J. Entomol. Res. Soc., 27(1): 1-14, 2025
Doi: 10.51963/jers.v27i1.2623
Review Article
Online ISSN:2651-3579

Association of Malarial Development with Climate Change: A Review

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ABSTRACT

Malaria is considered as the single most prevalent life-threatening infectious disease in the world which spreads to human populations by Anopheles mosquito. Malaria infection poses serious risks to adults, children and pregnant women. The adverse effects in pregnant women include anaemia, fetal demise and premature delivery. The incidence of malaria is higher in children younger than five years in endemic areas like tropical Africa. The vector potential of female species Anopheles varies due to different meteorological conditions. Climate based models have also shown an enhancement of disease following extreme weather changes. This review gleans an insight into the association of malaria with different climatic variables. It covers etiology, symptoms' manifestation, life cycle of the parasite, transmission, epidemiology, drug resistance, impact of El Niño cycle, malarial association with climatic change and conclusions and technological innovations.

Keywords: Malarial mosquito, climate change, Plasmodium, Temperature, Malaria transmission.

Zafar, S., Sarwar, I., Iftikhar, S., Asam Riaz, M., Zafar, M.I., Yang, M., & Hussain, I. (2025). Association of malarial development with climate change: A review. *Journal of the Entomological Research Society*, 27(1), 1-14.

Received: March 21, 2024 *Accepted: January 29, 2025*

INTRODUCTION

Malaria is a major global health concern, causing 350-500 million infections and 1 million deaths annually. Its transmission has been reported from large areas of Central and South America, Africa, Asia, Eastern Europe, and the South Pacific. In lower-income countries, half of the world's population is at risk of malaria. In the Americas, approximately 132 million people live in areas which are at risk of malaria. Mosquitoes preserved in amber nearly 30 million years ago provided the first evidence of this protozoan. Due to its prevalence in Roman times, the disease was also named as Roman fever. The parasite was identified by Charles Louis Alphonse Laveran, a French physician, who was awarded Nobel Prize for his research. The term malaria has been derived from two Italian words "mala aria" meaning foul or bad air (Gelband, Panosian, & Arrow, 2004; Townson, 2017). This name originated due to prevalence of malarial cases in areas where bad air was found associated with the accumulation of pools (Amorosa, Corbellini, & Coluzzi, 2005; Nureye, 2021).

Etiology

Malaria is a vector-borne disease in which *Plasmodium* spp. causative pathogens are transmitted via the bite of the infected female Anopheles mosquito (Meibalan & Marti, 2017). A single-celled parasite known as a sporozoan causes malaria. This sporozoan belongs to the genus *Plasmodium*.

The genus *Plasmodium* is composed of more than 200 species, but only five species viz. *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae* and *P. knowlesi* are involved in human-to-human transmission (Sato, 2021; Boualam, Pradines, Drancourt, & Barbieri, 2021; Nureye, 2021). Three simian parasites i.e. *P. cynomolgi*, *P. inui*, and particularly *P. knowlesi* (Sharp, Plenderleith, & Hahn, 2020; Antinori, Galimberti, Milazzo, & Corbellino, 2012) relate to human malaria (Sharp et al., 2020; Boualam et al., 2021). Other species affect animals like rodents, monkeys and reptiles (Gueirard et al., 2010). Among human pathogenic species, *P. falciparum* is the most dangerous form, responsible for majority of deaths throughout the world. *P. ovale* and *P. vivax* cause relapsing malaria. The five species of plasmodium such as *P. falciparum, P. vivax, P. malariae, P. ovale* and *P. knowlesi* are available but *P. falciparum* and *P. vivax* causes malaria widely in Asia (Sato, 2021).

Symptoms' Manifestation

Symptoms are similar to flu and can last for 06 to 10 hrs. Some strains may have a longer cycle or produce mixed symptoms (Abdelwahab et al., 2023). Typical symptoms include fever, chills, sweating, headaches, nausea, vomiting, body aches, chest pain, convulsions, bloody stools, blood in urine, weakness, anemia, liver enlargement, mild jaundice, impaired consciousness, high acidity in the blood and body fluids, seizures, coma and a higher breathing rate (Burke et al., 2019; Abdelwahab et al., 2023; Daily, Minuti, & Khan, 2022). Complications of malaria include liver/kidney failure, low blood glucose, swelling and rupturing of spleen, pulmonary edema and acute respiratory distress syndrome (Abdelwahab et al., 2023). Severe malaria becomes a medical emergency. It is also responsible for causing child mortality and kill about half a million children every year (WHO 2023).

Life Cycle

All *Plasmodium* species have a similar life cycle comprising two parts. The parasite infects a person or a vertebrate host in the first part. In the second, it is transmitted from the malarial patient or infected vertebrate host to another host by an insect vector (Votýpka, Modrý, Oborník, Šlapeta, & Lukeš, 2016; Sato, 2021). Five *Plasmodium* species which naturally infect humans are transmitted by mosquitoes of genus Anopheles. These mosquitoes also act as vector for other *Plasmodium* species parasitizing mammals (Amino et al., 2006; Perkins, 2014; Sato, 2021).

Malaria parasite exists in the form of a motile uninucleate sporozoite. Its life cycle starts when an infected adult female Anopheles mosquito bites a person and feeds on his blood. Following feeding, sporozoites are released into the blood stream of the host through mosquito's saliva (Frischknecht & Matuschewski, 2017; Sato, 2021). Upon entry of parasites into human blood stream, they rapidly move to liver cells where they develop and multiply during a stage called as schizogony (Prudêncio, Rodriguez, & Mota, 2006). Rupturing of infected liver cells releases many merozoites (Sturm et al., 2006; Josling & Llinás, 2015; Bancells et al., 2019) into the blood which further invade red blood cells (RBCs). This stage is completed within 9-14 days. The parasites develop into blood schizonts within the RBCs. RBCs are ruptured by schizonts and numerous merozoites are released which invade new RBCs. On rupturing of infected red blood cells, typical symptoms of malaria like chills and fever are manifested due to production of a toxin hemozoin. The period between the first infective bite and manifestation of symptoms is named as the incubation period. The incubation period is for 7-10 days but it may be shorter in *P. falciparum* and longer in *P. vivax* and *P. malariae* (McConnaughey, 2014).

Some infected blood cells don't follow asexual multiplication. Instead of replication, the merozoites in these cells differentiate into the sexual forms known as gametocytes that circulate in the blood stream. A mosquito biting an infected human ingests the gametocytes which are pre-destined to differentiate into either male or female gametes (gametogenesis). The activation of gametocytes occurs when they are exposed to the environment of mosquito mid gut lumen. The male and female gametocytes differentiate to produce microgametes and macrogametes, respectively (Bennink, Kiesow, & Pradel, 2016). The macrogamete is fertilized by the microgamete to produce a zygote. When zygote undergoes meiosis, it develops into a motile form, the ookinete containing four haploid genomes in its nucleus (Sinden & Hartley, 1985). After penetrating the wall of the mosquito midgut, ookinete forms an oocyst on the exterior surface (Siciliano et al., 2020). Inside the oocyst, mitosis takes place repeatedly and thousands of active sporozoites develop by sporogony (Vaughan, 2007; Araki et al., 2020). When oocyst bursts, it releases sporozoites into the body cavity which travel to the mosquito's salivary glands. They gain the ability to infect human cells and the cycle of human infection initiates when the mosquito bites new person (Baer, Klotz, Kappe, Schnieder, & Frevert 2007).

Transmission

As the malarial parasites affect red blood cells, people may pick malaria by exposure to infected blood. It can be transmitted from mother to unborn child, blood transfusions, organ transplant and use of shared needles or syringes. Transmission rates vary depending upon factors like rainfall distribution, types of mosquito species and closeness of mosquito breeding sites to human population (Burke et al., 2019). Transmission can also occur when infected mosquitoes are transported from malaria hit area to unaffected area.

Epidemiology

The epidemiology of malaria varies significantly even within small geographic regions. Epidemics can occur in some areas with seasonal unstable malaria such as Northern India, Afghanistan, Iraq, Turkey, Ethiopia, Eritrea, Burundi, Sothern Africa (Botswana, Mozambique, Namibia, South Africa, Swaziland, Zimbabwe) and Madagascar. Devastating epidemic occurs when changes are observed in environmental, economic and social conditions i.e. heavy rainfall pattern following drought, prevalence of wet conditions and aggravation by floods or migration of population from non-malarious to affected area. Economic, political and social disturbance in Venezuela has led to several hundred thousand cases of malaria in residents and refugees (Breman, 2009). Recent deluge and heavy monsoon downpour in Pakistan were intensified by climate change. Stagnant water spread over hundreds of kilometers in flood hit areas of Pakistan which could not recede in days led to cases of malaria and other diseases.

The major epidemiological parameters of malaria include the thermic environment, density, the indoor or outdoor human biting habits and the longevity of the female anopheline vectors. Longevity is much important because the part of Plasmodium's life cycle taking place in mosquito (sporogony) continues from 08 to 30 days depending on the species and temperature conditions. The effective mosquito vectors like *Anopheles gambiae* in Africa are long lived, occur in high density in tropical climate, breed readily and bite human beings compared to other animals (Breman, 2009).

The malarial risk is dependent on interactions between the host, parasite, mosquito vector, and environment. This interactive relationship is known as the epidemiologic triad of disease. Variation in these elements may significantly affect risk of infection (Baird, Bangs, Mauire, & Barcus, 2002). The regional risk may be gauged empirically by the criteria defined by Bruce-Chwatt, Draper, & Konfortion (1973):

Hypoendemic: Little transmission with non-significant effect of malaria on the community.

Mesoendemic: Variable transmission that differs with changes in local conditions, e.g. weather or disturbance to the environment.

Hyperendemic: Intense seasonal malarial transmission with disease in all age groups.

Holoendemic: Perennial intense transmission with protective clinical immunity among adults (Bruce-Chwatt et al., 1973; Baird et al., 2002).

The mosquito vectors in the genus Anopheles are prone to the environmental parameters viz. temperature and humidity. Therefore, altitude, rainfall and temperature determine the activity and abundance of anopheline mosquitoes and malarial transmission. Life span of mosquito is increased at high relative humidity and infective mosquito can infect more hosts (Baird et al., 2002). Malarial transmission does not occur in all parts of the malaria-endemic countries. Transmission has not been reported even within tropical and subtropical areas at very high altitudes, during colder seasons in some areas and in deserts (excluding the oases) (Bassa et al., 2018). Transmission is more intense in warmer regions closer to the equator. The highest transmission has been observed in Africa, South of the Sahara and in parts of Oceania such as Papua New Guinea. It is less intense and more seasonal in cooler regions (Grover-Kopec et al., 2005).

Drug Resistance

The two malaria parasites viz. *P. falciparum* and *P. vivax* which frequently cause malaria in human beings have shown resistance to most of the recommended antimalarial drugs. The development of resistance in *Plasmodium* species is determined by the large number of parasites in the infected individual's blood stream at the time of asexual blood stage infection in association with the mutability of their genomes (Cowell & Winzeler, 2019). Resistance to chloroquine in *falciparum* occurs due to point mutations in the gene encoding pfcrt (*P. falciparum* chloroquine resistance transporter) and pfmdr (*P. falciparum* multidrug resistance protein [P-glycoprotein transporter proteins]), causing minimized drug accumulation in the food vacuole (Bray et al., 2005). In 1989, chloroquine-resistant *vivax* was reported for the first time from Papua New Guinea. In Indonesia and Oceania, high grade chloroquine-resistant *vivax* has been reported to be prevalent (Bray et al., 2005). Resistance to antimalarial drugs has spread rapidly. WHO suggests continuous monitoring to support drug observation efforts.

Malarial Association with Climatic Change

The World Health Organization (WHO) has reported approximately 247 million malaria cases in 84 malaria endemic countries and 619,000 deaths worldwide during the year 2021. In sub-Saharan Africa, a child dies every minute from malaria. Exploring the relation between climate and malaria is essential (Caminade et al., 2014; Cella et al., 2019) for effective management in future. Malaria has been regarded as one of the most climate-sensitive infectious diseases. It has recently been described as a complex interaction between humans, mosquitoes, the *Plasmodium* parasite, and the climate (Lubinda, Haque, Hamainza, & Moore, 2021; Kulkarni, Duguay, & Ost, 2022). Climatic variables viz. temperature, humidity and rainfall patterns have significant effect on the mosquito population dynamics, behavior, development of parasites in the mosquito and malaria outbreaks in epidemic transmission areas (Hoshen & Morse, 2004; Wickremasinghe, Wickremasinghe, & Fernando, 2012; Kreppel et al., 2019; Beloconi et al., 2023).

Altered Vector Distribution and Abundance

Climate change can influence the distribution and abundance of malaria vectors by modifying their habitat suitability, geographical range, and seasonal activity patterns (Benedict, Levine, Hawley, & Lounibos, 2007). Anopheles mosquitoes exhibit varying degrees of temperature and humidity preferences, with different species responding differently to changing climatic conditions (Rogers & Randolph, 2000). Warming temperatures may lead to the expansion of the geographical range of certain Anopheles species into higher altitudes and latitudes, increasing the risk of malaria transmission in traditionally non-endemic areas (Parham et al., 2015). Changes in vector distribution and abundance can alter the spatial and temporal patterns of malaria transmission, affecting human populations living in affected regions (Lafferty, 2009).

Impact of El Niño Cycle

Climate change leaves its impact on El Niño cycle which is linked with increased risks of infectious and mosquitoes' transmitted diseases in the tropics particularly malaria (Anyamba et al., 2019; Kreppel et al., 2019; Lubinda et al., 2021). The warm phase of *El Niño-Southern Oscillation-ENSO* (El Niño) relates to increased precipitation and eruption of many vector-borne diseases, while the cold phase (La Niña) causes drought during the short rains in East Africa (Kreppel et al., 2019). Dry conditions produced by El Niño have reportedly increased the malarial cases by more than one third in Colombia and Venezuela. A study conducted by Kreppel et al. (2019) confirmed the effect of ENSO and microclimate on abundance of malaria vector and host-seeking behavior. During warm conditions, higher outdoor biting showed that indoor vector control strategies might be less effective during this period. El Niño warms the atmosphere in the tropics which lasts for several months to a year after the occurrence of event (Tyrrell, Dommenget, Frauen, Wales, & Rezny, 2015; Kreppel et al., 2019).

Impact of temperature on malaria transmission

Temperature plays a critical role in shaping the transmission dynamics of malaria by influencing the development rates of both Anopheles mosquitoes and Plasmodium parasites. Warmer temperatures accelerate the development of mosquitoes from eggs to adults, shorten the extrinsic incubation period (EIP) of the malaria parasite within the mosquito vector, and increase the biting rates and survival of adult mosquitoes (Mordecai et al., 2013). These temperature-mediated changes can lead to higher rates of malaria transmission and increased vectorial capacity in regions experiencing warming trends (Hoshen & Morse, 2004). Conversely, extreme temperature events such as heatwaves may disrupt mosquito breeding habitats, reduce vector longevity, and temporarily suppress malaria transmission (Huang, Zhou, Zhang, Wang, & Tang, 2011).

The ecology of mosquitoes, biology of *Plasmodium spp.,* and proneness of humans to malaria are all affected directly/indirectly by extreme climatic conditions (Adewuyi & Adefemi, 2017). As the vectors or pathogen carriers are sensitive to climate, their perpetuation and spread are much affected by climate change. Climate forecast connected with the increased carbon dioxide concentrations in the atmosphere and rising atmospheric temperature has forced the Intergovernmental Panel on Climate Change (IPCC) to predict about threat of malaria in previously unaffected regions globally causing a 50% rise in malaria cases in 2050 (Cella et al., 2019). The global temperature has shown warming trend since the mid-1950s (Stark, Mataya, & Lubovich, 2009). This increased warming is expected to enhance the transmission rates of mosquito-borne disease and its geographical spread as well (Lubinda et al., 2021; Chandra & Mukherjee, 2022). Reemergence of malaria has been reported in areas where transmission was previously eliminated (Baldari et al., 1998; Krüger, Rech, Su, & Tannich, 2001; Wickremasinghe et al., 2012). An increase in temperature facilitates *Plasmodium* sp. to develop faster intensifying transmission of malaria. A Celsius increase may make the population vulnerable to the disease (Samarasekera, 2023). According to a study conducted by Gondwe et al. (2021) in Malawi, for each 1°C increase in daily minimum temperatures, malaria cases increased in the South East of Malawi by 3.8 percent two months later.

Duration of parasitic development in the vector, larval development time, vector population dynamics, vector's existence and mosquito biting rates are all determined by moderate temperature range (Bayoh & Lindsay, 2003, 2004; Shapiro, Whitehead, & Thomas, 2017; Nissan, Ukawuba, & Thomson, 2021; Beloconi et al., 2023). Below this range, a minimum temperature is needed by mosquitoes to ensure their survival for parasite development. Above this range, due to harmful temperature thresholds, the adult population of mosquitoes may drop sharply (Bayoh & Lindsay, 2003;Shapiro et al., 2017; Nissan et al., 2021). Specifically the parasite's life cycle inside the mosquito cannot be completed below 17ºC and above 35ºC, the further transmission of malaria is hampered (Andriamifidy, Tjaden, Beierkuhnlein, & Thomas, 2019).

Alteration in vector body temperature due to varying ambient temperature may change the metabolic rates of insect vectors and the parasites hosted by them (Gillooly, Brown, West, Savage, & Charnov, 2001; Hundessa et al., 2018; Cella et al., 2019). Anopheline mosquitoes inhabiting environment affected by climate heating show a higher metabolic rate which further causes interference in the development of larvae taking less time for maturity (Kibret et al., 2016; Cella et al., 2019).

Greenhouse Gas Concentrations

Global emissions of greenhouse gases caused by human activities have increased to >70% since the pre-industrial period (Cella et al., 2019). The intensifying effects of climate change are carried along by greenhouse gas emissions (Thomson & Stanberry, 2022). Climatic variations are observed on manifold timescales covering daily weather and seasonal cycles to inter-annual variations (Alexander et al., 2006; Donat et al., 2013a; Nissan et al., 2021). Superimposed on this are nonlinearly increasing greenhouse gas concentrations which have led to detectable trends in average temperature regimes and daily weather changes (Alexander et al., 2006; Donat et al., 2013b; Nissan et al., 2021). Climate change influences risk of malaria due to these seasonal changes (Nissan et al., 2021) and varying weather patterns

The elevated atmospheric CO_2 level enhances the habitat availability for reproduction of mosquitoes leading to higher vector density and increased malaria incidence (Beloconi et al., 2023). Vegetation acclimation activated by elevated CO_2 under climate change also increases the risk of malaria (Le, Kumar, Ruiz, Mbogo, & Muturi, 2019). A study conducted at the University of Liverpool suggests that climate change, brought about by greenhouse-gas emissions and land-use changes may cause patterns of malaria infection to change during the next 50 years. Reduction of greenhouse gas emissions is a significant pathway for protection of people from malaria (Li & Managi, 2022).

Influence of precipitation on malaria transmission

Precipitation patterns, including rainfall duration, intensity, and frequency, influence the availability of mosquito breeding sites and the suitability of habitats for Anopheles mosquitoes (Siraj et al., 2014). Increased rainfall can lead to the expansion of breeding habitats, higher larval densities, and greater adult mosquito emergence rates, thereby enhancing malaria transmission in affected areas (Kibret, Glenn Wilson, Ryder, Tekie, & Petros, 2019). Conversely, drought conditions may reduce the availability of suitable breeding sites, limit mosquito survival, and decrease malaria transmission (Hashizume, Terao, & Minakawa, 2009). However, changes in precipitation patterns can also lead to the creation of new breeding habitats, such as stagnant water pools formed by flooding events, which may facilitate the emergence of malaria vectors in previously unaffected regions (Ebi, Ogden, Semenza, & Woodward, 2017). Malaria is sensitive to rainfall patterns as heavy rainfall contributes to the development of mosquito breeding sites which ultimately increase vector population (Thomson et al., 2017; Beloconi et al., 2023). The time interval between rainfalls spells results in phase proliferation permitting mosquito population to increase rapidly. However, longer gaps limit the growth of mosquito population (Bouma, 1997; Shaman & Day, 2007). According to a study conducted at Malawi, for each 1 mm increase in mean daily precipitation, childhood (under 5) malaria increased by 1.7 percent in the South East and by 2.3 percent in South West, and North, all one month later. In people over 5 years of age, 1 mm increase in daily mean precipitation showed an increase in malaria incidence by 1.6 and 3.3 percent in South East and South West, respectively with a 2- months lag (Gondwe et al., 2021).

Impact of humidity on malaria transmission

Humidity is essentially required for mosquito survival because desiccation adversely affects insects. High humidity near soil surface, leads to an increase in mosquito survival, flight activity and host-seeking trend. These changes are favourable for malaria transmission within an optimum humidity range of 60-80% (Garg, Dhiman, Bhattacharya, & Shukla, 2009; Haque et al., 2010). Duque et al. (2022) concluded in their studies that throughout the dry season, periodic conditions of sustained humidity occurred which allowed foraging by resting mosquitoes followed by increased incidence of malaria.

Ecological Impacts on Parasite Development

In addition to influencing vector biology, climate change can directly impact the ecology and transmission dynamics of Plasmodium parasites, particularly during their development within the mosquito vector (Ermert, Fink, Jones, & Morse, 2011). Temperature plays an important role in determining the rate of parasite development within the mosquito, with higher temperatures accelerating parasite growth and maturation (Mordecai et al., 2013). Warmer temperatures can shorten the EIP of malaria parasites, leading to more rapid development of infectious sporozoites and higher transmission rates (Paaijmans et al., 2010). However, extreme temperatures or fluctuations in temperature regimes may disrupt parasite development, reduce the infectivity of mosquitoes, and influence the timing and intensity of malaria transmission.

Human Health Vulnerability and Adaptation

Climate change poses significant challenges to human health and well-being, particularly in vulnerable populations living in malaria-endemic regions (Ebi et al., 2017). Changes in temperature and precipitation patterns can affect human exposure to malaria vectors, alter the timing and seasonality of malaria transmission, and influence the effectiveness of vector control interventions (WHO, 2021). Vulnerable populations, including children, pregnant women, and individuals with weakened immune systems, are at increased risk of malaria infection and related complications in the context of climate change (Greenwood & Mutabingwa, 2005). Adaptation strategies such as early warning systems, improved surveillance and response mechanisms, and targeted vector control measures can help mitigate the impacts of climate change on malaria transmission and reduce the burden of disease in affected communities (Campbell-Lendrum & Woodruff, 2016).

Technological Innovations

The climate change needs to be addressed wisely to combat emerging global health issues particularly malaria. IPCC has already issued alert about changing weather patterns which may affect migration of human population, plants, animals and pathogens. The direct and indirect effects of climate change may impact epidemiology (Zhou, Minakawa, Githeko, & Yan, 2004; Hussien, Eissa, & Awadalla, 2019) of vector borne diseases, on-going malaria control programs and elimination efforts in different countries of the world. According to UN reports, it is difficult to accurately assess the effect of climate change on malaria transmission as it is dependent on various factors like population and demographic dynamics, insecticides' resistance, human activities like deforestation (Kar, Kumar, Singh, Carlton, & Nanda, 2014) and temperature fluctuations. Many researchers and health professionals assert that global warming, an unpleasant result of climate change, may be linked to the persistence as well as the resurgence of malaria epidemics (Adewuyi & Adefemi, 2017). It is imperative to analyze and understand the effects of climate change on health problems to anticipate important changes in risk (Kulkarni et al., 2022) and devise effective strategies to thwart its negative impact. Key technological innovations need to be developed including advanced surveillance system using apps, micro-planning, prevention, diagnosis (Chibi, Wasswa, Ngongoni, Baba, & Kalu, 2023), novel interventions and gene drive technology (James, Dass, & Quemada, 2023) along with climate change mitigation approaches.

CONCLUSION

In conclusion, climate change represents a significant driver of malarial development, influencing the distribution, abundance, and transmission dynamics of malaria vectors and parasites worldwide. Changes in temperature and precipitation patterns can alter mosquito breeding habitats, vector distribution, and parasite development rates, leading to shifts in the spatial and temporal patterns of malaria transmission. Vulnerable populations living in malaria-endemic regions are particularly susceptible to the impacts of climate change on human health, highlighting the urgent need for adaptive strategies and interventions to mitigate the risks of malaria transmission in a changing climate. By understanding the complex interplay between climate variables, vector biology, parasite ecology, and human health outcomes, researchers and public health authorities can develop effective strategies for malaria control and prevention in the face of ongoing climate change.

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