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Review Article

Drug Resistant in Malaria

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Abstract

The following is an explanation of the main factors that theoretical models suggest influence the emergence of drug resistance in malaria. The development and pace of drug resistance propagation are significantly influenced by the proportion of infected hosts receiving medication treatment. The second important effect is the medication's capacity to eliminate parasites. The average transmission rate, recombination, the biological cost of resistance, and the mode of gene action are among the factors that also impact the rate of spread, albeit very slightly. the artemisinin derivatives. The process by which drug pressure selects resistant parasites, the following local transmission of those parasites, and the migration of reservoirs are all crucial components in the dynamics of drug resistance. Pharmacokinetics, pharmacodynamics, immunological factors, and the human host all play a major part in the selection effect of parasite interactions. Resistance spread is influenced by eco-epidemiological variables, such as migration. The goal of eliminating malaria is being hampered by the emergence and dissemination of drug resistance to antimalarials, which is also shortening the time that these medications can effectively treat patients. Treatment for malaria parasite infections in human hosts mostly consists of chemotherapy and chemoprophylaxis; nevertheless, medication selection pressure has been discovered to play a role in the emergence and dissemination of resistance. The restricted supply of compounds that have been shown to be suitable for therapeutic use throughout the preceding 75 years since the introduction of synthetic antimalarials has been seriously harmed by the emergence of drug-resistant parasite strains.

Key words: drug resistant; malaria; antifolate; chloroquine; combination therapies

1.Introduction

The parasitic tropical disease malaria is carried by vectors in 91 countries worldwide. Only six Plasmodium species are known to regularly infect people out of the over 120 species that infect birds, reptiles, and mammals. Plasmodium falciparum produces high quantities of blood-stage parasites that sequester in important organs in all age groups and cause severe anemia in African children, who make up the majority of malaria fatalities (Ashley et al., 2018) . The latter question is addressed by theoretical models of drug resistance. It is intended that by doing this, drug use policies that maximize a drug's useful life will be put into place (Mackinnon, 2005). Malaria treatment and control are severely hampered by medication resistance, particularly multiple drug resistance. The tropical world is seeing an increase in the propagation of resistance to practically all medications, including mefloquine, pyrimethamine, and chloroquine. As a result, there is an urgent need for new medications as well as a preventative measure (Mackinnon and Hastings, 1998). Plasmodium richen (which infects chimpanzees), Plasmodium cynomolgus (which infects Macaca fascicular), Plasmodium bergheim (which infects rodents), Plasmodium chabad (which infects Mus musculus), and Plasmodium gallinacean (which infects birds) are some of the models used in malaria research (Su et al., 2019) . Southeast Asia is home to the zoonotic Plasmodium knowlesi, a species that jumps from macaque monkeys. Recently, human instances of the zoonotic Plasmodium simoom and Plasmodium cynomolgus have been detected by molecular diagnostics; nevertheless, the prevalence and clinical significance of these species remain uncertain (Plewes et al., 2019) . A few species of anopheline mosquitoes carry the parasitic Mato protozoan infection known as malaria (Figure 1). Although people are frequently infected by four different species of Plasmodium, the majority of cases of illness and mortality are caused by Plasmodium falciparum (White, 2004a). The recently made-available P. falciparum genome offers intriguing new directions for medication research and valuable information for comprehending resistance mechanisms (Arav-

Boger and Shapiro, 2005) . For circumstances when trustworthy microscopy would not be accessible, antigen detection techniques have been devised. Based on the identification of histidine-rich protein-2 (HRP-2; ICT malaria P.f.), these innovative, quick techniques for treating Plasmodium falciparum (Huong et al., 2002).

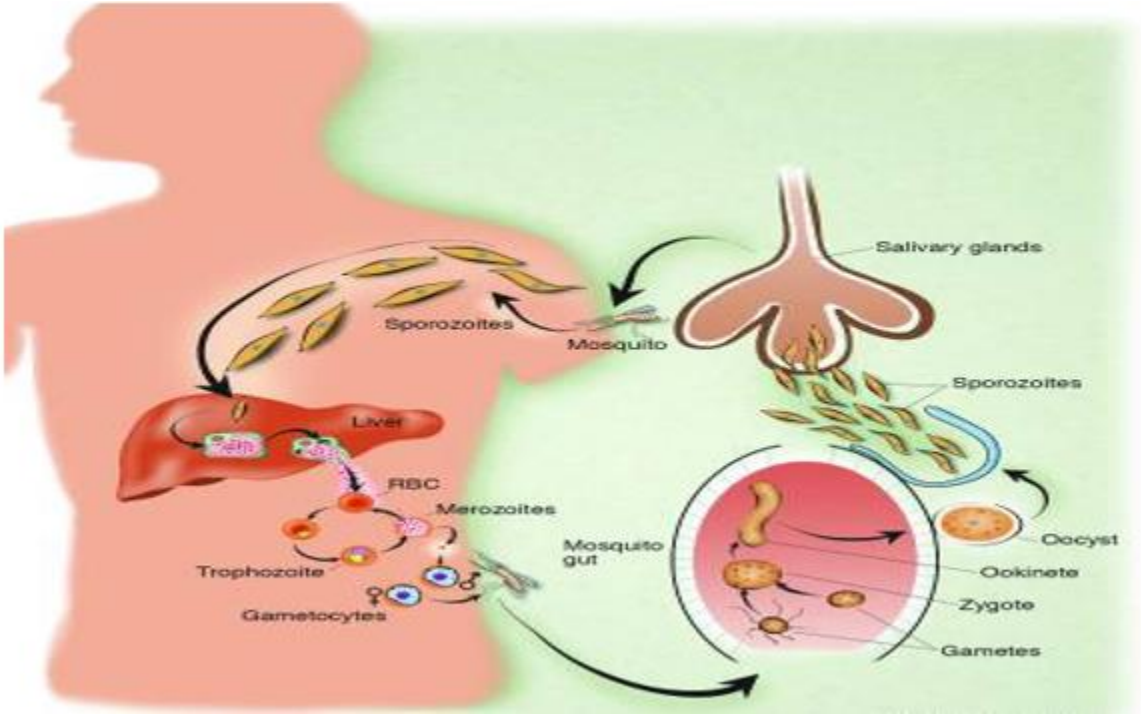

Figure 1: The life cycle of malaria parasites in humans and their vector, anopheline mosquitoes (White, 2004a).

2. The Diagnosis

Effective treatment and containment of malaria require a prompt and accurate diagnosis. Among the contemporary methods for diagnosing malaria include flow cytometry, molecular approaches, automated blood cell analyzers, serology-antibody detection, laser desorption mass spectrometry, and fluorescence microscopy (Murray et al., 2003). Lateral flow immunochromatographic technique is used in both malaria rapid diagnostic tests (RDTs) and rapid pregnancy tests (RPTs). In these tests, the clinical sample migrates as a liquid across the surface of a nitrocellulose membrane through capillary action. Two sets of monoclonal or polyclonal antibodies are used for a particular targeted parasite antigen: a capture antibody and a detection antibody. Monoclonal antibodies have the ability to be exceedingly selective, in contrast to polyclonal antibodies, which may be more sensitive. Furthermore, depending on the source of antigen used—peptides, recombinant proteins, or pure native protein—the performance characteristics of RDT can vary greatly (Murray and Bennett, 2009).

2. 1. Microscopy

Microscopic slide analysis of peripheral blood is still the most popular and reliable test for identifying malaria parasitemia in the majority of endemic locations. According to the WHO estimate from 2011, there were 165 million microscopic slide exams conducted globally in 2010. Diagnostic sensitivity estimates for microscopic slide examination vary depending on the type of infecting species, region, and other criteria. However, generally speaking, diagnostic sensitivity is considered to be no more than 75%. Based on the proportion of patients with clinical malaria who had parasitemia detected, this number was calculated (Wilson, 2013) . The most reliable method for determining whether someone has malaria is still microscopy. The methods for preparing slides, staining them, and reading them are widely accepted and standardized. An additional benefit of microscopy is the ability to estimate parasite density, which may be done with ease on a thick film (Figure 2) (Bisoffi et al., 2012).

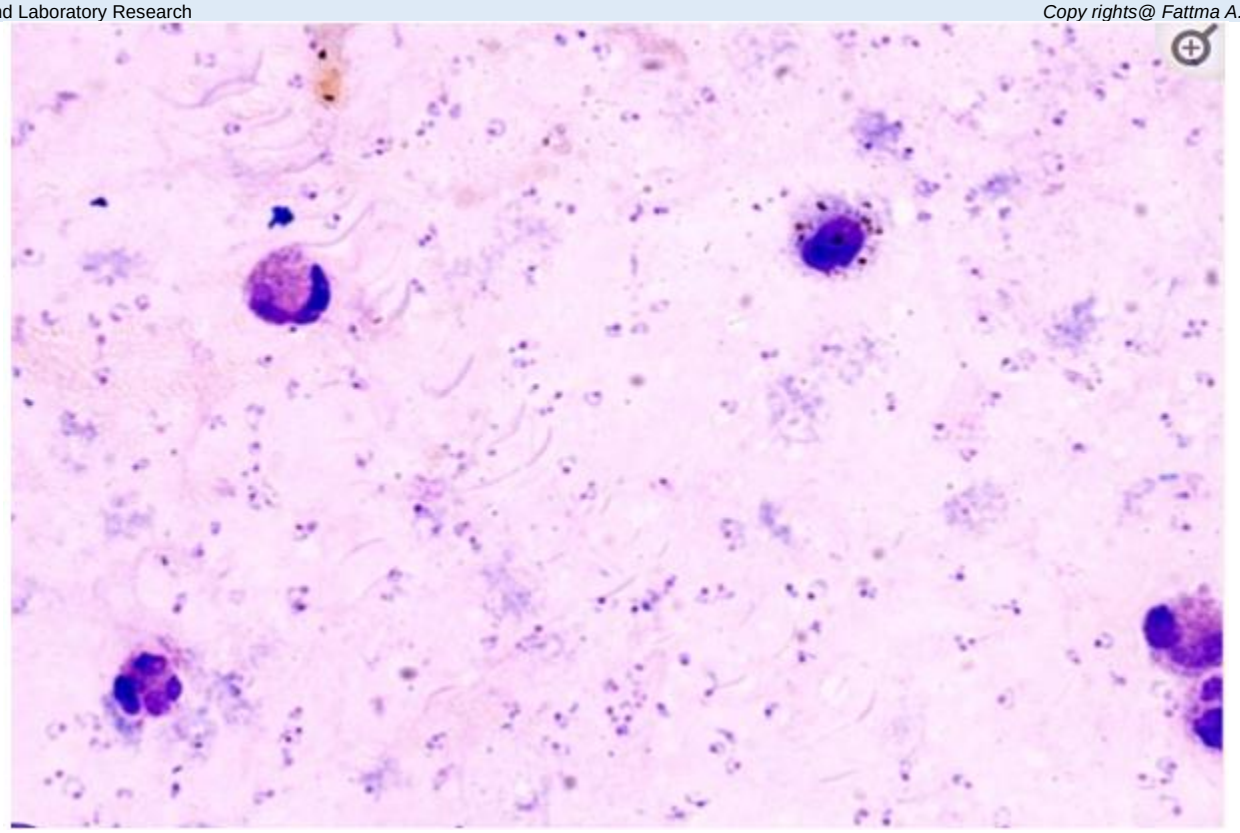

Figure 2: Giemsa-stained thick film containing a high P. falciparum parasite density (Photo courtesy of CTD Negrar; Maria Gobbo) (Bisoffi et al., 2012).

2.2. Antigen Detection Tests

The first blood sample obtained from each patient was a fingerpick sample, which served as a control for thick and thin smears and ICT malaria P.f./P.v.Ò (AMRAD, NSW, Australia), Precheck Ò (Orchid Biomedical System, Goa, India), and Optimal (DioMed AG, Switzerland) tests. There is an expiration date on each test that is used. Three knowledgeable technicians—each in charge of a particular test type—performed antigen testing in accordance with the manufacturer's instructions (Huong et al., 2002). Based on consensus reference genomic sequence alignment, the LAMP-PfK13 LAMP primer set was created for the detection of P. falciparum's gene Kelch 13. All human-infective Plasmodium species were among them, along with a few zoonotic species like P. Knowles and P. cynomolgus that have lately spread to infect human hosts (Malpartida-Cardenas et al., 2019).

3. Medications Available to Treat Malaria

3 .1. Quinine and Related Compounds

A member of the aryl amino alcohol class of medicines, quinine is a cinchona alkaloid. It is always provided as salt because it is a very basic chemical. There are several different formulations available, such as the gluconate, bicolpate, sulphate, dihydrochloride, and hydrochloride salts; the dihydrochloride is the one that is most frequently utilized. Quinine works against intraerythrocytic malaria parasites as a fast-acting schizonticide. Furthermore, it is not gametocytocidal against Plasmodium falciparum but gametocytocidal against Plasmodium vivax and malaria. Quinine also acts as an analgesic, but not as an antipyretic. It is uncertain how quinine works as an anti-malarial agent (Achan et al., 2011). Quinine, a naturally fluorescent substance, has been used for many years to treat malaria infections. Quinine's mode of action is still unknown, despite some data indicating that it functions in the parasite food vacuole. The multidrug resistance of Plasmodium falciparum (Bohórquez et al., 2012).

3.2. Antifolate combination Drugs

By blocking dihydrofolate reductase (DHFR), antifolate antimalarial drugs like cycloguanil and pyrimethamine (Fig.3) rob the parasite of essential cofactors for folate. In Plasmodium falciparum and other protozoa, DHFR serves as a bifunctional enzyme in conjunction with thymidylate synthase (TS), which uses methylenetetrahydrofolate to methylate d-UMP to d-TMP (Yuthavong, 2002).

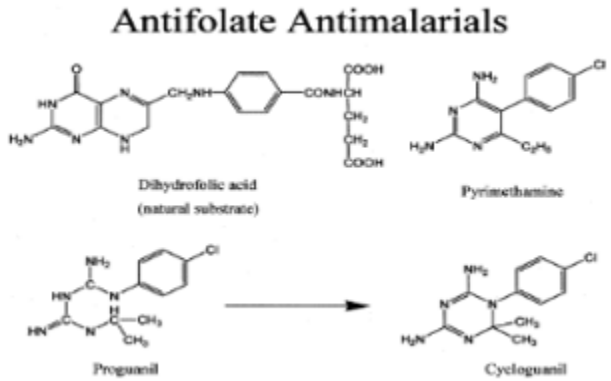

Figure 3: The structures of P. falciparum dihydrofolate reductase (DHFR) substrate and inhibitors (pyrimethamine and cycloguanil). Proguanil is the prodrug from which cycloguanil is generated in vivo (Yuthavong, 2002).

3.3. Antibiotics

Any substance that has been used to treat bacterial infections, as well as any analogues created if they were effective against Plasmodium falciparum, were considered antibiotics in this review. Two families, previously covered in two reviews, have been the subject of numerous investigations during the past thirty years: tetracyclines and macrolides and their derivatives. In the future, though, more medications that combat malaria parasites might be created. The activity of co-trimoxazole, quinolones, tigecycline, mirginiamycin, ketolides, fusaric acid, and thiopeptides against P. falciparum was detailed in this third and last review on the use of antibiotics as anti-malarial medications (Gaillard et al., 2016). The broad-spectrum antibiotics known as tetracyclines were discovered at the beginning of 1940. They are highly effective against a variety of bacteria, including intracellular bacteria and protozoa like Plasmodium, as well as lymphatic filariasis (Briolant et al., 2008).

4. Causes of Resistance

4.1 Definition of Antimalarial Drug Resistance

In non-falciparum species, antimalarial resistance has been slower to develop. This is likely because there are less parasites in the human host, which leads to fewer mutation events. For P. vivax and P. oval, this is because they can avoid blood schizonticides by generating hypnozoites in the liver (White, 2004b). Antimalarial drugs work primarily by eliminating the erythrocytic stages of malaria parasites, which infect humans and cause illness. The two most prevalent malaria parasites, P. falciparum and P. vivax, require distinct medication regimens for treatment. Because artemisinin-based combination therapy (ACT) is commonly resistant to earlier versions of the drug, it is currently recommended in almost all locations for the treatment of uncomplicated falciparum malaria. Chloroquine plus primaquine is still the standard first-line treatment for vivax malaria in most regions. The two medications that make up ACT are a potent artemisinin component that rapidly kills most parasites and a partner drug that acts more gradually to eliminate any remaining parasites and stop the emergence of artemisinin resistance (Cui et al., 2015).

4.2. Mechanism of antimalarial resistance

A closer examination of the parasite's metabolism and the antimalarial medications' method of action is required to appropriate the physical nature of resistance. Hemoglobin is taken up by the malaria parasite's intra-erythrocytic stage and stored in its feeding vacuoles. Here, hemoglobin is broken down into hemozoin pigment by exopeptidases and endopeptidases, of which ferriprotoporphyrin IX's cytotoxicity is a significant component (Farooq and Mahajan, 2004) . The effective use of antimalarial medications depends on their price, accessibility in endemic areas, short course regimens, good tolerance, and safety (especially in young children). Nowadays, almost all antimalarials must be used in combination with one another, with each medicine focusing on a distinct parasite pathway in order to prevent the emergence of parasites that are resistant to drugs (Petersen et al., 2011). Even after years of usage, little is understood about the majority of the malarial medicines currently on the market, including their mechanisms of resistance and manner of action. Even though this wasn't thought to be a big deal when these treatments worked well, it's becoming painfully clear that our capacity to come up with a solution is greatly constrained by our lack of understanding. Further understanding of parasite sensitivity spots, basic drug action mechanisms, and the development of resistance is necessary to not only create new medications with unique modes of action (Olliaro, 2001). Different antimalarial drugs function at different rates, or Figure 4 illustrates how the growth of drug-resistant parasites is accompanied with a relative increase in the likelihood of carrying gametocytes, which initiates a "vicious cycle." (Nosten and Brasseur, 2002) .

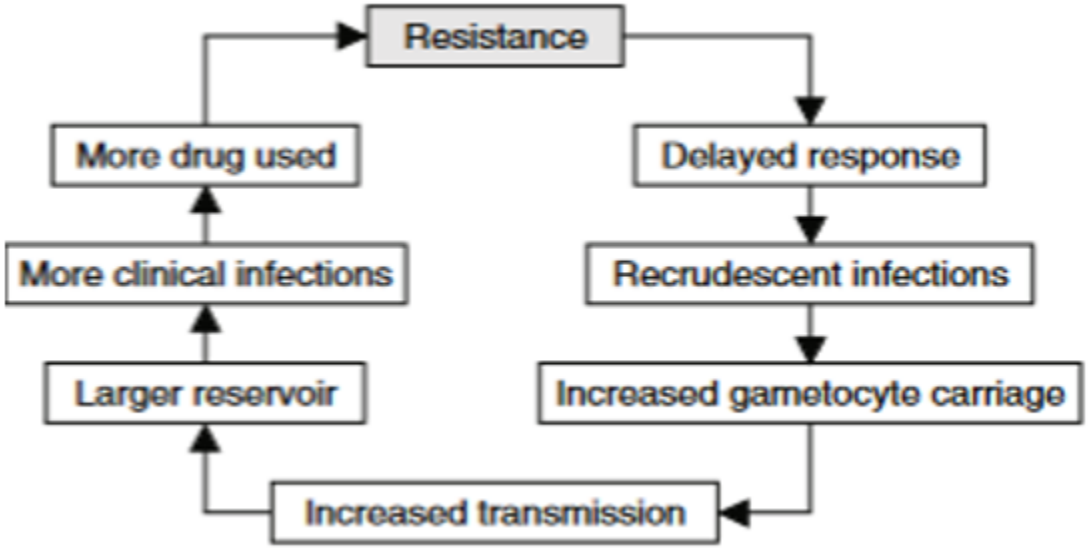

Figure 4: 'A vicious circle of medication resistance to antimalarials (Nosten and Brasseur, 2002).

4.3. Chloroquine

The detoxication of heme is how chloroquine and the other 4-substituted quinolines kill malaria parasites. Hemoglobin is one of the main nutritional sources for the parasite during its intraerythrocytic development and proliferation. It is carried into the acidic food vacuole where it is progressively broken down into smaller peptide fragments by metalloid, aspartic, and cysteine proteases. Free hem is a hazardous result of hemoglobin breakdown (Arav-Boger and Shapiro, 2005). Similar to antifolate resistance, chloroquine (CQ) resistance has been recognized for more than 40 years, but less progress has been made in identifying the underlying mechanism or mechanisms. Fast infection and hyde/microbes. The significantly slower onset and spread of CQ resistance suggested that its genetic makeup was probably more complex than that of antifolate resistance. As with any medication, understanding how it works is crucial to comprehending how an organism develops resistance, even though its final target and the molecules that mediate resistance to it don't always have to be linked, as the antifolates amply demonstrate (Hyde, 2002). For simple P. vivax malaria, the WHO recommends either ACTs or chloroquine (although chloroquine is no longer used in certain countries, such as Indonesia). Acts are being used more frequently due to the rising prevalence of chloroquine-resistant P. vivax, especially in Asia. While only artesunate-pyronaridines are licensed to treat P. vivax malaria in the blood stage, other ACTs are similarly useful and are used off-label. Relapses of P. vivax malaria pose a challenge to the management of malaria (Phillips et al., 2017). The most often used antimalarial medication in the world is still chloroquine. Every year, 200–400 million doses are taken. Despite broad resistance, it remains the medicine of choice for almost all cases of Plasmodium vivax, P. malaria, and P. oval malaria. It is also still widely used to treat falciparum malaria. Ten years ago in Papua New Guinea, resistance in P. vivax was first recorded, while in the late 1950s, resistance in P. falciparum emerged separately in South-East Asia and South America (White, 1999). Westerner I recently investigated the epidemiological elements linked to the emergence and transmission of drug-resistant malaria in a work in which he examined the parasite-drug human-vector interactions that influence the occurrence and dynamics of drug resistance (Schapira et al., 1993). There have been no reports of dormant parasites in humans after ART treatment, in contrast to evidence from in vitro studies. This might just be the result of researchers failing to notice these strange-looking parasites in patients' blood smears following therapy. Another possibility is that human organs like the spleen eliminate highly injured and dead parasite-infected red cells, leaving only a very tiny percentage of latent parasites circulating at densities below microscope detection thresholds (Cheng et al., 2012).

5. Detection of resistance

5.1 In vivo tests

The effectiveness of ACT is waning in several domains. Traditional 48-hour in vitro assays are not useful as an epidemiological tool for tracking artemisinin resistance since they have not shown comparable decreases in vitro susceptibility, despite clear resistance in vivo. We postulated that the observed discrepancy could be clarified by a reduction in vulnerability during the ring stage, devoid of a commensurate decline in sensitivity during the more developed stages of the parasite. Consequently, we developed a simple adaptation of the standard WHO in vitro 48-hour antimalarial drug susceptibility test, focusing on the growth of the parasite's ring stage, and assessed its efficacy as an indicator of artemisinin resistance in vivo (Chotivanich et al., 2014).

5.2 In vitro tests

an in vivo susceptibility tests. Artesunate (Guilin Pharmaceutical Co., Ltd., China) was prepared as 60 mg/ml of stock solution diluted in 1 ml of 5% NaHCO3. was stored at 30°C and utilized within a month of production. After being further diluted to 1 mg/ml in RMPI-1640 culture medium (which was then kept at 4°C and used within a week after production), artesunate (ATS) was then serially diluted twice to get final concentrations ranging from (Chotivanich et al., 2014). It is poorly known how P. vivax malaria affects expectant mothers, who are particularly susceptible to P. falciparum malaria. There is conflicting evidence regarding a higher morbidity of P. vivax malaria during pregnancy. In contrast, neither the risk nor the severity of malarial infection was shown to be significantly impacted by pregnancy or the infant in a recent study carried out in an area of Sri Lanka where P. vivax is the main endemic (Witkowski et al., 2013). In vitro techniques have been employed to track medication resistance against malaria. Radioisotope uptake is one of the methods utilized for P. falciparum in vitro growth inhibition investigations. Artemisinin resistance testing methods include serological assays, fluorescence-based assays, and, more recently, ring-stage

survival assays. In laboratories with limited resources, radioisotope and serological assays are unfeasible due to their specific equipment and supply requirements (Cheruiyot et al., 2016) The primary basis for antimalarial drug susceptibility testing methods is the in vitro culture of the parasite. The malarial parasite can be cultured in vitro using one of two methods: continuous culture or short-term culture. The short-term culture approach is easy to use in the field, involves minimal laboratory equipment, and is straightforward. The continuous cultivation approach is more complex and requires technical, logistical, and well-equipped laboratory support. It is a vital tool for basic research, efficacy trials, and the development of anti-malarial drugs. Early in the 20th century, the first short-term culture technique for Plasmodium falciparum was described (Bass, 1911).

6. Combination Therapies and Resistance Mitigation

6.1. Artemisinin-based combination therapies

With an expected 241 million infections and 627,000 deaths from malaria in 2020, the disease is still a serious worldwide health concern. Approximately 98% of cases are caused by Plasmodium falciparum, the most virulent causative species. On the plus side, the total disease burden has significantly decreased during the previous 20 years. This is partially due to the fact that artemisinin-based combination therapies (ACTs)—such as dihydroartemisinic-piperaquine (DHA-PPQ), artemether-lumefantrine (AL), artesunate-amodiaquine (ASAQ), artesunate-mefloquine (AS-MQ), artesunate-sulfoxide-pyrimethamine (AS-SP), and artesunate-pyronaridine (AS-PND)—have been adopted as the primary treatment for uncomplicated P. falciparum malaria in endemic nations across the globe. While AS-MQ and DHA-PPQ have been the most widely used ACTs in Southeast Asia, almost 98% of doses given worldwide are delivered with AL and ASAQ (Table 1) (Ward et al., 2022).

derivative of ART	Associated medication	Shorthand	World use	areas where first-line				
Artemether	Lumefantrine	AL	74%	AFRO	AMRO	SEARO	EMRO	WPRO
Artesunate	Amodiaquine	ASAQ	24%	AFRO				
Dihydroartemisinic	Piperaquine	DHA-PPQ	1%	AFRO		SEARO		WPRO
Artesunate	Pyronaridine	AS-PND	0.1%			SEARO		WPRO
Artesunate	Mefloquine	AS-MQ	1%		AMRO	SEARO		WPRO

Table 1: The WHO recommends artemisinin-based combination therapy as initial treatments for P. falciparum malaria that is not complex (Ward et al., 2022).

As ACTs, which are currently the first-line treatment for P. falciparum throughout the world where malaria is endemic, artemisinin derivatives are well-tolerated, fast-acting medications that are frequently combined with longer-acting partner medications. Southeast Asia has seen the emergence of artemisinin resistance, which shows up as a delayed clearance of parasitemia after treatment with an artemisinin derivative (Takala-Harrison and Laufer, 2015). which pair a medication with a prolonged half-life with the quick potency of an artemisinin derivative. However, resistance to both artemisinin and its companion medications has once more expanded throughout Southeast Asia, and there have been isolated reports of artemisinin-resistant parasites in other areas.2- 6. As ACTs are currently the sole therapy option accessible in Africa that is still universally effective, well-designed surveillance measures are required to safeguard artemisinin and its partner drugs throughout the continent (Ehrlich et al., 2020). Researchers have found over 20 distinct mutations in P. falciparum that confer artemisinin resistance. Artemisinin resistance is produced by mutations in the parasite gene kelch13. It is challenging to monitor the spread of resistance using standard molecular marker techniques due to the variety of mutations involved and the possibility that the same mutation may emerge independently in many places (Project, 2016).

7- Future plans for combating drug-resistant malaria

The majority of malaria control programming have been threatened by the significant challenge posed by drug resistance in malaria parasites. Drug-resistant malaria is a global issue, but it is particularly bad in Africa. When resistance to chloroquine develops, SP combination is used as a first-line medication in a number of countries worldwide. Particularly in some areas of east Africa, the widespread use of SP combination has quickly led to sensitivity loss, raising the possibility of multidrug resistance developing there. A variety of presumptions describe the future antima35.larial drug resistance and measures to combat it. First, antimalarial medications will be required for a very long time (Farooq and Mahajan, 2004). Countries shifted to SP as their nationally approved treatment once resistance to CQ spread. Countries returned to using artemisinin combination treatments (ACTs), as advised by the World Health Organization (WHO), when resistance to SP also increased. Future attempts to control malaria must focus on creating and executing control techniques to impede the spread of resistance, as it will likely take a minimum of ten years for a new compound to achieve the efficacy of artemisinins. There have now been reports of resistance to medications in the artemisinin class, suggesting the potential establishment of resistance (Klein, 2013). The population genetic structure and malaria control are being studied at different regional scales and with different concepts. A first theory is to identify genetically different parasite populations, suggesting little gene flow between them (Koepfli and Mueller, 2017).

Methodology

To determine the chloroquine-resistant P. falciparum strains that are actively spreading malaria in Orissa, India, we have tried screening the main malaria vectors in the area for the presence of resistant parasite strains. Female Anopheles mosquitoes that were sleeping indoors were collected from a variety of malaria-endemic areas in the Indian state of Orissa using CDC light traps and mechanical aspirators. Areas with high endemicity were selected for the study (Mohanty et al., 2009).

Qualities for inclusion

Male or female, at least eighteen years old, and willing to provide informed consent to participate in the study will be the inclusion criterion.

Disqualification standards

If a participant's intellectual and/or cognitive handicap has been diagnosed, it may hinder their capacity to understand the project's information and prevent them from being recruited for the study.

As shown in Table2, a purposive sample of five types of respondents was chosen for interviews in each of the chosen countries (Tindana et al., 2021).

Nigeria	Respondent	Number	Interview/FD(
Policy	National regulatory authorities	2	Interview
	National Malaria Control Program	2	Interview
Distributor	Public sector drug wholesalers/distributors	6	Interview
	Private sector wholesalers/traders	6	Interview
Health service providers	Public sector: clinicians, pharmacist	4	Interview
	Private sector: clinicians, nurses, pharmacist, drug store	4	Interview
	Village health workers	3	FGD
Researchers	Malaria researchers	5	Interview
End users	Parents /caregivers	3	FGD
	Parents/caregivers	4	Interview
	Community leaders	3	FGD

Table 2: Sample for semi-structured interviews and focus group discussions (FGDs) in Nigeria (Tindana et al., 2021).

Discussion

Thailand's efforts to combat malaria have been quite successful, as seen by the more than 80% drop in incidence between 2007 and 2017. Nonetheless, the prevalence of malaria remains a problem for public health. The Thai government has set a 2024 deadline for the national eradication of malaria, with a strategy that emphasizes early detection and efficient treatment for asymptomatic cases. Thailand's socioeconomic structure and geographic location present considerable obstacles to the eradication of malaria. Controlling malaria is made more difficult in areas that border other endemic countries due to human and vector migration, as well as the fact that most of these areas are rural, which increases transmission and results in a lack of health services (Noisang et al., 2019). The current study shows how pesticide resistance to pyrethroids, which are used to control malaria vectors, is quickly emerging, especially in Tanzanian regions where ITNs have been in use for more than 20 years. The results of this study showed that the mosquito population's reactions to WHO insecticide-treated paper differed depending on the sentinel site. In contrast to organochlorine, some vector populations were able to withstand exposure to all three synthetic pyrethroid compounds that were tested: permethrin, deltamethrin, and lambda cyhalothrin., chemicals include carbamate and organophosphate, to which the vectors were completely sensitive. The Moshi and Muheza mosquito populations of Anopheles gambiae s.l. demonstrated resistance to deltamethrin, whilst the Rumeru, Dar es Salaam, Handeni, and Kilombero mosquito populations were suspected of having resistance. Additionally, compared to those in the other four sentinel districts, the mosquito population in Arumeru, Moshi, and Muleba districts was resistant to lambda cyhalothrin (Kisinza et al., 2011). The ex vivo evaluation of medication susceptibility can help track and monitor antimalarial drug resistance. Assessing the parasites' reaction in the absence of host factors that can influence a therapy's in vivo efficacy is made possible by measuring ex vivo susceptibility. Several techniques, including those based on DNA and antigens (Chotivanich et al., 2014). This is the first paper that we are aware of regarding the use of the SYBR green I assay in conjunction with the WWARN standardized procedure for 384-well fast ex vivo testing to profile drug responses in field isolates via in vitro malaria medication sensitivity. The WWARN test was improved by using higher quantities of dye, detergent, and culture time (Cheruiyot et al., 2016). Your findings show that the created LAMP assays in conjunction with the LoC platform are excellent choices for clinical settings, offering great promise for point-of-care integration. This is accomplished by utilizing an ISFET-based platform and a Lab-on-Chip technique to modify amplification chemicals to be compatible with electronic detection (Malpartida-Cardenas et al., 2019). Despite being the first medication used to treat malaria, QN's exact mode of action has never been established (Bohórquez et al., 2012). While humans rely solely on salvage mechanisms to meet their metabolic demands, many infections rely on their own metabolic route to create folate. This makes targeting the folic acid synthesis route for the treatment of several illnesses in humans appealing. While drug-resistant microorganisms can proliferate rapidly, the effective life of individual medications is extended when they are combined to treat diseases (Ding et al., 2013).

Conclusion

Drug laws should ideally vary depending on the regions of a nation and the degree of resistance present. This could be challenging based on how the health services are set up. However, during epidemics at least, programs to

control malaria should be ready to step in and provide more potent medication, which may be required when entire communities are unexpectedly exposed to very high transmission levels. The clear historical pattern of the availability and use of inferior antimalarials coinciding with the evolution and propagation of resistance is particularly alarming if we are to meet the objectives of the WHO's Global Technical Strategy for Malaria 2016–2030. We propose to use mathematical modeling to evaluate the urgent need for P. vivax and P. falciparum drug resistance surveillance in Southern Thailand's rural and border regions, given the scarcity of complete datasets available. Continuous molecular surveillance reaching community malaria centers may be the most efficient way to achieve this given the conditions covered in this paper, which include the concealment of early treatment failure, inherent resource constraints, and sociopolitical obstacles to malaria control in these areas. The Thai and Southeast Asian plans for the eradication of malaria would suffer if this important region was not completely covered. Malaria is a potentially fatal virus that affects both the world's most industrialized nations and those with inadequate access to basic medical care. Rapid and accurate diagnosis of malaria patients is becoming more important due to the rising disease burden, the emergence of antimalarial drug resistance, and the widespread use of antimalarial therapy (ACT). Alternative diagnostic approaches are required because to the challenges associated with doing microscopy, particularly in endemic locations. However, the majority of fevers linked to malaria can already be detected by the majority of currently available techniques, making them sufficiently sensitive for therapeutic care. The issue is the clinical malaria test's poor specificity, particularly in areas with high transmission rates. Both the identification of clinically important malaria biomarkers and the detection of malaria infection would make an ideal diagnostic tool (capable of discriminating illness from simple infection). There are already known potential biomarkers. Furthermore, a more sophisticated RDT for malaria would provide a semi-quantitative evaluation of the parasite density. As an alternative, research should concentrate on combining many disease markers into a single device, such as adding a bacterial illness biomarker to a malaria RDT. The main foundation for all antimalarial drug susceptibility assay techniques is the growth and maturation of parasites in in vitro culture medium with various known concentrations of antimalarial agents. Every method has different costs, costs of sensitivity, and costs of practicality. For a long time, the radioisotope assay method was the gold standard; nevertheless, its widespread application was constrained by the risks involved in the disposal of radioactive materials. DNA-specific fluorochrome assaying techniques such as flowcytometry and fluorometric assay are very sensitive, fast, automated, and highly DNA-specific; nevertheless, they require expensive equipment, and the presence of leukocytes increases background noise.

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