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Review Article

An Overview of the many Methods that may be used to Diagnose and Treat Malaria

Abdulaziz Radhi S AL Johni[1]*, Omar Ali H Alsariry[2], Mohanad Mohammad Ayash[3], Amal Mohammed A Alaslai[4], Mohammed Ali Jaber Khubrani[5], Mariam Ahmed M A Yamani[6] and Amirah Ahmed M Alyamani[7]

[1]Ph.D. Microbiology Department of Laboratory at King Fahad Hospital, Medina, Saudi Arabia

[2]Technician Pharmacy Shmeisy Medical Complex Makkah, Saudi Arabia

[3]Technician Pharmacist Assistant Shmeisy Medical Complex Makkah, Saudi Arabia

[4]Non-physician Medical Education Specialists King Abdul-Aziz Hospital in Makkah, Saudi Arabia

[5]Lap Technicial Shmeisy Medical Complex in Makkah, Saudi Arabia

[6]Clinical Laboratory Sciences king Abdul-Aziz hospital in Makkah, Saudi Arabia

***Corresponding Author:** Abdulaziz Radhi S Al Johni, Ph.D Microbiology Department of Laboratory at King Fahad Hospital, Medina, Saudi Arabia.

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Abstract

The global spread of malaria is a serious public health concern. Parasites belonging to the genus Plasmodium are responsible for this condition. Plasmodium falciparum and Plasmodium vivax are responsible for the vast majority of human malaria cases, however the former is the more dangerous species. During their blood stages, Plasmodium falciparum and Plasmodium vivax cause similar anemia. Nearly a third of all malaria deaths are attributable to severe cases of malarial anemia induced by P falciparum. Multiple factors seem to contribute to malaria-related anemia. Red blood cell clearance increases and bone marrow erythropoiesis decreases characterize this condition. Still poorly understood at the molecular level are the mechanisms that cause malarial anemia. Malaria parasite ligands have been investigated for their potential roles in the destruction of adult erythrocytes and the remodeling of younger erythrocytes. The risk of developing severe malarial anemia has been linked to polymorphisms in cytokines. It is believed that the goal of these cytokines and the "toxins" generated by malaria is to interfere with erythropoiesis. The inflammation brought on by malaria is likely to be exacerbated by co-infections, making malarial anemia more likely to develop [1].

Keywords: The Origins of Malaria; Cause of malaria; Malaria as a Cause of Poverty; Types of malaria; symptoms; Diagnosis; Treatment

Introduction

Malaria is one of the most prevalent parasitic diseases seen around the world. It is caused by the parasites Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, and Plasmodium ovale, in addition to additional zoonotic malaria parasites as Plasmodium knowlesi [1]. There are now 95 nations in which an estimated 3.2 billion people are at risk of contracting the malaria parasite [2].

According to the latest recent estimate from the World Health Organization (WHO), there were 212 million new cases of malaria worldwide in 2015 [2]. (range 148 million to 304 million). Africa accounted for the majority of reported cases of malaria across the globe (90%), followed by Southeast Asia (7%) and the Eastern Mediterranean (2%) respectively. This high endemicity all over the world is responsible for what is estimated to be 429,000 deaths (with a margin of error ranging from 235,000 to 639,000). Children less than five years old accounted for 306,000 of the total fatalities. Estimates suggest that the African area of the WHO was the location of 92% of the fatalities that occurred in 2015, while the Southeast Asian region of the WHO was responsible for 6% of the fatalities, and the Eastern Mediterranean region of the WHO was responsible for 2% of the fatalities. P. falciparum is by far the most lethal of the malaria parasites that can infect humans, and it is responsible for 99% of all deaths that are caused by malaria. These figures from the WHO witness to the severity of the current malaria epidemic and the consequences it is having on the well-being of people all around the world [2].

The World Health Organization (WHO) has developed a Global Technical Strategy for Malaria 2016-2030, which includes a list of objectives that are intended to be completed by the year 2030 [3]. These include the eradication of malaria in at least 35 countries where it was still present in 2015, a reduction in the global incidence and death rates of malaria of at least 90 percent by 2030 compared to the levels seen in 2015, and the prevention of the spread of malaria in all countries that are currently free of the disease. These WHO targets are geared toward achieving the relevant Sustainable Development Goal, which calls for the eradication of AIDS, tuberculosis, malaria, and other pandemics associated with neglected tropical diseases by the year 2030 [4].

Malaria is now only found in the southwest region of the kingdom, which includes the areas of Aseer and Jazan. This is due to the fact that the national malaria control program in Saudi Arabia, which was initiated in 1948, has significantly reduced the number of cases of malaria that are reported each year. The World Health Organization (WHO) has included Saudi Arabia in the E-2020 initiative, which has the objective of reaching the target of zero autochthonous illnesses by the year 2020 [5]. The number of instances of autochthonous or indigenous (locally transmitted) malaria in the nation had a significant reduction between the years 2000 and 2014, going from 511 in 2000 to barely 30 in 2014 [6]. After 2014, however, there was an increase in the number of cases, which resulted in 5,382 cases of malaria being documented in 2016 [6, 7], including 272 cases that were locally transmitted (270 falciparum and 2 vivax malaria). This number of incidents is considerable when compared to international norms; hence, the government is still dedicated to making major efforts toward being compliant with E-2020.

Researchers from a variety of institutions have been looking at Saudi Arabia's efforts to rid the country of malaria by the year 2014 [7, 8].

The Origins of Malaria

In 1880, a French military surgeon named Alphonse Laveran made the discovery of the protozoan parasite while serving in Algeria. Laveran was stationed in Algeria at the time. The Nobel Prize in Physiology or Medicine was bestowed to him in 1907 as a token of appreciation for the work he had done in this field. In the year 1890, two researchers from Italy named Grassi and Filetti made the discovery that the parasites Plasmodium vivax and Plasmodium malaria were the same. In 1897, a researcher from the United States of America gave the parasite the name Plasmodium falciparum. P. ovale was the designation that Stephens gave to the fourth and last species in 1922. In the year 1897, in the city of Calcutta, India, an officer in the Indian Medical Service named Sir Ronald Ross made the discovery that mosquitoes are capable of passing malaria from one bird to another. In 1902, the Nobel Prize in Physiology or Medicine was bestowed to Sir Ronald Ross for this study. Since the beginning of human history, people have been aware of the disease known as malaria. Around 7,000 to 12,000 years ago, there were many bodies of water and pools of water due to an increase in temperature in Africa, a rise in humidity that generated new water sources, and the development of agriculture in the Middle East and North East Africa. These factors all contributed to the presence of a great deal of water. As a consequence of this, the environment and location became favorable for the growth of the parasites that cause malaria and for the transmission of the disease by the mosquito that is responsible for spreading it [5].

Cause of Malaria

Poverty as a Cause of Malaria

Because it increases a person's likelihood of contracting the disease, poverty is a contributor to the progression of malaria. People living in poverty are more likely to have dwellings where mosquitoes may flourish. It has been shown that the characteristics of the wall construction are connected to the prevalence of the disease malaria. It is impossible for those with the lowest incomes to afford preventative treatments like insecticide-treated bednets since these procedures require payment [10].

Expenses incurred by a family due to malaria include out-of-pocket payments for travel, fees associated with consultations, the cost of drugs, and the cost of meals at a distant medical facility. It's possible that these costs are prohibitive for low-income families, so they could put off seeking treatment in anticipation that their loved one will get well on their own, or they might skip medical attention altogether. When appropriate treatment is expensive, other coping techniques include utilizing pharmaceuticals obtained from friends and neighbors, sharing medicines with siblings who are also sick, and conserving some tablets for the next disease episode after the child has recovered from the current one. This practice is common in households that have a number of young children: In most cases, just the youngest or sickest child is sent to the hospital, while the other children in the family are given medicine to take care of their symptoms. This approach not only has an effect on the final outcomes of the therapy, but it also contributes to the evolution of medicine resistance [11].

It is typical for those at the bottom of the economic ladder to lack simple access to medical treatment, particularly in rural regions. This is notably the case in the United States. They often live in remote areas that are difficult to reach because of a lack of financial resources and transportation infrastructure. However, in addition to the financial burden and difficulty of gaining access, there are other obstacles that prevent individuals from accessing treatment and prophylaxis for malaria. Social and cultural marginalization is one of the most powerful elements that both encourage the spread of illness and makes it more difficult to get medical care. The implementation of healthcare models that require patients to pay for the services they get in order to reduce overall government spending has another effect on access to treatment. Access to health care for the poor has been hampered by the imposition of user fees [12].

The lack of economic opportunity in rural areas is often the driving force behind migration to metropolitan centers. The fast and uncontrolled urban growth that occurs on the outskirts of towns and cities in tropical countries leads to the establishment of conditions that are suitable for the spread of malaria. People who move to urban areas from more rural areas sometimes end up living in substandard housing in densely populated, underdeveloped periurban areas. These people carry with them their traditions and routines from the countryside, which may foster the growth of mosquitoes [13].

To earn a livelihood in agriculture, road construction, logging, and gem mining, poverty drives people daily into malaria-infested jungles and woodlands. For instance, colonization initiatives in the Brazilian Amazon have attracted nonimmune settlers for agricultural purposes, which has resulted in a proliferation of malaria vectors in artificial habitats. This is due to the fact that agricultural purposes are the primary motivation for these settlers. Inadequate housing, logistical challenges for disease management, significant population movement, a lack of disease awareness, and the poverty of new settlers are all factors that contribute to the deterioration of the situation and provide ideal circumstances for the explosive outbreak of epidemics. In many cases, an insufficient amount of nourishment contributes to the severity of these epidemics [14].

If people are unable to work because of malaria, there may be less food available for consumption in many rural areas of Africa, which is where the bulk of the population lives and where subsistence agriculture is practiced. Even a brief period of illness may have profound repercussions on the financial stability and nutritional well-being of families and communities. Planting and harvesting seasons tend to coincide with times of the year when there is a significant risk of transmission. There is a correlation between malnutrition which is rich in calories but poor in protein and increased rates of malaria morbidity and mortality [15].

There is evidence to suggest that the perceived risk of malaria could impact crop choices as a coping mechanism in case a labor scarcity is brought on by malaria. As a result, farmers would choose crops that need less work in comparison to those that are more profitable [16].

It is common practice to evaluate the effects of malaria on families in the near term; nevertheless, it is anticipated that malaria would, over time, have an effect on levels of poverty and vulnerability at the household level [16].

Many studies don't look at how households and businesses change their ways of making money or getting by based on how many people have malaria. In rural Kenya, where a study was done, the most common way for household members to make up for lost work time was to work for each other. Most of the time, households paid for direct costs by using their savings and cash on hand, selling animals, or getting gifts from other households. These plans can backfire and make it harder for a family to deal with other problems in the future [16].

The potential for malaria infection may have a broad variety of implications on economic behavior, planning, and incentives. Because malaria is so widespread, some of the expenditures that are associated with it will someday be reduced or eliminated altogether: War, which drives millions of people from their homes and destroys what little infrastructure they have, unhealthy working conditions, and poverty, which makes it difficult for individuals and countries to pay for preventative measures and high-quality medical care are all factors that contribute to global poverty. In this scenario, the mere presence of malaria in a community results in expenses for the whole group. This is due to the fact that social and economic choices are altered depending on how probable individuals believe they are to get ill. The danger of malaria influences a variety of choices, including those in agriculture, commerce, investments, and fertility. This may have a significant impact on the rate of economic growth as well as productivity. Studies that are often conducted in households are unable to quantify these impacts, and as a result, they do not demonstrate them. One example of this kind of cost is the way that the fear of malaria may make it less probable for a country to engage in international commerce and investment. Malaria has the potential to become an even more serious issue in a global economy that is undergoing rapid transformation, further isolating an already impoverished African continent [16].

Types of malaria

There are five types of Malaria

Plasmodium falciparum (P. faliparum)

The most severe form of the disease's symptoms. It is most widespread in sub-Saharan Africa, although it may be found all throughout Africa. The most current figures indicate that cases are now being reported in places of the world where it was previously thought that this species had been eradicated completely.

Plasmodium vivax (P. vivax)

In most instances, the less severe form of the sickness does not pose a risk of death. However, sick animals still need treatment since the growth of the illness, if left untreated, may lead to a number of other health concerns. This species has the widest geographic distribution throughout the whole planet. P. vivax is responsible for around sixty percent of the infections that occur in India. This parasite goes through a stage in which it lives in the liver, and it may stay in its host for years without causing sickness. If the patient is not treated, the liver stage of the malaria parasite may become active again, even if it has been dormant for many months or even years, and cause relapses, also known as malaria episodes.

Plasmodium malaria (P. malaria)

The less severe type of illness does not often result in death for the patient. However, the sick animal still has to be treated since avoiding treatment may also result in many negative effects on the animal's health. This particular form of parasite has been present in the blood of certain individuals for more than three decades.

Plasmodium ovale (P. ovale)

In most cases, the less severe version of the disease does not result in fatalities. However, treatment is necessary for the sick individual since the infection may get more severe and lead to a variety of adverse health effects. This particular parasite has a stage that takes place in the liver, and it is capable of surviving inside of a human for years without causing illness. In the event that the patient is not treated, the liver stage of the parasite may become active once more, which may result in a second attack of malaria several months or even years after the patient's most recent episode.

Plasmodium knowlesi (P. knowlesi)

Malaria is produced in macaques, but it may potentially infect people.

Symptoms

Symptoms of malaria often appear anywhere from 10 days to one month following infection. The symptoms might change based on the kind of parasite that is present. After being bitten by a mosquito, some people may not experience any symptoms of illness for up to an entire year. Parasites may live inside of a host for a number of years without causing any noticeable symptoms. Malaria may come back in many different forms depending on the parasite that causes it. Before being released into your circulation, the parasites lie dormant in your liver for years at a time. When the parasites make a comeback, so do the symptoms they caused. The signs and symptoms of malaria are often confused with those of the flu. They are composed of.

The flu-like symptoms of shivering chills, a headache, and painful muscles, as well as feeling weary and feverish, are common symptoms of malaria. It's also possible that you'll feel queasy, vomit up, or have diarrhea. Malaria may result in the loss of red blood cells, which can lead to anemia as well as jaundice, which is characterized by a yellowing of the skin and eyes. In the event that the infection is not treated as soon as it is discovered, the condition might worsen and result in renal failure, convulsions, mental disorientation, coma, or even death.

It usually takes between 10 and 4 weeks for a person to start feeling unwell after being infected with the virus, but it can take as little as 7 days or as long as a year. There are two different strains of malaria, P. vivax, and P. ovale, that have the potential to reappear (relapsing malaria). After a person is bitten by an infected mosquito, some of the parasites that cause P. vivax and P. ovale infections can remain latent in the liver for a few months to roughly four years. "Relapse" is the term used to describe what happens when these parasites awaken from their dormant state and begin taking over red blood cells. This causes the host to get ill.

When they first get sick, most people have fever, sweats, chills, headaches, malaise, muscle aches, nausea, and vomiting. Malaria can quickly become a very bad disease that can kill you. The best way for you and your doctor to know for sure if you have malaria is for a drop of your blood to be looked at under a microscope to see if there are malaria parasites. If you are sick and there is any reason to think you might have malaria like if you just got back from a trip to a country where malaria is common, the test should be done right away.

Malaria infection and Pregnancy

Pregnant women, particularly those carrying their first child, have an increased risk of contracting malaria. It has been proven that the severity of the illness lessens with each successive pregnancy that a woman has. The production of antibodies against variable surface antigens (VSA) such as PfEMP-1, refine, and savors is considered to be the cause of this phenomenon. Because these antigens are identified on parasitized RBCs that infect the placenta, they are sometimes referred to as Variant Surface Antigens of Pregnancy-Associated Malaria (VSA-PAM). It is necessary to investigate the ways in which the immune system is affected by the biological components connected to malaria in the absence of symptoms. There is a connection between high levels of IL-10 and G-CSF in the blood of pregnant women who have no symptoms, according to studies that looked at cytokines and growth factors in pregnant women [17, 18].

Diagnosis

Rapid diagnosis of malaria is essential for ensuring that patients receive treatment as soon as possible and that the disease is not disseminated further by local mosquito populations.

Because it has the potential to be a life-threatening condition, malaria has to be treated as though it were an emergency. Patients diagnosed with malaria who are unable to receive treatment in a timely manner are the primary cause of mortality in the United States.

It is possible to diagnose malaria in a patient by considering where they have traveled, how they are feeling, and what the attending physician observes when they examine them. However, the final diagnosis requires that laboratory testing demonstrated the presence of malaria parasites or sections of parasites [1].

The parasitological confirmation of a malaria diagnosis using optical microscopy or lateral flow immunochromatography has to be done as promptly and correctly as possible so that appropriate disease treatment may be administered [19]. Blood smears taken from fever are used to determine whether or not a patient needs immediate medical attention or has died from malaria. Malaria can become more severe if the diagnosis is delayed for too long. Because they are more dense, blood smears that contain a higher number of parasites are simpler to identify. Malaria species may be identified using thin smears. In regions where malaria is prevalent, fevers are frequently mistaken as being caused by malaria, particularly in children. Even if a blood smear or microscopic test for malaria comes back negative, the disease may frequently be detected and treated in a clinical setting. Children who are diagnosed and treated for malaria without the use of microscopic confirmation frequently pass either as a result of a mistake or because they did not receive treatment for another condition [20]. Evidence of severe falciparum malaria may be seen in the form of parasitized red blood cells, P. falciparum schizonts, and pigment deposits in peripheral polymorphonuclear leukocytes. 11 Although serological testing can reveal a history of malaria infection, they are not helpful in treating acute infections. Babies and young children are unable to utilize them because maternal antibodies prevent them. Diagnostic tools for malaria include rapid dipstick and polymerase chain reaction (PCR) assays [20].

A clinical diagnosis is arrived at by taking into account both the patient's symptoms and the findings of the doctor's physical examination of the patient.

The earliest symptoms of malaria, which are often fever, chills, sweats, headaches, muscular pains, nausea, and vomiting, are not always obvious and can also be caused by other illnesses, such as the flu or common viral infections. Malaria is a parasitic disease spread by mosquitoes. Additionally, the outcomes of the physical examinations are not always crystal apparent (elevated temperature, perspiration, tiredness).

Plasmodium falciparum is the parasite that often causes severe malaria, which is characterized by more obvious symptoms such as disorientation, coma, focal neurologic indications, severe anemia, and difficulty breathing. Because of this, the likelihood of someone having malaria may increase [18].

The results of malaria tests conducted in the laboratory should always support what is observed in the clinic. The healthcare practitioner should undertake an initial workup and order a full blood count and a regular chemistry panel in addition to ordering the malaria-specific diagnostic tests that are described below. If the person does have a positive test for malaria, these further tests will assist determine the severity of the infection and determine whether or not treatment is necessary. These tests are particularly useful for diagnosing severe cases of anemia, low blood sugar, renal failure, elevated bilirubin levels, and acid-base imbalances [20].

Malaria parasites can be identified by the process of placing a drop of the patient's blood on a microscope slide and spreading it out in the manner of a "blood smear." Following that, the drop is examined by means of a microscope. Before the sample is examined, it is dyed, and the Giemsa stain is the one that is typically used. This gives the parasites a distinct appearance. This test is still the most accurate approach for a laboratory to determine whether or not a patient has malaria. However, this is contingent on the quality of the reagents, the microscope, and the level of expertise possessed by the laboratory technician.

Molecular Diagnosis The polymerase chain reaction is utilized in the process of locating the parasites' nucleic acids (PCR). Even though this approach could be a bit more sensitive than smear microscopy, it is not particularly effective for identifying patients who are extremely unwell in a normal hospital scenario. This is because smear microscopy is the gold standard for making such diagnoses. The majority of the time, the findings of PCR tests do not come back quickly enough to be of any assistance in making a diagnosis of malaria. After the diagnosis of malaria has already been determined by smear microscopy or an RDT, PCR is most useful for confirming the species of the malarial parasite that is present.

Serology employs either enzyme-linked immunosorbent assay (ELISA) or indirect immunofluorescence (IFA) to identify antibodies against malaria parasites (ELISA). The purpose of serology is not to detect active illnesses; rather, it determines how long ago a person was exposed to a pathogen.

Drug resistance tests and Tests need to be conducted in specialist labs in order to determine whether or not the parasites taken from a particular patient are responsive to antimalarial chemicals. There are primarily two types of laboratory procedures: Tests performed in vitro: The parasites are cultured in a dish in the laboratory with progressively higher concentrations of the medications. The amount of medicine that is effective enough to stop the growth of the parasites is the endpoint. Molecular characterization: PCR or gene sequencing may also be used to look at molecular markers that can be used to predict certain drug resistance. This can be done in the context of the study of drug resistance. The Centers for Disease Control and Prevention (CDC) recommends that each and all cases of malaria that are discovered in the United States be investigated for possible indications of medication resistance [20].

Treatment

Malaria, which may be treated, is responsible for the deaths of over 600,000 people every year. In order to properly treat malaria and keep the disease under control, it is necessary to diagnose the condition at an early stage and begin treatment as soon as possible. The artemisinin-based combination treatments (ACTs) are now the most effective treatment that is available, particularly for the strain of

malaria caused by P. falciparum (ACTs). The elimination of all Plasmodium parasites from a patient's circulation in the shortest amount of time and in the most thorough manner feasible is the primary objective of the treatment. A straightforward case of malaria does not develop into a serious illness or result in death thanks to this measure. By decreasing the size of the infectious reservoir and putting a stop to the development and spread of drug resistance to antimalarial medications, effective treatment not only makes it less likely that the infection will be passed on to other people, but it also has positive implications for public health. Microscopy or a rapid diagnostic test (RDT) should be done to confirm the parasitological diagnosis of malaria in a person before antimalarial therapy is administered to that individual since there is a possibility that they have the disease. Only provide therapy that is based on clinical evidence in the event that diagnostic testing cannot be performed on the patient immediately or within two hours of their arrival for treatment. Anti-malarial medication that is both effective and secure has to be administered within twenty-four hours after the initial fever in order to treat malaria. This is the only treatment that will heal the condition and keep any potentially fatal consequences at bay.

It is believed that the usage of oral artemisinin-based monotherapy (also known as GMAT), is one of the key factors that led to the emergence and subsequent dissemination of artemisinin resistance. The World Health Organization (WHO) has requested that nations that experience a high rate of malaria cease production and distribution of ACTs, as well as provide assistance to individuals in gaining access to ACTs that have been evaluated for their level of effectiveness against falciparum malaria [22, 23].

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