

Prevention and Elimination of Malaria in India

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Abstract. India, just like many other countries in the world, has been combating malaria for a long time. Its geographical location along with its climate and general economic situation, have been causing the country to be a common habitat for malaria, which is a vector-borne disease carried by mosquitoes, as they mainly thrive in swamps or undrained ponds that are prevalent in India throughout the year. Witnessing the rise of the spread of malaria in India, the government does not just sit back and practice non-intervention, rather, over the past decades, the government, though not often entirely successful, have been developing various strategies and programs in countering the disease. Some of the most crucial ones include the National Malaria Control Programme in 1953 and agencies established include the National Vector Borne Disease Control Programme that has been developing plans for total eradication of malaria by 2030. Some of the strategies include traditional use of pesticides, while others are about distributing medications and improving surveillance programs in tracking the disease.

Keywords: Malaria, India, National Malaria Control Programme, eradication.

1. Introduction

In the South Asian subcontinent where India is located, the climate can be described as having abundant rainfall and strong temperature which are the perfect conditions for plant growth. But at the same time, the excessive precipitation and continuous high temperature also make the local residents suffer. The hottest places in the world are ranked, and India is on the list every year. Humidity and scorching heat are breeding grounds for germs. The dense jungle has a wide variety of species, and the sanitary conditions in ancient India were quite limited. Diseases spread quickly here because the humid and hot climate makes it easy for bacteria and viruses to reproduce and spread among people. The first thing that makes Indians suffer is the infectious disease "malaria" that is highly prevalent in hot flash areas. This disease, which is rapidly spread by mosquitoes, will always come unexpectedly during the alternation of dry and rainy seasons in India. Under the hot and humid climate, every small puddle hidden in the bushes is populated by mosquitoes for several generations. In a good house, a large number of mosquitoes carry germs and enter the crowd, causing countless Indians to suffer from the painful malaria. People at that time did not have a particularly good way to treat this disease, so they had to suffer from malaria once a year. Some people tried to use local remedies for treatment, while more people were at a loss and depended on begging for the protection of religious gods, some local people don't believe and even refuse to get treatment because of the limited education. The number of people who lost their lives to malaria in ancient India is immeasurable, and the disease has been an almost unsolved problem on a global scale for a very long time. Nearly 70 percent of malaria cases in India are contributed by five out of 36 States and Union Territories. These include Odisha (36%), Chhattisgarh (12%), Jharkhand (9%), Madhya Pradesh (9%) and Maharashtra (5%). Historically, the above-mentioned states and northeastern States such as Meghalaya, Mizoram, Nagaland, which have a wide coverage of forest, hilly, tribal and conflict-affected areas accounted for the most of the malaria burden in the country [1].

There are many ways to prevent malaria, as many of the techniques have been developed since the beginning of the struggle of humans against malaria in ancient times. For example, back in the 1900s,

people in North America contributed to the decline of malaria by draining swamps, water ponds, or any other places that contain a fair amount of stagnant water where malaria's vector mosquitoes inhabit and breed and later switch to more modernized surveillance programs [2]. In the present time, there are medications developed in countering malaria and people also continue using pesticides such as ITN to eliminate mosquitoes, and both of these strategies are wielded by India in its ongoing fight against malaria.

2. Process Malaria infection

The parasite affects in three stages once it affects the human body. After a mosquito has bitten a person, the parasites are transmitted into the body, and they head for the liver, which is the first stage of malaria. When an invasion is successful, the sporozoite is established inside a parasitophorous vacuole (PV), with a membrane generated from hepatocytes creating the interface with the cytoplasm of the hepatocytes. The parasite undergoes substantial remodeling in the PV, which is necessary for parasite survival. This remodeling helps the parasite bypass hepatocyte defenses like the autophagosomal system and use the PV as a pathway for nutrition intake from host cells. The processes of substantial organellar and genome replication occur without cytokinesis if these first perturbations are successful, leading to the creation of a multinucleated schizont. After LS development, cytokinesis takes place, resulting in the production of exo-erythrocytic merozoites. All *Plasmodium falciparum* liver stages immediately go through schizogony, but hypnozoites, a latent stage of *Plasmodium vivax* liver infection, are a reduced population of the liver stage [3]. Hypnozoites can stay inactive for many years before reactivating to go through secondary schizogony and bring on relapses of the infection of the blood.

After the infection stage described in stage one, where the liver is the targeted organ, the infection crosses to the second phase or stage 2. As previously described, the life cycle of the parasite in humans begins through infected Anopheles mosquito bites injecting into the host the parasites [4]. The motile sporozoites cross the epithelium traveling through the blood circulatory system to the liver, where it develops further into thousands of merozoites. These merozoites mark the beginning of the second stage. According to Milner, the parasites invade the red blood cells (RBCs), with the *Plasmodium falciparum* preferring erythrocytes invasion while the *Plasmodium vivax* responds or shows a tropism for reticulocytes.

Erythrocyte invasion requires the merozoites to undergo various complex maneuvers hence a more than one-step process. Merozoites and erythrocytes initial contacts occur at the merozoite surface at any point. The process is then followed by the reorientation of the polar merozoite relative to the erythrocyte, which is apical with a tight junction formed through the formation of an electron-dense contact between the two cells [4]. At the same time, the parasite's protein-coated surface sheds, and the parasitophorous vacuole forms, the ovoid shape of the parasite is maintained by a moving junction and an actin-myosin motor. Milner further states that the moving intersection closes behind the parasite forming an iris diaphragm enclosing the merozoite, which is the parasite within the parasitophorous vacuole. The parasite post-invasion replicates asexually where it is enclosed, producing daughter merozoites.

When the cell breaks, the daughter merozoites are liberated, and they move to invade the RBCs maintaining the blood stage. Malaria, or its clinical manifestation, including fever, anemia, and exhaustion, is caused by a continual cycle of attacking, replicating, and lysing the aforementioned blood cells; as a result, the host exhibits malaria symptoms. The parasites within the RBCs traverse into organs and tissues, sustaining the infection and preventing clearance by the spleen [4]. Some percentage of the parasites though small during the blood stage, undergo gametocytogenesis and are taken by the second feeding of a female Anopheles mosquito during a blood meal initiating the sporogonic or sexual phase.

3. Prevention policies against Malaria

Prevention Policy 1: In 1953, the Government of India launched the National Malaria Control Programme (NMCP). India is a major player in malaria research. Among these players, the CSIR-Central Drug Research Institute in 2011 noted it was the largest publisher on antimalarial drug discovery for the past five years. Take the contributions by the CSIR-Central Drug Research Institute as an example of malaria control measures in the country. Some of the molecules that India helped develop, like tafenoquine, pyronaridine and dihydroartemisinin are today part of standard treatments for malaria. Bulaquine (Elubaquine, CDRI-80/53) successfully completed clinical trials and has been marketed in India since 2000 [1]. The commitment to find new cures for relapsing *P. vivax* malaria is a good example. Since the 1950s, the WHO-recommended regimen for preventing relapse has been a 14-day course of primaquine, in patients with adequate G6PD (glucose-6-phosphate dehydrogenase) activity [1]. The issue is that since the disease is asymptomatic for this stage, patient compliance with the regimen was poor, and a new, simpler therapy was needed. Early work was supported by the use of *P. cynomolgi* infections of Rhesus monkeys at the CSIR as a model for *P. vivax* infection of humans. This model was set up and used since the late 1970s in collaboration with the WRAIR (the U.S. Walter Reed Army Institute of Research), testing 80–100 compounds over the next decade. One of the compounds, WR238605, was of particular interest, as it had established a curative dose in the experimental model. Subsequent clinical studies showed that it had a long duration of effect, and could potentially replace 14 days of primaquine with a single dose. This early work formed the basis of further clinical development for the compound, now called tafenoquine, which was taken on by GlaxoSmithKline and MMV as collaboration in 2008 [1]. India participated in the tafenoquine Phase-2b dose finding studies. Subsequent clinical trials culminated in the submission and approval in 2018 by both the US and Australian regulators. The next stage for this important medicine is the regulatory submission, approval and distribution of this medicine throughout countries with a significant *P. vivax* burden.

Prevention Policy 2: In 1997, the Government of India shifted its focus from the eradication of malaria to the control of the disease and switched from the blanket spraying of insecticides to selective spraying indoors. In 2003, malaria control was integrated with other vector borne diseases under the National Vector Borne Disease Control Programme (NVBDCP) as all such diseases share common control strategies such as chemical controls (e.g. indoor residual spraying), environmental management, biological control (e.g. larvivorous fish), and personal protection strategies (e.g. insecticide treated bed-nets) [1].

4. Available prevention methods

Within the program developed by India in combating its domestic malaria situation, one of the commonly used methods is related to the use of medications in both areas endemic to malaria or not. Some of the medications recommended include but is not limited to chloroquine. Also, the widely applied ACT (artemisinin-based combination therapies) treatments, which involve in the combination use of two or more drugs at the same time, are recommended and used in India, despite the relative weakness manifested for use by pregnant women. Both medications are still in use although as time progresses and as the situation of malaria in India gets better, but the specific application of each of them is different.

For chemoprophylaxis, or specifically chloroquine, it has a great potential and proven to be especially effective for pregnant women and children, and they are very useful in combating two types of malaria: *P. falciparum* and *P. vivax*. Other recommended ones belonging in the same category include doxycycline, having 95 percent efficacy, and atovaquone-proguanil, with about at least 95 percent efficacy [5]. Their period of use is different as well. For chloroquine, the use will be 4 weeks after the exposure while for atovaquone-proguanil, it will be 7 weeks after the exposure to the disease. The Artemisinin-based combination treatment was introduced in 2011 and became recommended nationwide. The treatment used in combination of drugs, is also very effective as it

exceeds the 95 percent of efficacy, even though there are few cases of hypersensitivity recorded, but for majority of the time, the medications work. In India, one of the common and effective combination is artesunate + sulfadoxine-pyrimethamine, also known as AS + SP, which has reached as high as 100 percent effectiveness, and other combinations proven safe include AS + MQ, which has the efficacy of 99.2 percent [6].

The combinations vary of ACTs in India from state to state, as the malaria variants also change from area to area; for instance, the ACTs might not be working as much in the northwest region of the country, in comparison with all other places in India. However, like all drugs in relation with targeted diseases, there is drug resistance developed, meaning new combinations for the case of ACTs need to be developed as well, and a promising one will be artesunate + lumefantrine, artesunate+piperaquine. With the implementation of both types of major medications, the government has to also monitor closely on the development of the disease region by region so that the specific medications can be used. Moreover, the government of India needs to also find suitable medications for people in northeastern regions of the country, where the status of malaria has been rampant.

Other than the use of medications, which contribute greatly to India in its fighting against malaria, India has also been implementing several different strategies. Some of the most effective and common ones in other countries are the use of pesticide and development of surveillance systems so that cases can be more easily tracked down for treatment. In order to make the aforementioned strategies better, India has made numerous plans trying to improve. Starting from 2015, the government of India has set several milestones on progress towards the elimination of malaria in the country, from 2016 to 2030, in cooperation with several major agencies in the country, such as “National Center for Vector Borne Disease Control, also known as NVBDCP which acts to provide guidelines and also monitor the enforcements of approved measures [7].

For surveillance programs, the government will make the reporting of cases, as long as fitting the symptoms, mandatory for individuals, which to do that, the government has to expand the surveillance on the status of diseases for individuals, basically putting malaria as a disease that the public should pay attention to. Furthermore, having individuals just reporting is not enough, as the government intends to also allocate medical specialists to different regions in order to provide the needed medical support for those being exposed to malaria [8].

In addition to just trying to improve the tracking of the disease, as a major player in eliminating malaria, pesticides also deserves attention from the government, as there are planned tracking in pesticide resistance or in cases even the use of it, as in India, the use of insecticides such as ITNs and IRS, which the ITNs can have as high as 80 percent of effectiveness in protecting people, only covers at most 60 percent [9]. At last, the government of India should not only focuses on surveillance of cases, which the medical specialists certainly need to be equipped with latest knowledge on the development of the variants in various areas, but also, focuses more on tracking pesticide resistance to see if the pesticide is effective to the specific malaria variant and expanding the use of pesticide.

5. Conclusion:

For decades, India has been trying to contain and eliminate malaria through the practice of providing effective medications, improving while expanding surveillance on malaria, along with continued pesticide use, as the deaths due to malaria has dropped from 1707 in 2007 to 93 cases in 2020, with the trend still on decline, except the cases from 2018 to 2020 remain pretty steady in trend. Nonetheless, the concerns of medication resistance, lack of supply of medications to people in need, along with problems of potential poor disease surveillance network and resistance developed by vectors against the use of pesticides, still remain, thus making the government of India having to watch closely on the status of their programs and methods so that the progress and efforts of combating malaria gained throughout years will not be wasted. Therefore, several things that could have been done include not only accepting and distributing the anti-malarial vaccines in the upcoming years, but also building up strong network in providing medications for people in heavily affected

areas in addition to setting up local agenda on closely monitoring the resistance of pesticides and making any adjustments when necessary in ensuring the elimination of vectors habitats.

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