



Review on Pathology and Chemoprophylaxis of Malaria

Ajinkya V Devkar, Dhanashri Puri, Vijaysingh Sabale, Rahul Jadhav

Lokmangal College of Pharmacy Wadala

ABSTRACT

Malaria is the most common parasite disease in the world and is spread by female Anopheles mosquitoes that bite between dusk and early. Human disease can be caused by five types of parasites: Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, and, as of late, Plasmodium knowlesi. Anorexia, vomiting, shivering, high fever, and joint and stomach discomfort are some of the initial, nonspecific signs of malaria. Plasmodium falciparum is the primary cause of severe kind. The significance of behavioural preventative strategies (bed nets, repellents, etc.), sufficient chemoprophylaxis, and raising public understanding of pathophysiology and disease prevention methods. The primary method of diagnosing malaria has been microscopic analysis of blood, which involves using blood films to confirm the diagnosis and improve sanitation and chemoprophylaxis.

Keywords :- Malaria, Anopheles mosquitoes, Chemoprophylaxis

INTRODUCTION

The parasites that cause malaria, Plasmodium ovale, P. malariae, P. knowlesi, P. vivax, and P. falciparum, are the ones that spread the disease. The latter two are the most prevalent; malaria, in particular, is mostly an infection of the red blood cells that results in recurrent fever that appears suddenly. P. falciparum malaria is extremely dangerous and can result in various organ damage, unconsciousness, and even death. It is female Anopheles mosquitoes that transmit malaria. When a person is bitten by an infected mosquito, the parasite enters the body through the saliva of the mosquito. The parasite first enters the body through the liver, where it multiplies. The resultant parasites proliferate for a few days before being discharged into the bloodstream to infect red blood cells, where they eventually burst the cells, spreading the infection to others. They have the potential to cause fatalities or serious illnesses in large numbers. A portion of the parasites found in red blood cells mature into gametocytes, which are the sexual stages. If a mosquito bites an individual who is sick and these stages are consumed, grow for ten to fourteen days in the mosquito's stomach before entering the salivary glands to await the next bite. All of the world's tropical and subtropical regions are home to malaria. High transmission zones are mostly located in rural areas in the Western Pacific (Papua New Guinea, Solomon Islands, and Vanuatu), South America (such as Brazil), South East Asia (such as Thailand, Indonesia, and East Timor), and sub-Saharan Africa [1, 2]. The World Health Organisation (WHO) declared Australia malaria-free in 1981, with the last locally acquired malaria case occurring in the Northern Territory in 1962. There are several Anopheles mosquito species in the Northern Territory, though, and if foreign visitors who are bitten here reintroduce the malaria parasite to the indigenous mosquito population. Interactions among the parasite, host, and surroundings determine the course of a malaria infection. Accordingly, attempts to connect outcomes using a single immunological marker frequently lead to misleading relationships that break under various conditions. A significant portion of our knowledge of malaria immunity is derived from phenomenological observations or extrapolated from in vitro observations, which is made worse by the absence of natural animal models for human malaria from which data could be consistently extrapolated [2]. Malaria immunity is a result of a combination of acquired or adaptive immunity, non-adaptive immunity, and hereditary resistance, just like immunity to other illnesses. The majority of sickness and nearly all malaria deaths are caused by Plasmodium falciparum, so immunity to this parasite will be the main topic of discussion in this chapter.

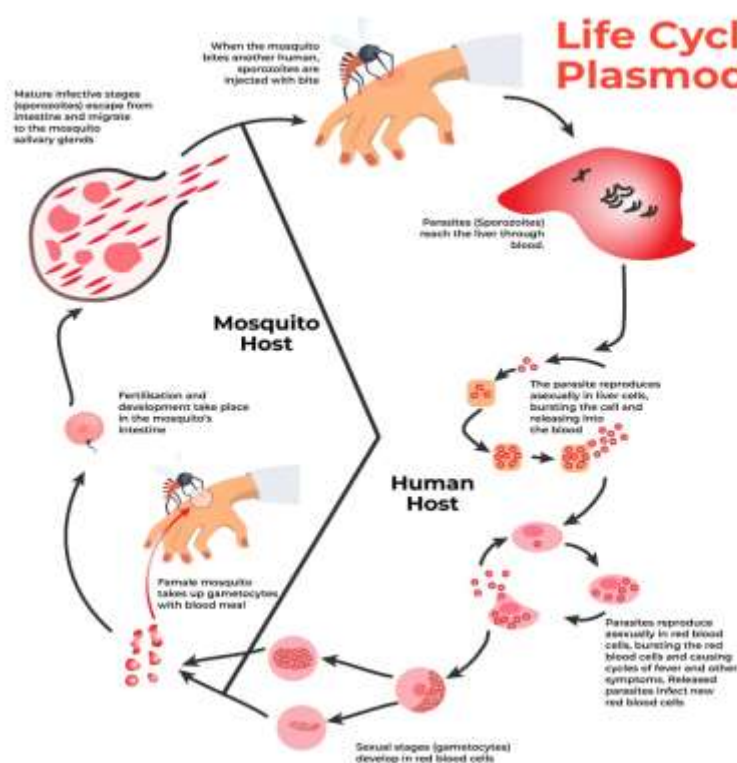
Defination of malaria :-

an infectious disease that can be spread by the bite of an Anopheles mosquito, infected needles, or contaminated transfusions. It is brought on by protozoan parasites from the plasmodium family. The most fatal kind of malaria is falciparum malaria. Anopheles mosquitoes spread the parasite that causes malaria, a blood sickness that affects humans. It is possible to prevent and treat malaria [2]. The Italian terms "bad" (mala) and "air" (aria) from the 18th century are the origins of the word malaria. Dr. Francisco Torti of Italy most likely coined the phrase when people believed the illness was brought on by contaminated air in marshy places.

History of malaria :- Malaria has a long history because it was a disease that existed before humans. Throughout most of human history, people have been plagued by malaria, a contagious

disease that can be fatal and has impacted migration patterns. For hundreds of years, scientists and medical professionals have studied the disease's biology in an effort to prevent and treat it. This interest stems from the identification of the parasite that causes it. Since there is currently no vaccine against malaria and many of the earlier anti-malarial medications are becoming less effective due to the parasite's high levels of drug resistance, these investigations have persisted. Given that malaria still poses a serious threat to public health, accounting for 250 million fever episodes and around one million fatalities yearly, it is imperative to comprehend its past [3]. The origins of human malaria are most likely in Africa, where it coevolved with mosquitoes and non-human primates, its hosts. Mosquitoes from the Paleocene era, which is roughly 30 million years old, that were preserved in amber were the first to contain malaria parasites. It's possible that malaria has infected humans throughout human history. Plasmodium falciparum may have first infected humans through gorillas.[5]. Given that malaria still poses a serious threat to public health, accounting for 250 million fever episodes and around one million fatalities yearly, it is imperative to comprehend its past [3]. The origins of human malaria are most likely in Africa, where it coevolved with mosquitoes and non-human primates, its hosts. Mosquitoes from the Paleocene era, which is roughly 30 million years old, that were preserved in amber were the first to contain malaria parasites. It's possible that malaria has infected humans throughout human history. Plasmodium falciparum may have first infected humans through gorillas.[5].

Life cycle of malaria :- Female Anopheles mosquitoes are the main hosts and vectors of transmission for Plasmodium parasites. Vertebrates, including humans, are secondary hosts. The parasite is initially acquired by mosquitoes by their consumption of an infected person's blood.



Control efforts :-

In Brazil, entomologist Raymond Corbett Shannon found *Anopheles gambiae* mosquitoes carrying illness, which were probably transported there by swift mail boat or aeroplane [21]. This African native mosquito species is a particularly effective malaria vector. [22] The largest malaria outbreak to ever strike the novel World occurred in 1938 as a result of the arrival of this novel mosquito vector. However, by carefully applying Paris green to breeding sites and pyrethrum spray-killing to adult resting spots, *A. gambiae* was completely eradicated from northeastern Brazil, and consequently from the New World, in 1940 [7]. DDT was employed as an insecticide beginning in World War II to fight malaria, which was endemic in most tropical regions of the world, and its insect vectors. Although its initial purpose was to safeguard soldiers, it was eventually used as a public health tool. For instance, during the war in Liberia, the United States conducted extensive military operations there, and the U.S. Public Health Service started using DDT as a larvicide and for indoor residual spraying (IRS) in an effort to reduce malaria in the country's capital, Monrovia. The initiative was extended to neighbouring settlements in the early 1950s. In order to ascertain if it would be possible to eradicate malaria in tropical Africa, the World Health Organisation (WHO) initiated a trial antimalaria programme in several regions of Liberia in 1953. Nevertheless, a number of setbacks to these initiatives predicted the widespread withdrawal of attempts to eradicate malaria in tropical Africa by the middle of the 1960s [8].

Netic resistance to malaria :-

Genetic resistance to malaria arises from alterations in human red blood cells that prevent the malaria parasite from invading and replicating within these cells, as well as immune system modifications that boost immunity to this infection. Thus, blood cell genes like aberrant haemoglobins, glucose-6-phosphate dehydrogenase deficiency, and Duffy antigens—which confer innate resistance—as well as immunity-related genes like the major histocompatibility complex genes—which control adaptive immune responses—are all involved in host resistance to malaria.[25] Modified blood cells offer resistance that helps people survive the perilous early years of life, but older people and adults who live in areas where malaria is widespread are more likely to benefit from the powerful defence mediated by adaptive immune responses [9]. The greatest known selective pressure on the human genome since agriculture first emerged 10,000 years ago has been exerted by malaria.[26][27] Due to this parasite's selection, a number of hereditary erythrocyte variations have grown widespread in previously malarial regions of the world. [11].

Pathology of malaria within Human Hosts :-

The malaria parasite passes through two phases after it enters humans: the erythrocyte phase and the exoerythrocytic phase.

Exoerythrocyte phase :-

The liver is where the parasites mature and develop during the exoerythrocytic phase. The sporozoites in an infected mosquito's saliva enter the bloodstream and move to the liver, where they spread the infection or sporozoites while the insect feeds on blood. After a mouthful, the migration process takes about thirty minutes. Hepatocytes are infected by sporozoites. The proliferation of sporozoites comes next. We refer to this as asexual multiplication or reproduction. It takes six to fifteen days to complete this multiplication. Within the hepatocytes, the parasite then produces thousands of merozoites. The large number of merozoites causes their host cells to burst, allowing them to escape into the circulation. Occasionally, the sporozoites may produce productive hypnozoites that are latent in the liver rather than immediately developing into exoerythrocytic phase merozoites. Plasmodium vivax and Plasmodium ovale are examples of this. Dormant periods can last for a number of months, usually ranging from six to twelve months to three years. In these two malaria species, hypnozoites are the cause of extended incubation periods and delayed relapses [12]. The red blood cell involvement phase is referred to as the erythrocytic phase. The merozoites in the RBCs continue to multiply asexually, bursting the RBCs and releasing the merozoites into the blood. Each burst is associated with a specific level of fever. The young merozoites then penetrate fresh red blood cells, causing further multiplication. Several such amplification cycles occur. Each such amplification is accompanied by a wave of fever. Some merozoites grow into male and female gametocytes, which can be transmitted to mosquitoes. This concludes the life cycle [13].

Diagnosis of malaria :-

Malaria diagnosis has traditionally relied on microscopic inspection of blood films. Although blood is the most frequently utilised sample to make a diagnosis, saliva and urine have been studied as alternate, less invasive specimens. [14] More recently, modern techniques utilising antigen testing or polymerase chain reaction have been discovered, however these are not routinely implemented in malaria endemic countries. Ancus who cannot afford laboratory diagnostic testing frequently utilise a history of subjective fever as the basis to treat for malaria. Because the four principal parasite species have unique characteristics, microscopy on blood films is the most cost-effective, favoured, and reliable method of diagnosing malaria. Two types of blood film are traditionally utilised. Thin films, like usual blood films, enable species identification because the parasite's appearance is best preserved in this preparation. Thick film permits the microscopist to screen a larger amount of blood, approximately eleven times more sensitive than thin film, making it easier to detect low levels of infection on thick film; however, the appearance of the parasite is much more varied, making distinguishing between species much more difficult. After considering the advantages and disadvantages of both thick and thin smears, it is crucial to utilize both smears while seeking to make a clear diagnosis [15]

Antigen Test :-

For locations where microscopy is accessible and laboratory staff are not competent in malaria diagnosis, there are commercial antigen detection assays that require only a drop of blood. Immunochromatographic tests (also known as malaria fast diagnostic tests, antigen-capture assays, or "dipsticks") have been created, distributed, and field tested. These tests require a finger stick or venous blood, take 15-20 minutes to complete, and the results are visible as the presence or absence of coloured stripes on the dipstick, making them suited for field use. The threshold of detection by these quick diagnostic tests is in the range of 100 parasites/ul of blood (commercial kits range from roughly 10.002% to 0.1% parasitemia) and compared to 5 by thick film microscopy [16].

Molecular method :-

Molecular approaches are available in some clinical laboratories, and rapid real-time assays (such as QA-NASBA based on polymerase chain reaction) are being developed with the goal of deploying them in endemic areas. PCR (and other molecular techniques) are more precise than microscopy. However, it is costly and requires a specialised laboratory. Furthermore, parasitemia levels do not always correlate with disease progression, especially when the parasite can cling to blood vessel walls. PCR (and other molecular techniques) are more precise than microscopy. However, it is costly and requires a specialised laboratory. Furthermore, parasitemia levels do not always correlate with disease progression, especially when the parasite can cling to blood vessel walls. As a result, more sensitive, low-tech diagnosis techniques must be developed to detect low levels of parasitemia in the field [17].

Cause of malaria :-

Plasmodium, a single-celled parasite, is the cause of malaria. There are over 100 distinct Plasmodium species. They cause malaria in a variety of animals and birds, as well as humans. Four Plasmodium species usually infect humans. Plasmodium falciparum causes the vast majority of malaria deaths, particularly in Africa. The infection can strike rapidly and cause a number of life-threatening consequences. Plasmodium malariae infections not only cause conventional malaria symptoms, but they can also remain in the blood for extended periods of time, possibly decades, without creating any symptoms. Plasmodium ovale is a rare parasite that can induce relapses and is most common in Western Africa. Plasmodium vivax, the most widely distributed of the species, causes less severe symptoms. [18].

Signs and symptoms :

The typical fever pattern of the different type of malaria

Malaria symptoms usually appear 8-25 days after infection (36); however, symptoms may appear later in patients who have used antimalarial drugs for prevention.[37] The disease's initial manifestations, which are typical to all malaria species, are comparable to flu-like symptoms[38] and can mimic other disorders such as septicemia, gastroenteritis, and viral infections.[37] The symptoms may include Symptoms include headache, fever, shivering, joint pain, vomiting, hemolytic anaemia, jaundice, haemoglobin in urine, retinal damage [19], and convulsions.. The characteristic symptom of malaria is paroxysm, which is a cyclical occurrence of sudden coldness followed by rigour, fever, and sweating that occurs every two days (tertian fever) in P. vivax and P. Ovale infections every three days (quartan fever) in P. malariae. P. falciparum infection might result in recurrent fever every 36-48 hours or a less severe and nearly continuous fever [20]. P. falciparum (also known as falciparum malaria) is typically responsible for severe malaria. The symptoms of falciparum malaria appear 9-30 days after infection.[38] Individuals with cerebral malaria typically exhibit neurological symptoms, such as aberrant posture, nystagmus, conjugate gaze palsy (failure of the eyes to turn together in the same direction), opisthotonus, seizures, or coma. [21].

Treatment of malaria :-

The CDC (Centres for Disease Control and Prevention) recommends the following medications to treat malaria: Artemisia derivatives (not licenced in the USA, prevalent elsewhere), atovaquone-proguanil (Malarone), chloroquine doxycycline, mefloquine (Lariam), quinine, and sulfadoxine-pyrimethamine (Fansidar). Primaquine is also effective against hypnozoites, which are dormant parasite liver forms, and it helps to avoid relapses. Primaquine should not be provided to pregnant women or patients with G6PD deficiency. A screening test rules out G6PD deficiency [22].

Conclusion :-

The findings lead to numerous noteworthy conclusions. First, it is very feasible for an economy to fall into a "malaria trap," in which sickness breeds poverty and poverty becomes disease prevention unsustainable. In the model economy, we can calculate the size of this "malaria trap." It has the potential to cut average income in half. Gallup and Sachs (2000) highlight that in 1995, the 44 nations with intensive malaria burdens had a per capita income of \$1,526, compared to \$8,268 for the 106 countries without intensive malaria burden. Our model implies that the sickness alone could account for little less than half of this income discrepancy. Some investigations have revealed that malaria-mediated evolutionary selection has included two primary aspects: high selective pressure (for example, in the instance of the more common HbS allele prevalent in malaria-exposed populations) and independent evolutionary responses generated by various groups on a global and local scale. The HBB gene is the finest example on a worldwide scale, with three distinct SNPs (HbS, HbC, and HbE) found to confer malaria resistance because the mutations caused influence haemoglobin functioning. The disease burden is terrible, but there are solutions available to significantly reduce death and suffering. Investing in control and elimination will yield significant dividends for personal health, as well as cumulative advantages for a safer and healthier world. This generation's leaders must ensure that future generations will benefit from a significant investment during the coming decade.

References :-

1. Carter R, Mendis KN (2002). "Evolutionary and historical aspects of the burden of malaria". Clin Microbiol Rev
2. Poinar G (2005). "Plasmodium dominicana n. sp. (Plasmodiidae: Haemospororida) from Tertiary Dominican amber". Syst. Parasitol.
3. Poinar G (2005). "Plasmodium dominicana n. sp. (Plasmodiidae: Haemospororida) from Tertiary Dominican amber". Syst. Parasitol.
4. Joy DA, Feng X, Mu J, Furuya T, Chotivanich K, Krettli AU, Ho M, Wang A, White NJ, Suh E, Beerli P, Su XZ. (2003). "Early origin and recent expansion of Plasmodium falciparum".
5. Hayakawa T, Culleton R, Otani H, Horii T, Tanabe K (2008). "Big bang in the evolution of extant malaria parasites".
6. Liu W, Li Y, Learn GH, Rudicell RS, Robertson JD, Keele BF, Njanga J-BN, Sanz CM, Morgan DB, Locatelli S, Gonder MK, Kranzusch PJ, Walsh PD, Delaporte E, Mpoudi-Ngole E, Georgiev AV, Muller MN, Shaw GW, Peeters M, Sharp PM, Julian C, Rayner JC & Hahn BH (2010). "Origin of the human malaria parasite Plasmodium falciparum in gorillas".
7. Hempelmann E, Tesarowicz I, Oleksyn BJ. (2009). "Kurzgefasste Geschichte der Malaria-Chemotherapie. Von Zwiebeln bis zum Artemisinin".
8. Canali S (2008). "Researches on thalassemia and malaria in Italy and the origins of the "Haldane hypothesis"".
9. Sallares R, Bouwman A, Anderung C (2004). "The Spread of Malaria to Southern Europe in Antiquity: New Approaches to Old Problems".

10. Allison AC. (2009). "Genetic control of resistance to human malaria".
11. Neghina R, Neghina AM, Marincu I, Iacobiciu I (2010). "Malaria, a Journey in Time: In Search of the Lost Myths and Forgotten Stories".
12. Cox F (2002). "History of Human Parasitology". Clin Microbiol Rev .
13. Lalremruata A, Ball M, Bianucci R, Welte B, Nerlich AG, Kun JF, Pusch CM. "Molecular identification of falciparum malaria and human tuberculosis co-infections in mummies from the Fayum depression (lower Egypt)".
14. Stagl V, Sattmann H, Horweg C (2010). "Der Schrecken der Miasmen: Österreichische Forscher an Bord der Fregatte Novara auf den Spuren der Malaria". Wien Klin Wochenschr 122: 6–9.
15. Opekina BR (2009). "Malaria in Pacific populations: seen but not heard?". Journal of Population Research .
16. Dobson MJ (1994). "Malaria in England: a geographical and historical perspective". Parasitologia.
17. Knottnerus OS (2002). "Malaria Around the North Sea: A Survey". Gerold Wefer, Wolfgang H. Berger, Karl-Ernst Behre, Eynstein Jonsen (ed.), Climatic Development and History of the North Atlantic Realm: Hanse Conference Report. Springer-Verlag:
18. Reiter P (2000). "From Shakespeare to Defoe: malaria in England in the Little Ice Age". Emerg Infect Dis.
19. Breman J (2001). "The ears of the hippopotamus: manifestations, determinants, and estimates of the malaria burden". Am J Trop Med Hyg .
20. Worrall E, Basu S, Hanson K (2005). "Is malaria a disease of poverty? A review of the literature". Trop Med Int Health.
21. Parham PE, Christiansen-Jucht C, Pople D, Michael E (2011). "Understanding and Modelling the Impact of Climate Change on Infectious Diseases", InTech-Progress and Future Challenges, in Climate Change. Blanco J, Kheradmand H .
22. Spielman, Andrew; D'Antonio, Michael (2002). Mosquito: The Story of Man's Deadliest foe. Hyperion. p.