An Analysis of Several Aspects of Malaria

Dr Jyotirmaya Sahoo, Professor

Department of Health & Allied Science, Arka Jain University, Jamshedpur, Jharkhand, India

Email Id- dr.jyotirmaya@arkajainuniversity.ac.in

ABSTRACT: ***Malaria is a serious illness caused by Plasmodium parasites that is spread to humans via the bite of an infected female mosquito of the Anopheles species. Malaria is still the world's top cause of death, and early detection and treatment may help avoid negative consequences. Malaria is the most prevalent illness in Africa and certain Asian nations, while it is imported from endemic regions in the industrialized world. In China, the sweet sagewort plant was used to cure malaria fever as early as the second century BC. Quinine was first utilized as an antimalaria medication many years later. In 1955, the worldwide fight against malaria began, and Croatia proclaimed 1964 to be the year of malaria eradication. Malaria is controlled by the World Health Organization on a worldwide scale, with an emphasis on local strengthening of primary health care, early illness diagnosis, prompt treatment, and disease prevention. Malaria is now less prevalent globally than it was 10 years ago. However, there has been a rise in the number of malaria cases worldwide in recent years. It is making progress toward the WHO's goals, albeit at a slower pace.***

KEYWORDS: ***Antigen, Disease, Malaria, Parasite, Plasmodium.***

1. INTRODUCTION

Malaria afflicted an estimated 219 million people worldwide in 2017, killing 435,000 people. More than a century of worldwide effort and research targeted at improving malaria prevention, diagnosis, and treatment has resulted in this burden of illness and death. Malaria is the most prevalent illness in Africa and Asia, with the greatest number of indigenous cases in certain nations. Malaria death rates vary from 0.3 to 2.2 percent worldwide, and from 11 to 30 percent in tropical climates when severe forms of malaria are present. According to several research, the frequency of malaria parasite infection has risen since 2015. Malaria is caused by a tiny protozoon belonging to the Plasmodium species group, which includes various subspecies. Plasmodium species may cause illness in humans. Plasmodium is an internal amoeboid parasite that accumulates malaria pigment (an insoluble metabolite of hemoglobin). Parasites on various vertebrates; some are found in red blood cells, while others are found in tissue. Only five of the 172 Plasmodium species may infect humans. The zoonotic malaria P.knowlesi has been discovered in Southeast Asia. Humans are seldom infected by other animals. The illness known as malaria is caused by all of the Plasmodium species listed. Similarly, all species have morphology and biology that are identical[1].

Plasmodium has a complicated life cycle that is divided into two phases: sexual and asexual, vector mosquitoes and vertebrate hosts. The sexual phase of the parasite's life cycle occurs in the vectors, mosquitoes. Humans, the intermediate host for malaria, go through the asexual phase of the life cycle. Only female mosquitoes of the species Anopheles transmit human malaria. After being bitten by an infected female mosquito, the parasite, in the form of sporozoite, enters human blood and, after half an hour of blood circulation, reaches the hepatocyte. Plasmodium asexual development begins in the hepatocytes and continues in the erythrocytes. The rupture of erythrocytes is caused by all Plasmodium species[2].

1.1 Discovery of Malaria:

Malaria outbreaks are thought to have a long history dating back to the dawn of civilisation. It is the most common illness, and many people have died as a result of it. It is also believed to be the cause of significant military losses and the extinction of certain countries. Malaria was first described around 2700 BC in ancient Chinese medical documents, and 1200 years later in the Ebers Papyrus. Malaria killed Alexander the Great, the military commander. The fact that Christopher Columbus, Albrecht Dürer, Cesare Borgia, and George Washington all suffered from the illness shows that it was prevalent across society. Despite the fact that the ancient people were regularly exposed to malaria and its symptoms, the fever that afflicted patients was ascribed to a variety of supernatural forces and furious divinities. As a result, the Assyrian-Babylonian god Nergal, like the Canaan Zebub, was depicted as a stylised two-winged bug. Hippocrates characterized the illness in the 4th century BC in a manner that totally refuted its demonic roots, instead linking it to

evaporation from marshes, which produced the disease when breathed. That interpretation was held until 1880, when Laveran discovered the disease's etiology. Laveran, a French military physician, was the first to detect parasites in the blood of malaria victims, and he was awarded the Nobel Prize in 1907 for his discovery. Malaria, according to Cartwright and Biddis, is the most common African illness. Malaria is caused by a tiny protozoon belonging to the Plasmodium species group, which includes various subspecies[3].

1.2 The Development of Diagnostic Tests for Proving Malaria through History:

If left untreated, malaria may persist three to five years and, depending on the cause, may recur. The persistence of merozoites in the blood or hypnozoites in hepatocytes may induce recurrence months or years after the original infection in P. vivax and ovale infections. In Southeast Asia, vivax malaria recurrence is also frequent following P. falciparum infection. Infections with P. falciparum have been known to relapse, resulting in a fast rise in parasitemia and subsequent erythrocyte destruction. Malaria infection is particularly dangerous for children, pregnant women, immunocompromised and splenectomized patients, as well as healthy individuals who have never been exposed to Plasmodium. A malaria laboratory test should always be used to corroborate clinical results. Direct techniques, such as proof of parasites or portions of parasites, and indirect ones, such as demonstrating antibodies to the causal agents, are used to confirm malaria[4].

The gold standard technique for diagnosing malaria is light microscopy of Giemsa-stained blood films. This technique is not accessible in many areas of Sub-Saharan Africa due to a lack of appropriate staining material and qualified personnel. The method's sensitivity is dependent on the expert's knowledge, and an infection may be detected with 10–100 parasites/L of blood. A negative result in individuals with symptoms does not rule out malaria, but if the illness is still suspected, smears should be performed three times at 12-hour intervals. Immunofluorescence antibody testing has historically been used to diagnose malaria via serologic testing (IFA). IFA takes time and is subjective. It's useful for assessing potential blood donors in epidemiological research. Fluorescence microscopy and trained technicians are also required[5].

Rapid Diagnostic Assays (RDT) for antigen detection in the blood are immunological chromatographic tests that may be used to verify the presence of parasite antigens. These tests do not need the use of any electrical equipment, nor do they necessitate any particular knowledge or abilities. RDTs are currently recommended by WHO as the first-line test in all malaria-endemic regions throughout the globe. The antigen test's sensitivity varies based on the antigens represented in the test. Some RDTs have 50–100 parasites per liter (PfHRP2) to 100 parasites per liter.

In 2007, the FDA authorized the first RDT test. It is advised that all RDT test findings be verified via microscopic blood analysis. Antigens identified by RDT tests are known to persist in the blood following antimalarial therapy, although the presence of these antigens varies. The percentage of false positives should be fewer than 10%. Several RDT tests showed malaria at a low density parasite (200 parasites/L) in the eight rounds of testing, had low false-positive rates, and could identify P. falciparum or P. vivax infections or both. P. vivax false-positive rates were usually low, ranging between 5% and 15%. P. falciparum, on the other hand, has a false-positive rate of 3–32 percent. If the parasite density is low or if fluctuations in parasite antigen production limit the RDT's capacity to detect the parasite, good RDTs may sometimes produce false-negative findings. The percentage of false negative RDT test findings for P. falciparum varied from 1% to 11%. RDTs have an overall sensitivity of 82 percent (with a range of 81–99 percent) and a specificity of 89 percent (with a range of 88–99 percent)[6].

1.3 Malaria Treatment through History:

In China, a sweet sagewort plant known as Qinghai (Latin Artemisia annua) was used to cure malaria as early as the 2nd century BC. Much later, in the 16th century, Spanish conquerors in Peru took over the cinchona malaria medicine made from the Cinchona tree's bark (Latin Cinchona succirubra). In 1820, French scientists Pierre Joseph Pelletie and Joseph Bienaimé Caventou discovered the active component quinine from this plant, which had been employed in the chemoprophylaxis and treatment of malaria for many years. In 1970, a group of Chinese scientists headed by Dr. Youyou Tu discovered the antimalarial artemisinin from the herb Artemisia annua, which has shown to be extremely effective in the treatment of malaria. Youyou Tu was awarded the Nobel Prize in Physiology or Medicine in 2015 for this discovery.

The majority of artemisinin-related medicines on the market today are prodrugs that are activated by hydrolysis into the metabolite dihydroartemisinin. Antimalarial action of artemisinin medicines is mediated by the formation of a radical through a peroxide bond. To guarantee a high cure rate of P. falciparum malaria and prevent the development of drug resistance, WHO advises the use of artemisinin-based combination treatments (ACT). Because of the significant resistance to chloroquine, sulfadoxine-pyrimethamine, and amodiaquine, ACT treatments are employed. There is a lot of room for further study into artemisinins because of their unusual structure. Clearing pharmacological targets and modes of action, improving pharmacokinetic characteristics, and finding a new generation of artemisinins against resistant Plasmodium strains are all priorities[7].

During his Ph.D., German scientist Othmer Zeidler developed dichlorodiphenyltrichloroethane (DDT). There were no applications for DDT at the time, thus it became a worthless chemical. DDT's insecticidal properties were discovered by Paul Müller in Switzerland in 1939. DDT was first employed to combat malaria towards the conclusion of World War II. The success of DDT during WWII soon led to the introduction of additional chlorinated hydrocarbons, which were used in huge quantities to prevent illnesses spread by mosquitos. Two-thirds of the world's population had been exposed to malaria from the late Middle Ages until 1940, when DDT was introduced, posing a serious health, demographic, and economic issue. DDT is an organochlorine insecticide that was used to kill insects in liquid and powder form. People were sprayed with DDT during World War II. DDT became a strong method to combat malaria after the war by targeting the vector[8].

Efforts to develop an efficient antimalarial vaccine, as well as clinical trials, are under ongoing. Numerous attempts have been undertaken over the last few decades to produce effective and inexpensive antimalaria vaccines. Several clinical studies have been conducted in recent years. Clinical studies for the development of next-generation malaria vaccines are under underway. The major concern is the P. vivax vaccine, which needs further study to find new vaccine candidates. Despite decades of vaccine development research, a viable antimalaria vaccine has yet to be produced (i.e., with efficacy higher than 50 percent). The European Union Clinical Studies Register presently lists 48 clinical trials for malaria with a EudraCT protocol, 13 of which are still in progress. Because the malaria parasite is a complicated organism with a complex life cycle that may evade the immune system, developing a vaccine is very challenging. Plasmodium goes through morphological alterations and antigenic variants as it progresses through its life cycle. Plasmodium proteins are extremely polymorphic, with redundant roles. In addition, the Plasmodium species plays a role in the development of malaria illness. A greater effectiveness may be achieved by combining various adjuvants types into antigen-specific formulations. Clinical studies revealed that the majority of drugs were unsuccessful. Many experts across the globe, however, are trying to produce an efficient vaccine. Since existing malaria-prevention techniques, such as medicine, insecticides, and pesticide-treated bed nets, have failed to eliminate the illness, the World Health Organization has designated the quest for a vaccine as one of the most essential public-health research initiatives (WHO)[9].

The easiest method to avoid malaria is to avoid being bitten by insects. Antimalarial medicines that have developed from quinine are used to treat malaria. Malaria vaccines are classified as pre-erythrocytic (sporozoite and liver-stage), blood-stage, or transmission-blocking, depending on their main impact. The majority of the medicines used in therapy work against parasite forms in the blood. Artemisinin, produced from the plant Qinghao, and quinine, derived from Cinchona, are the two most important antimalarial medicines presently in use. Quinine, along with artemisinin, is one of the most effective antimalarial medicines now available. For malaria chemoprophylaxis in endemic regions, doxycycline is recommended. When ACT is unavailable or when the treatment of severe malaria with artesunate fails, it is sometimes used in conjunction with quinine or artesunate to treat malaria. Doxycycline has the drawback of being ineffective in youngsters and pregnant women. Because P. falciparum has developed a worldwide resistance to chloroquine, ACTs are suggested for the treatment of malaria, with the exception of the first trimester of pregnancy. ACTs are made up of a mixture of an artemisinin derivative that reduces parasitemia quickly and a companion medication that kills any residual parasites over a longer period of time. Artemether-lumefantrine, artesunate-amodiaquine, dihydroartemisinin-piperaquine, artesunate-mefloquine, and artesunate with sulfadoxine-pyrimethamine are the most often used ACTs. ACTs were very effective against

all strains of P. falciparum until recently, when the frequency of treatment failures in Southeast Asia increased. Atovaquone-proguanil is a non-artemisinin-based therapeutic alternative for those who have failed to respond to standard ACTs. However, due of the potential for fast development of atovaquone resistance, it is not authorized for widespread usage in endemic areas. Quinine is still effective, despite the fact that it requires a lengthy course of therapy, is poorly tolerated, particularly by youngsters, and must be used in conjunction with another medication, such as doxycycline or clindamycin. Except in the event of chloroquine-resistant P. vivax, when an ACT is employed, uncomplicated vivax, malariae, and ovale malaria are treated with chloroquine[10].

1.4 Malaria in Europe:

Malaria epidemics occurred in Europe throughout the Roman Empire and the 17th century. It was treated like any other fever that individuals had at the time until the 17th century. The techniques used, which included the discharge of blood, fasting, and bodily cleaning, were insufficient. The medicinal bark of the Cinchona tree, which contains quinine, was cited as the first effective antimalarial medicine and was originally utilized by the Peruvian people. It is thought that it was introduced throughout Europe by Spanish Jesuit missionaries in the fourth decade of the seventeenth century. The effort of a few researchers has resulted in current understanding of malaria therapy. Alphonse Laveran, Ronald Ross, and Giovanni Battista Grassi are among the researchers. Laveran, a military doctor in Algeria, identified the causative agents of malaria in the blood of mosquitoes in November 1880 and determined that it was a protozoa. Protozoa, like bacteria, may have a parasitic lifestyle inside people and therefore cause illness, according to Laveran. In the same year, Ronald Ross, a military doctor in India, discovered the transmission of avian malaria in the saliva of infected mosquitos, and Giovanni Battista Grassi, an Italian physician, demonstrated that malaria could be transferred from mosquitos to people.

1.5 Malaria in Croatia:

The Statute of the Town of Korula from 1265 is the earliest recorded document in Croatia that attests to the prevention of malaria. The Law on Health Care of Croatia and Slavonia, enacted in 1874, created a public health service aimed at treating malaria. Although there was no awareness of malaria or appropriate medical expertise, drainage was carried out in order to provide ‘healthy air' to the towns. In 1798, physician Giuseppe Arduino reported malaria in Istria to the Austrian authorities. Vincenzo Benini, a government official, agreed to a suggested sanitary measure for wetlands drainage.

The draining of wetlands near Pula and on the coastal islands started in 1864, and a program to control malaria by treating patients with quinine has been in place since 1902. The Malaria Institute was established in Trogir in 1922. In 1923, Dr. Otmar Trausmiller launched a mission on the island of Krk to eliminate malaria via the cleaning of water surfaces and the treatment of patients with quinine. Biological control of mosquitoes has been developed since 1924, in addition to chemical treatment, by introducing the fish Gambusia holbrooki to Istria and the seashore. In 1930, legislation was enacted to ensure village cleanliness, which included the building of water infrastructure and safe wells, all of which contributed to malaria control. Regular arsenic green (copper acetoarsenite) mosquito fogging was implemented, as well as larvicidal treatment of stagnant water.

2. DISCUSSION

Malaria is a parasitic illness that is spread by female anopheles and is caused by infection with a parasite of the genus Plasmodium. P. falciparum infection is the most dangerous of all the other species, particularly in terms of morbidity and death, which is why so much study has been focused on it. The illness affects up to 40% of the world's population, with an estimated 300-500 million individuals afflicted worldwide, mostly in the tropics. It has a significant morbidity and death rate, particularly in resource-poor tropical and subtropical areas, resulting in an annual economic loss of about US$ 12 billion in Africa alone. An effective human malaria vaccine is urgently needed for those living in malaria-endemic areas as well as non-immune travellers, particularly those traveling to malaria-endemic areas; this would provide a cost-effective way of preventing disease and death while also filling the gap left by other control measures. Several resources have been sunk in the last decades in an effort to enhance the existing available control methods, but without much

success, owing in part to the malaria parasite's continued resistance to medicines and mosquitoes' resistance to insecticides.

3. CONCLUSION

The worldwide effort to eliminate malaria started in the 1950s, but it failed owing to mosquito resistance to the insecticides employed, malaria parasite resistance to the medicine used in treatment, and administrative difficulties. Furthermore, the majority of Africa, where malaria is the most prevalent, was never included in the initial eradication efforts. Despite the fact that the majority of types of malaria may be effectively treated with currently available antimalarial, malaria-related morbidity and death are on the rise. This problem has emerged as a result of growing parasite medication resistance, as well as increased mosquito pesticide resistance, and has become one of the most pressing issues in malaria management in recent years.

All antimalarial medicines have been shown to be resistant. Because of the unexpected mass movement of people (birds, parasite disease vector insects) from regions with a big and varied infestation, research into discovering and testing novel antimalarial, as well as a possible vaccine, is currently underway. In certain countries, the eradication effort has shown that existing technologies may be adequate to eliminate malaria. The development of pesticide resistance among vectors and increasing ACT failures suggest that current malaria eradication methods may not be sufficient.

REFERENCES:

[1] R. H. Morrow and W. J. Moss, “Malaria,” in *The Development of Modern Epidemiology: Personal Reports from Those Who Were There*, 2009.

[2] G. D. Burchard, “Malaria,” *Internist*. 2014, doi: 10.1007/s00108-013-3390-9.

[3] R. M. K. Adanu, “Malaria,” in *Queenan’s Management of High-Risk Pregnancy: An Evidence-Based Approach: Sixth Edition*, 2012.

[4] N. F. Walker, B. Nadjm, and C. J. M. Whitty, “Malaria,” *Medicine (United Kingdom)*. 2018, doi: 10.1016/j.mpmed.2017.10.012.

[5] S. Sitalakshmi, A. Srikrishna, and P. Damodar, “Plasmodium malariae malaria - A case report,” *J. Indian Med. Assoc.*, 2005.

[6] N. F. Walker, B. Nadjm, and C. J. M. Whitty, “Malaria,” *Medicine*. 2010, doi: 10.1016/j.mpmed.2009.09.017.

[7] K. H. Carter, R. P. Escalada, and P. Singh, “Malaria,” in *Arthropod Borne Diseases*, 2016.

[8] J. Goddard, “Malaria,” *Infect. Med.*, 1997, doi: 10.5694/j.1326-5377.1957.tb60481.x.

[9] P. A. Zimmerman and R. E. Howes, “Malaria diagnosis for malaria elimination,” *Current Opinion in Infectious Diseases*. 2015, doi: 10.1097/QCO.0000000000000191.

[10] L. S. Garcia, “Malaria,” *Clinics in Laboratory Medicine*. 2010, doi: 10.1016/j.cll.2009.10.001.