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The Impact of the Malaria Parasite on Global Health

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Abstract: Malaria is an acute, chronic, and disabling parasitic disease accounting for millions of deaths and huge amounts of suffering in the human population yearly. Around 3.2 billion people are currently at risk of infection from Plasmodium parasites. Despite the promising advances of recent years in research and public health addressing malaria control, this disease remains one of the main health concerns in developing countries. In this review, we outline some of the key peculiarities of malaria, including epidemiology, biological aspects of the malarial parasite, host responses to malaria infection, and also discuss the clinical manifestations associated with the parasite. We also highlight the current strategies for disease control, before conveying how this often dismissive or short-sighted approach of many campaigns results in many health and social consequences for a large proportion of the world's population.

This paper aims to give an outline of

knowledge regarding malaria thus far and key future research directions in regard to both the parasite and its current control strategies. It gives a clear view of what we already know regarding epidemiology, biology, and clinical symptoms resulting from the malaria parasite, and the many knowledge gaps still existing that hinder further understanding of the malarial infection and block possible future new treatments and interventions against the disease.

1. Introduction

2. Epidemiology of Malaria

Epidemiology is the study of the distribution and determinants of health-related states among specified populations and the application of this study to control and prevent health problems. The principles are the same when dealing with the global distribution of any disease, infections, or deaths due to a particular disease. Malaria has held humans in its grip since the early dawn of the human race. Malaria is caused by four species of the Plasmodium parasite: P. vivax, P. falciparum, P. malariae, and P. ovale. However, the most dangerous one is P. falciparum. Nearly half of the world's population is at risk of malaria. In 2019, there were an estimated 229 million cases of malaria worldwide. The African Region carried a disproportionately high share of the global malaria burden. In 2019, the region was home to 94% of malaria cases as well as deaths due to malaria. Epidemiology, which is the distribution and determinants of malaria, is still a challenge for researchers because socioeconomic factors, demographics including population growth, and biosocial perspectives are the reasons for the increasing number of malaria cases.

The global trends of increases in malaria cases have taken place in all regions between 2010 and 2019. Malaria-free areas are still prone to malaria; thus, surveillance and control programs must be initiated. The malaria burden varies in different regions depending on geographical areas. The African and South-East Asia regions are the most affected areas of Plasmodium falciparum, which is responsible for about 80% of cases and almost all deaths. Children under five years of age and pregnant women are the most vulnerable to malaria infection due to their reduced immunity. Malaria is an occupational disease in miners, forestry workers, or fishers who work in high-risk areas. Generally, the Maldives, Namibia, and South Africa declared an absence of malaria cases in at-risk border areas by certified health methods. Malaria has both seasonal and epidemic transmission in forested areas and continuous transmission in urban areas from September to May in the whole island nation. Therefore, strict surveillance and a multi-sector approach should be initiated in order to eliminate malaria by 2030. [1][2]

2.1. Global Burden of Malaria

Malaria is an ancient and modern-day killer that continues to impact a large portion of the world. Despite the successful reduction of malaria by half from 2000 to 2019, the COVID-19 pandemic reversed this trajectory. Current estimates suggest that around 229 million cases and 409,000 deaths occurred in 2019, disproportionately affecting sub-Saharan Africa. High-risk populations include children under 5 years of age, who experience one in two deaths from malaria worldwide, and pregnant women, with approximately 872,000 women still experiencing malaria in 2019. Each year, around three-quarters of a billion people become infected with malaria. With 17% of Burkina Faso's healthcare burden due to malaria, the potential socioeconomic impact in high endemic areas is undeniable.

Global inequalities persist, with low-income regions still accounting for over 80% of the disease burden. Malaria cases continue to decline in the highest-burden countries, but 17 high-burden countries in sub-Saharan Africa reported increases in estimated cases in 2020, including eight among the Democratic Republic of the Congo, Kenya, and Nigeria, which make up 44% of the 19 million additional cases in 2020 compared to the previous year. Not solely across countries or in specific regions, malaria in particular places is often experienced differently in certain risk groups, owing to modifiable physiological and environmental factors including malnutrition, water and sanitation, and indoor air pollution. Multiple countries are reporting stockouts of the frontline falciparum combination therapy drug in the public sector in 2020, with 14 reporting substantial stockouts as compared to previous years, but advocating treatment from the healthcare system through low prompt care being sought often resorted to self-purchase of any therapy. [3][4]

3. Biological Aspects of the Malaria Parasite

The malaria parasites are members of the Plasmodium genus. These are characterized by a hugely elaborate life cycle comprised of both sexual and asexual stages of reproduction and multiple stages of disease. Consequently, they demonstrate an enormous immune adaptation, making the generation of a vaccine a significant challenge. Infection may proceed through one or more of the four species infective to humans. Before these Plasmodium species can cause bloodstream infection, pre-erythrocytic sporozoites and merozoites must first infect the liver, replicating and later being released upon the burst of the liver cells to generate erythrocytic merozoites, which are then spread around the body through the bloodstream. Subsequent interaction within the bloodstream with erythrocytes results in the development of trophozoites and schizonts, in the case of P. falciparum, with mature schizonts being responsible for the induction of the classical malaria fevers. Physical symptoms of the disease also manifest themselves as infected erythrocytes binding to blood vessel endothelia.

Immature gametocytes will also enter the human bloodstream and are taken in by an Anopheles mosquito when it ingests a blood meal. These gametocytes will successfully fertilize in the mosquito gut and develop into immature ookinetes, which move through the mosquito stomach wall and develop into oocysts, mitotically dividing and differentiating to produce sporozoites that will eventually be released and enter the bloodstream. Within 10 to 23 days, the mosquito will become infective in spreading the malaria parasite. The development of malaria in humans is determined by the immune status of the patient. Many children are born with resistance following the transfer of passive immunity from their placenta to protect against maternal malaria infection. In the absence of this immunity, the child’s own immune system will need to develop immunity over many years to have a chance of survival. [5][6]

3.1. Life Cycle of the Malaria Parasite

3.1.2. Life Cycle.

The life cycle of the malaria parasite is key to understanding the transmission and pathogenicity of the disease. The two critical aspects of the life cycle that are relevant to control and treatment are (a) when the parasite can be transmitted from one human to another and (b) the anatomical site in the human host in which the damage of importance to the disease occurs. The complete life cycle of Plasmodia within the mosquito or human host has been thoroughly reviewed. The life cycle is finally completed in its vertebrate host, where asexual reproduction by schizogony occurs in the bloodstream and is responsible for the general clinical condition of the patient.

The malaria parasite enters the body of a vertebrate host when an infected female Anopheles mosquito takes a blood meal. The sporozoon is presumably attached to the proboscis. Within 30 seconds of entering the vertebrate host, the sporozoon begins to penetrate endothelial cells of the venules of the body or feeds at the expense of the plasma in these blood vessels. Symptoms of transitory fever may appear within 12 to 30 minutes of the sporozoon's arrival in a host who has not been repeatedly infected in the past with malaria parasites, or these symptoms may be delayed for 8 to 12 days in a repeatedly infected person. In refrigerated blood samples, the sporozites move about as motile forms on the slides for many hours, and some can sometimes still be observed near, but outside the red corpuscles of cultured blood, for as long as 4 days. These free sporozites may, infrequently, come into contact with other blood meals arbitrarily taken by the mosquito. Preventing the transition from one segment of the life cycle to the next is a primary goal in interrupting malaria transmission. The potential points of inhibition are many, due to the complexity and duration of the life cycle. [7][8][9]

4. Clinical Manifestations and Complications

Malaria afflicts a broad range of populations, from the well-protected who reside for a short duration within malaria-endemic areas, to the local residents who have some acquired immunity, to young children residing in malaria-endemic areas with no protection. The clinical manifestations of malaria depend on the magnitude of the infecting inoculum, the duration of survival and multiplication of the asexual parasites, the immune response developed by the host, and the periodicity of parasitized erythrocyte rupture. Patients can be asymptomatic or have symptoms ranging from mild non-specific symptoms such as fever, chills, diarrhea, or vomiting, cough, and malaise to severe acute, life-threatening sequelae. An understanding of the clinical spectrum is vital in order to reach a proper diagnosis, to treat the patient, and thus reduce transmission of the parasite to the community, to provide chemoprophylaxis during a stay in malaria-endemic areas, and to detect and treat asymptomatic cases. An episode of acute, uncomplicated malaria is characterized by the sudden onset of fever, chills, intense headache, and myalgias, commonly associated with declining concentrations of circulating red cells from destruction and hemoglobin concentration from hemolysis. If anemia becomes severe, weakness, dizziness, and in children, a reduced level of consciousness can occur. On physical examination, tachycardia, splenomegaly, and orthostatic hypotension can also be present. Attention to the clinical history is important as exposure to malaria in malaria-endemic areas is the most significant risk factor for infection. Some travelers with no prior exposure to malaria may present with higher levels of parasitemia and more severe symptoms. Taken together, these symptoms and signs provide enough information for clinical suspicion and a subsequent diagnosis of acute malaria. Severe malaria is a manifestation of infection, which without effective antimalarial treatment will lead to a lifetime risk of mortality nearing 100%, due to complications including cerebral malaria, pulmonary edema, severe anemia, hypoglycemia, metabolic complications, acidosis, and more rarely, kidney complications. Children under five years of age bear the heaviest burden of severe disease and mortality. The timely diagnosis and appropriate clearance remain the foundation for rescuing lives from severe malaria. Detection approaches guided by awareness [10][11][12]and testing of symptomatic individuals form a fundamental strategy to make the diagnosis and ensure timely effective antimalarial treatment. It is also important to make the public aware of what symptoms to look for, the consequences of not seeking prompt medical care, and where to receive the appropriate treatment for malaria.

5. Prevention and Control Strategies

Preventing and controlling malaria are major components of the fight against the disease. The current strategy is based on four main components: vector control, early diagnosis and prompt treatment with effective antimalarial agents, education, and monitoring of communities at risk. Good strategies for mosquito vector control—the use of treated nets and spraying the inside of houses with residual insecticides—have been identified and are proving to be effective tools in the control strategies. The choice of antimalarials depends on the severity and complexity of the infection, the pattern of drug resistance, the age of the individual, and the knowledge of the safety, effectiveness, and reliability of different drugs.

To support effective therapeutic and prophylactic antimalarial strategies and, in the case of temporary visitors, to meet pre-travel health advice, a number of useful resources are available. Mosquito net coverage is considered a necessary malaria control measure to support the roll-out of indoor residual spraying or when conditions preclude spraying. Although it is recognized that net coverage yields a reduction in the prevalence of malaria and an increase in child survival, a gap exists between the distribution of LLINs and their use in most sub-Saharan African countries. Infection prevention strategies such as intermittent preventive treatment in pregnancy to reduce anemia in pregnant women and the incidence of low-birth-weight newborns' delivery should become an important part of the antenatal care in malaria-endemic areas. Combining IPT and nets could also be a useful strategy for further reducing the number of malaria deaths. Knowledge of malaria among society is a great asset in the fight against malaria; a community aware of the necessity to attend a primary health center for treatment of fever or cough is well placed to demand effective treatments. Indeed, community engagement and changes in behavior are key elements of the integrated approach advocated by the Global Malaria Action Plan, which is basic to the prevention of importation of malaria, early detection, and treatment at the local health facility. The roll-out of these packages should benefit from appropriate mapping methodologies, targeting of resources to the neediest, optimal case management, evaluation and impact assessment of interventions, and appropriate training at all levels of the health system. Most people in sub-Saharan Africa will continue to be exposed to malaria, with varying levels of intensity; it is therefore important to ensure all interventions are sustainable, as the profile of intervention required will change as malaria is suppressed. Significant challenges to their implementation, including weak health systems, shortage of health workers, and misinformation about the applicability and safety of long-lasting insecticide-treated nets, are real impediments to their implementation in many endemic African countries. These comprehensive approaches will help to ensure that expenditure on malaria control optimizes the health of the populations at risk. [13][14]

5.1. Vector Control Measures

A primary strategy in the fight against malaria is to reduce the abundance of the vectors or their survival, to limit the number of infections that can be transmitted. Anopheles mosquitoes are the vectors for human malaria, and control efforts need to target them. Full protection of households is effective, and some protection is also gained by unprotected people living close to protected households. However, this 'spatial repellency' of mosquito coils and mats is usually only a few hours, so personal protection is needed at dusk and dawn; at these times, indoor mass protection by long-lasting insecticidal nets is effective. Insecticide treatment of animals where mosquitoes rest, such as cattle and dogs treated with pyrethroids, saves human lives and may also protect the animals from mosquito-borne diseases. Some residual malaria transmission occurs from early evening outdoor biting and outdoor resting mosquitoes where bed nets are in use. Outdoor biting and resting mosquitoes can be controlled by using pyrethroids to treat the inner walls of houses, particularly the eaves of the walls where mosquitoes like to rest before finding a blood meal, thus reducing their numbers. Perhaps the most traditional and effective form of malaria control is through environmental management, decreasing mosquito breeding sites, draining swamps, and engineering landscapes to make them less prone to hosting vectors. Urbanization can also lead to a reduction in malarial prevalence, as urban areas often have better personal and public hygiene associated with those populations. Insecticides are a primary mode of controlling the vectors indoors, with long-lasting insecticidal nets and indoor residual spraying serving as the primary tools of vector control. In long-lasting insecticidal nets, a net good for about 5 years is coated with insecticide, and resistance to washing and fading, but remains safe for humans. The net is impregnated by dipping in an insecticide bath, or a net can be produced by treating filaments and weaving them. The former is common in most areas of South America and in the forests of Central and Western Africa. The specific insecticides and formulations of treatment have changed over the years as mosquitoes have developed resistance to the older treatments. Many novel types of treatments are being studied, including the release of sterile males or transgenic males, though challenges such as public acceptance and sustainability complicate the initiation of new techniques. A technique utilizing bacteria has also been developed. The bacteria reside in the mosquito gut and influence its ability to transmit the malarial parasite. The bacterium is spread by the mosquito in its offspring. Spraying bed nets with mixed chemicals, either pyrethroids or insect growth suppressors, broadly increases potency and delays the onset of mosquito resistance, as some mutants can be resistant to one drug but not the other. As such, when the net is used, it offers a broader intent for reducing malarial incidence. There are challenges with insect brackets, including biodegradation and splashing, and the administration of novel chemical regimens was used for large phases of the public to assure compliance. [15][16]

6. Conclusion and Future Directions

This parasitic disease has exerted a tremendous burden on global health for thousands of years and remains among the most significant infectious diseases. Over the past two decades, we have witnessed great progress in malaria control, primarily through the scale-up of ITNs and ACTs, vaccine development, and other insecticides. However, the genotypes of the malaria parasite are rapidly changing, leading to insecticide and drug resistance. Eliminating the spread of the malaria parasite would greatly assist with malaria eradication. Despite significant advancements, some problems remain, including vaccine toxicity, drug resistance, and high transmission rates. Continued research on the molecular biology of the disease, the introduction of new therapies, the discovery of new drug targets, the design of new vaccine strategies, and the development of new vaccines are all goals that should be considered.

Next-generation interventions include, but are not limited to, explorations of the gut microbiota, which are associated with timeliness and mosquito transmission, Wolbachia, gene therapies, and alterations to the genetic makeup of Anopheles. Furthermore, improvements in surveillance systems through the use of new diagnostic equipment and techniques should be investigated. Continued malaria research will assist in the creation of new strategies for the prevention and management of malaria. Over the last fifteen years, substantial investments in malaria research and development have been made; nonetheless, increased funding and international cooperation are required in order to reach a malaria-free world. Sustainable malaria control may be achieved by expanding research and education on the parasite and involving the public and health workers effectively. The government should have a program for malaria management. In order to eradicate malaria, strong commitment is essential. There is evidence of the substantial burden caused by malaria, and other feasible methods of eradicating malaria should be investigated and implemented in the future.

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