alone" diagnostic test, a lack of confidence among the community and health professionals, and an inability to detect mixed malaria infections (29–37).

- **Molecular Malaria laboratory diagnostic tests**

The use of molecular malaria techniques, such as PCR on blood or, more recently, saliva samples, developed in Zambia by Mharakurwa et al., microarray, mass spectrometry (MS), flow cytometry (FCM) assay, and loop-mediated isothermal amplification (LAMP), is primarily limited to research settings rather than routine patient care. However, new approaches and methods for diagnosing malaria are being provided by these molecular techniques (38,39).

- **Malaria Serological tests**

The basis of serology malaria diagnostic testing is the identification of antibodies directed against blood stage asexual malaria parasites. The most dependable of these tests is apparently immunofluorescence antibody testing (IFA). >1:20 IFA titres are considered positive, <1:20 indicate unconfirmed malaria, and > 1:200 titres indicate recent infections. IFA is easy to use, sensitive, but time-consuming and needs a costly fluorescence microscope in addition to skilled staff (40,41).

❖ **Microscopy**

Ever since Laveran made the first microscopic demonstration and identification of the malaria causal agent, Plasmodium, in 1880, microscopy has remained the "goldstandard" for diagnosing malaria. With the exception of a few minor staining techniques advances made by Romanowsky in the 19th century, almost nothing has changed in the technique. Thin and thick peripheral blood smears are stained (with Giemsa, Wright's, or Field's stains) for the traditional microscopy diagnosis. The method's ease of use, affordability, high specificity, and capacity to determine parasite density have led to its widespread acceptance on a global scale. Research keeps showing how beneficial it is for assisting with the efficient control of malaria in endemic nations like Sub-Saharan Africa, especially in this portion of Southern Africa. Despite having a high specificity, microscopy's sensitivity is regrettably quite limited, particularly at low parasite densities. According to a Tanzanian study involving ten hospitals, more than one-third (39%) of the slides that were first identified as positive were in fact false positives. A related study conducted on 17 outpatient clinics in Kenya revealed that the positive predictive value of "positive" slides was a mere 22%. In fact, O'Meara et al. have also shown that there is a significant inter-expert disagreement in malaria microscopy parasite readings, even among highly skilled microscopy personnel. Staff members, including microscopists, must continue to receive retraining in order to counteract these constraints, and in certain cases, this has shown to be beneficial. Other concentration techniques, including the Quantitative Buffy Coat (QBC), can also strengthen conventional routine microscopy. All things considered, microscopy still presents several difficulties, such as the labor-intensive nature of the procedure, poor sensitivity, the need for advanced diagnostic skills, and the necessity of a minimal infrastructure (microscope, power/electricity, etc.) (26,29,36,42,43).

❖ **Clinical diagnosis**

Malaria is diagnosed clinically by looking at the patient's signs and symptoms, history, and physical examination. It is the most extensively used and least expensive method of diagnosing malaria. The indistinguishable nature of malaria from other illnesses with comparable signs and symptoms, such as pneumonia, sepsis, the human immunodeficiency virus (HIV) infection, influenza, etc., makes clinical identification of malaria difficult and limited at all times. It is true that while clinical diagnosis has a 100% sensitivity, its 0-9% specificity is quite low (44). Due to the non-specificity of malaria symptoms and indications, overdiagnosis of malaria results in overtreatment of the disease and undertreatment of other conditions in malaria-endemic areas. However, in non-endemic places, there are cases of misdiagnosis. Therefore, relying solely on clinical diagnosis leads to a number of issues, as numerous reports have shown. These issues include: i) overdiagnosing malaria; ii) needless morbidity and mortality as other illnesses go undiagnosed and untreated; iii) overtreating and squandering health resources on cases other than malaria; iv) prescribing anti-malarials inappropriately, which contributes to anti-malarial drug resistance; and v) failing to treat other clinical conditions with similar symptoms. Thus, it is crucial to augment clinical diagnosis with laboratory-based diagnosis rather of relying primarily on it (43,45–50).

THE CURRENT POSSIBLE MEDICAL MANAGEMENT FOR MALARIA

Two crucial functions for medications exist in the battle against malaria. Initially, the goal of prompt and efficient therapy for malaria is to stop the disease from getting worse and to stop gametocyte proliferation, which stops the disease from spreading to mosquitoes. Second, medications, such as various chemoprevention techniques, intermittent prophylaxis, and widespread drug use, can be utilized to prevent malaria in endemic populations. Antimalarial drugs are used to both treat and prevent infections with malaria. The red blood cell stage of malaria infection, which is the stage at which the infection produces symptoms, is the target of the majority of antimalarial medications. The majority of antimalarial medications' pre-erythrocytic (liver stage) activity was not fully described when it first appeared in Wuhan, China, in late 2019. The disease is extremely contagious and has a 4.6% global mean death rate (51–53). The three primary classes of antimalarial drugs that are now on the market are derivatives of quinolines, antifolates, and artemisinins. The most used antimalarial medication for treating malaria is quinine. The first antimalarial medication used to treat the disease in the 17th century was quinine, an alkaloid that was extracted from the Cinchona tree's bark. Quinine is still used to treat severe malaria; to shorten treatment duration and limit adverse effects, it is frequently used in conjunction with other antimalarial medications. Due to their low toxicity and adverse effects, ease of production, and favorable pharmacokinetic qualities, quinine and chloroquine are the most researched antimalarials. While isoquine and other intriguing structural analogues have garnered a lot of interest, the lack of systematic synthesis methods to diversify 4-aminoquinoline may have impeded the creation of new medications (54–57). Amodiaquine, Piperaquine, Lumefantrine, Lumefantrine, and Tafenoquine are among the derivatives of artemisinin. Current research shows that compounds with urea and thiourea pharmacophores are effective against different cancer cells and strong inhibitors of human DNA-topoisomerase II (58).

❖ **Anti-malarial Drugs' Pharmacology**

The goal of treating malaria is to get rid of all parasites completely from the body and stop the illness from getting worse. Preventing the infection from spreading to other people and preventing the development and spread of resistance to antimalarial medication therapy are important aspects of treatment. The choice of the right medication, dose, length of therapy, and the medications' safety and effectiveness all affect the treatment's goal. Eleven groups comprise the pharmacological classification of medications used to treat malaria. They are quinoline-methanol, 4-aminoquinolines, biguanides, aminopyrimidines, chinona alkaloids, 8-aminoquinolines, sulfonamides, tetracyclines, amino alcohols, and naphoquinones (59).

❖ **Prevention of malaria**

When those with little or no prior exposure get malaria, the illness can proceed quickly to a severe and frequently deadly state. Chemoprophylaxis and avoiding the mosquito vector can prevent the majority of malaria cases in the United States.

From nightfall to dawn, the female Anopheles mosquito eats. Wearing protective clothing, using insect repellent containing N,N-diethyl-l-m-toluamide (DEET), staying in screened areas and spraying these areas with pyrethrum-containing insecticides, and sleeping under insecticide-impregnated bednets are some ways that people can avoid contact with mosquitoes during these hours (60). Travelers to endemic regions should receive advice on chemoprophylaxis as well as how to avoid the mosquito vector. It is important to note that chemoprophylaxis is not 100% successful; in the event that a person has traveled to an area where malaria is endemic in the previous two to three years, malaria must be taken into consideration in the differential diagnosis of any feverish condition. Chemoprophylaxis aims to eliminate the parasite after it has entered the body but before it can cause the host red blood cells to burst, which results in malaria symptoms. Medication may do this by targeting the parasite in the blood or liver. The goal of causal chemoprophylaxis is to eradicate the parasite in the liver before it has a chance to enter the bloodstream. Drugs that target blood-borne asexual parasites are used to achieve suppressive chemoprophylaxis. Since most antimalarial medications target blood-borne parasites, they are suppressive chemoprophylactics. The only antimalarial medication on the market that consistently eradicates organisms at the liver stage is primaquine. The individual's health (including variables like pregnancy, age, and chronic illness); the risk and kinds of malaria in the places to be visited; and the existence of drug-resistant P falciparum all influence the choice of chemoprophylactic regimen. For travelers visiting regions such as Mexico, Central America, Haiti, the Dominican Republic, and the Middle East where plasmodia are still susceptible to chloroquine, chloroquine is the advised chemoprophylactic. Chloroquine has extremely few contraindications. Nonetheless, the majority of tourists go to places where chloroquine resistance exists and alternative medications-typically more toxic-must be taken (61). Doxycycline is a suitable substitute for mefloquine, which is the preferred medication for the majority of these travelers. People traveling outside of Thailand prefer to take doxycycline due to widespread mefloquine resistance. Another viable regimen for chloroquine-resistant areas is mefloquine or doxycycline plus proguanil (proguanil is not accessible in the United States). However, this regimen is substantially less effective than mefloquine or doxycycline. Furthermore, recent research indicates that primaquine, which appears to operate against organisms in the liver stage, is just as efficient as mefloquine and

doxycycline for chemoprophylaxis in regions where chloroquine resistance is present (62). Chloroquine or mefloquine prophylaxis should start two weeks prior to entering the malaria-affected area (to ensure medication tolerance and to give acceptable blood levels). It should continue for four weeks after leaving the area as well as during the duration of the stay. Beginning one to two days prior to travel to a malaria-prone location, doxycycline should be taken every day while in the area and for four weeks following departure. Terminal prophylaxis, or taking the medication after leaving the contaminated region, is required to eradicate organisms that reappear in the liver after the patient goes home (63). To eradicate any residual liver stage parasites, primaquine should be administered for 14 days after returning home if there was a substantial chance of exposure to P vivax or P ovale. Anytime during the four weeks that the blood schizonticide is being administered, primaquine may be given (12,64).

DIFFICULTIES FOR PATIENTS WITH SERIOUS MALARIA

- **Pulmonary complications**

The patient's incapacity to wake up with a Glasgow score of 9 or below, the presence of the parasite P. falciparum, and additional factors (such as the fact that acute lung injury typically happens many days after the sickness starts) Even after a first response to treating malaria and getting rid of parasites, disease might spread quickly. Usually not related to the heart, pulmonary edema can develop into acute respiratory distress syndrome (ARDS), which is characterized by elevated blood pressure. Permeability of pulmonary capillaries Acute lung damage and a blood pressure/oxygen/inspiratory oxygen fraction of 200 mmHg or below are characterized as ARDS (65,66).

- **Renal complications**

Rarely nonoliguric, acute renal failure is typically oliguric (<400 ml/day) or anuric (<50 ml/day), and it may necessitate short-term dialysis. Usually, urine sediment is not very interesting. Acute tubular necrosis may arise in extreme situations as a result of renal ischemia (65,67).

- **Neurologic complications**

When adults contract severe malaria, cerebral malaria is the most prevalent clinical manifestation and cause of mortality. The. In order to be considered strictly as cerebral malaria, hypoglycemia, bacterial meningitis, and viral encephalitis must be ruled out (68).

II. CONCLUSION AND FUTURE DIRECTION

The first section of our review articles goes into extensive detail on the aetiology, pathophysiology, epidemiology, life cycle, and existing treatments for malaria, in addition to its signs and symptoms. Pharmaceutical medications have benefits, but they often have drawbacks, such as renal damage. More randomized controlled studies are needed to find out more about the most effective malaria treatment. We wish to continue our efforts on malaria research. In order to evaluate patients' physical and mental health and to provide a more thorough understanding of malaria and its improved treatment, a second study with counseling will be conducted in our nation or state with the help of our colleagues.

ETHICAL STATEMENT

Along with the right medications, a skilled pharmacist provides patients with empathy and understanding.

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CONFLICT OF INTEREST

The authors attest that they are free of any known financial or personal conflicts of interest that would taint the findings of this study.

INFORMED CONSENT

Using websites, review articles, and other sources to produce research content.

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