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Review Article

Epidemiological Burden and Management of Malaria in Rural Settings

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Abstract: Malaria is a complex and daunting problem with an intricate life cycle and nuanced interplay of agent, host, vector, and environment that is further complicated by challenging political, eco- nomic, and social factors. This article provides an overview of the relevant aspects of malaria focusing principally on the key public health-related issues including estimates of the current burden, description of the agent, life cycle, modes of transmission and vector aspects, discussion of epidemiological factors, basic information on clinical manifestations, diagnostic testing, treatment and chemoprophylaxis approaches.

Keywords: Malaria, Epidemiology, Clinical Features, Management.

INTRODUCTION:

Malaria is an acute febrile illness caused by *Plasmodium* parasites, which are spread to people through the bites of infected female *Anopheles* mosquitoes. There are 5 parasite species that cause malaria in humans, and 2 of these species – *P. falciparum* and *P. vivax* – pose the greatest threat. *P. falciparum* is the deadliest malaria parasite and the most prevalent on the African continent. *P. vivax* is the dominant malaria parasite in most countries outside of sub-Saharan Africa.[i]

The first symptoms – fever, headache and chills – usually appear 10–15 days after the infective mosquito bite and may be mild and difficult to recognize as malaria. Left untreated, *P. falciparum* malaria can progress to severe illness and death within a period of 24 hours. In 2020, nearly half of the world's population was at risk of malaria. Some population groups are at considerably higher risk of contracting malaria and developing severe disease: infants, children under 5 years of age, pregnant women and patients with HIV/AIDS, as well as people with low immunity moving to areas with intense malaria transmission such as migrant workers, mobile populations and travellers.[ii]

DISEASE BURDEN

According to the latest World malaria report, there were 241 million cases of malaria in 2020 compared to 227 million cases in 2019. The estimated number of malaria deaths stood at 627 000 in 2020 – an increase of 69, 000 deaths over the previous year. While about two thirds of these deaths (47 000) were due to disruptions during the COVID-19 pandemic, the remaining one third of deaths (22 000) reflect a recent change in WHO's methodology for calculating malaria mortality (irrespective of COVID-19 disruptions).[iii]

EPIDEMIOLOGY

Susceptibility to malaria is an important host-related factor that influences malaria transmission dynamics. In areas of high malaria transmission intensity with repeated exposure to the parasite, a level of partial immunity will develop and severe infections are seen predominantly in children, whereas most adults will be asymptomatic. In areas of lower transmission intensity all ages can be affected Individuals who are semi-immune may not develop severe disease, or any symptoms at all; however, they can still be infected and therefore serve as a source of infection for others. Without repeated exposure to the parasite, partial immunity will wane.[iv] Individuals who were born in a malarious region and then move away may be vulnerable if they return and therefore should be strongly encouraged to take malaria prophylaxis. Additionally, this partial immunity passes from mother to child *in utero*; however, passive immunity wanes and this

leaves children aged 6 months to 5 years the most vulnerable to infection with malaria since they are no longer protected by maternal antibodies and they have not yet survived repeated infections to develop partial immunity of their own. Climatic conditions, including temperature and rainfall, can have substantial effects on malaria.[v] Increasing temperatures shortens the duration of the extrinsic cycle in the vector making the mosquito infectious more quickly and increasing the probability of transmission. Excessive heat may make the use of bed nets uncomfortable and thereby reduce usage. Rain can create additional breeding sites for *Anopheles* mosquitoes and increase the density of vectors. However, in some circumstances, excessive rain may actually wash away breeding areas. The presence of water for irrigation around villages and houses, plays a major role in determining the risk of malaria. In some areas malaria transmission is driven by seasonal changes of the climate with the transmission and incidence being the highest in the rainy season. Increasing altitude decreases the risk of malaria transmission and, at high enough elevation, vector populations cannot be maintained and the disease will therefore be absent.[vi]

Vector competence, or the innate genetic factors that influence mosquito susceptibility to *Plasmodium* infection and subsequent ability of a vector to transmit a pathogen, is important and varies among species with some being totally refractory to infection. A related, but broader concept that has been used to conceptualize malaria transmission is vectorial capacity which integrates several important factors including vector density, host preference, and female mosquito longevity, as well as vector competence. Vectorial capacity, which is difficult to measure, can be assessed quantitatively as a function of the density of female anopheline mosquitoes relative to humans, the probability that a mosquito will feed on a human, the number of times a person is bitten, the proportion of the vector population that survives the extrinsic cycle in the mosquito, and the number of days this proportion is expected to survive.[vii] *An. gambiae*, an efficient malaria vector with high competence and vectorial capacity, is highly susceptible to infection, has relatively long survival, prefers to feed on humans (anthropophilic), feeds (endophagic) and rests (endophilic) indoors, and is active at night (nocturnal). Given that the extrinsic cycle in the vector may be as long as 18 days, mosquito longevity is of particular importance.

CLINICAL MANIFESTATIONS

The clinical manifestations of malaria vary with age, immunity, epidemiology, and geography. In highly endemic areas, the high- est risk groups include children (age 6–36 months), who can develop severe illness, and pregnant women, who can deliver low birth weight newborns. In geographic regions where malaria is transmitted year round, older children and adults develop partial immunity after repeated infections and are at lower risk for severe disease.

Malarial Fever

Early in the course of clinical malaria, febrile episodes occur at irregular intervals daily. The temperature of non-immune individuals and children may rise above 40°C (104°F) and can be associated with tachycardia, delirium, and febrile convulsions (in children). Later in the course of the infection (if untreated), the rupture of infected RBCs may become synchronized giving rise to febrile paroxysms every other day for *P. vivax*, *P. ovale*, and *P. falciparum*, and every third day for *P. malariae*.

Uncomplicated Malaria

Uncomplicated malaria can occur with any *Plasmodium* species. The initial symptoms of malaria are non-specific and may include fever, tachycardia, tachypnoea, chills, malaise, fatigue, diaphoresis, headache, cough, anorexia, nausea, vomiting, abdominal pain, diarrhoea, arthralgias, and myalgias.[viii] Laboratory evaluation of uncomplicated malaria may demonstrate parasitaemia (usually < 0.1 per cent parasitized RBCs), anaemia, thrombocytopenia, elevated transaminases, mild coagulopathy, and elevated blood urea nitrogen (BUN) and creatinine.

Complicated/Severe Malaria

Complicated malaria is generally defined as acute malaria with hyperparasitaemia (>5–10 per cent of parasitized RBCs) and/or major signs of organ dysfunction.[ix] Many of the clinical findings are the result of the parasitized (and non-parasitized) RBCs adhering to small blood vessels in a process known as cytoadherence. The clinical findings may include altered consciousness (with or without seizures), acute respiratory distress syndrome, circulatory collapse, metabolic acidosis, renal failure, haemoglobinuria (blackwater fever), hepatic failure, coagulopathy (with or without disseminated intravascular coagulation), severe anaemia, massive intravascular haemolysis, and hypoglycaemia.

Cerebral Malaria

Cerebral malaria is an encephalopathy that presents with impaired consciousness, delirium, and/or seizures.[x] Risk factors for cerebral malaria include no malarial immunity, age (young and elderly), pregnancy, poor nutritional status, HIV infection, and history of splenectomy. Cerebral malaria can rapidly progress to coma and death. If untreated, cerebral malaria is almost always fatal; with appropriate treatment mortality is 15–20 per cent. Laboratory evaluation of cerebral spinal fluid (CSF) may be normal or may have a slightly elevated total protein and cell count. Retinal haemorrhages and other ophthalmologic abnormalities may be observed. Survivors of cerebral malaria may have long-

term neurological sequelae. This is more common in children than adults and may include hemiplegia, cerebral palsy, cortical blindness, deafness, epilepsy, language deficits, and impaired cognition.

TREATMENT AND MANAGEMENT OF MALARIA

The treatment and management of malaria can be challenging and depends on the species of *Plasmodium*, the potential resistance, levels of parasitaemia, and clinical status.[xi]

Uncomplicated Malaria

Uncomplicated malaria is typically treated with oral medications and does not require hospitalization. However, young children, non-immune adults, and immunosuppressed individuals can deteriorate rapidly and should be followed especially closely.

Uncomplicated *P. Falciparum* Malaria

Selection of an appropriate treatment for uncomplicated *P. falciparum* malaria is dependent on drug availability, resistance patterns, and individual patient-specific factors. When possible, uncomplicated *P. falciparum* malaria should be treated with a combination of two agents to inhibit the development of further antimalarial resistance. Chloroquine is the drug of choice for patients where chloroquine-sensitive *P. falciparum* can reliably be predicted based on geographic resistance patterns. For chloroquine-resistant *P. falciparum* malaria first-line treatment consists of one of the following agents: artemisinin derivative combinations, atovaquone/proguanil, quinine (in combination with doxycycline or clindamycin), or mefloquine (in combination with artesunate or doxycycline).

The WHO recommends artemisinin combination therapies (ACTs) as the first-line treatment of uncomplicated falciparum malaria as they are potent against all developmental stages of the asexual forms of malaria, resulting in the most rapid clearance time relative to other agents.

Uncomplicated Non-Falciparum Malaria

The treatment of choice for the erythrocytic forms in uncomplicated non-falciparum malaria is chloroquine as it is well tolerated and highly effective. There are small pockets of chloroquine-resistant *P. vivax* that can be treated with mefloquine, atovaquone/proguanil, or quinine in combination with doxycycline or clindamycin.

In order to prevent relapse of *P. vivax* or *P. ovale* infections, treatment directed at the hypnozoites should be considered. The drug of choice for the clearance of presumed hypnozoites is primaquine. Primaquine can cause severe and potentially fatal haemolysis in individuals with G6PD deficiency. Patients should be screened for G6PD deficiency prior to administration of primaquine. Patients that have G6PD deficiency should be educated about the possibility of relapsing infection. Primaquine is contraindicated in pregnancy.

Complicated and Severe Malaria

Treatment of severe malaria typically requires hospitalization for high-level supportive care and the prompt administration of par- enteral antimalarials. There are two major classes of drugs available for parenteral treatment of severe malaria, the cinchona alkaloids (quinine and quinidine) and the artemisinin derivatives (artesunate, artemether, and artemotil). Intravenous artesunate is the preferred treatment of children, adults, and pregnant women in the second and third trimesters with severe malaria (in areas where artesunate is of reliable quality and is immediately available). Otherwise, intravenous quinine (in combination with doxycycline or clindamycin) is the regimen of choice.

CONCLUSION

Malaria is a preventable disease but remains one of the world's great scourges. However, renewed resources and international resolve have resulted in progress towards reducing the burden of malaria and led to cautious optimism about the future elimination of this disease. Given the availability of proven methods for malaria control, as well as the promise offered by innovative approaches for vector control, improved diagnostics and therapy, and the potential for vaccine development, such cautious optimism is not unwarranted. The science of malaria may be reaching the point of making elimination, and even eradication, possible. However, science alone will be insufficient to conquer malaria and both significant resources and unflagging resolve, at the international and local level, will be necessary to consolidate the recent gains made and to make additional progress. Yet, both resources and resolve are not unlimited, and areas impacted by malaria have many pressing problems such as HIV/AIDS, tuberculosis, food shortages, poverty, pollution, and other critical issues. Reducing the burden of malaria will have to be part of a broader dialogue to determine priorities.

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