THE BURDEN OF MALARIA AND CHALLENGES/OPPORTUNITIES FOR IMPROVED TREATMENT AND CONTROL 1

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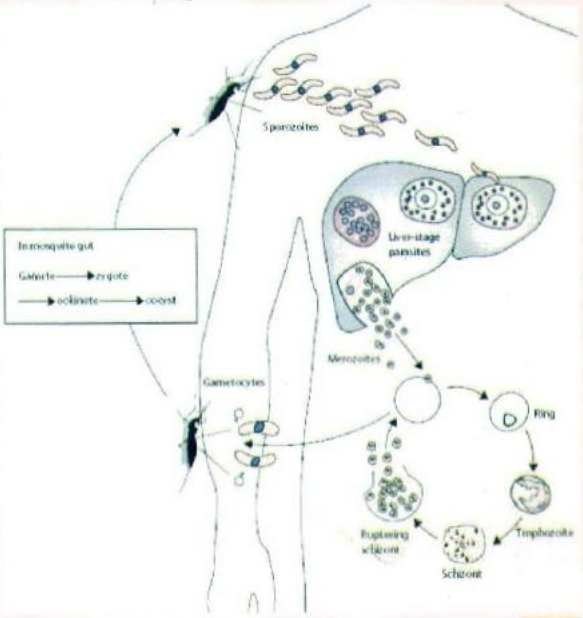
Summary: Malaria continues to be a major medical and developmental challenges in endemic areas, mostly sub-Saharan African countries. A number of factors, such as drug and insecticide resistance, war and civil disturbances, environmental and climatic changes, travel and population increase, are responsible for the worsening malaria situation in African continent. Despite the huge challenges of the disease burden, efforts to drastically reduce the impact or completely eliminated the disease has increased over the years. Several national and international organizations are more committed ever than before in the fight against this deadly disease. Today, the interventions that have proven effective in prevention and control of malaria include early diagnosis, prompt and effective therapy, prevention of contact between human and the vector by using insecticide treated bed net, and intermittent preventive therapy in pregnancy.

Introduction: Malaria is a febrile illness characterized by a number of symptoms because of its impact on several organs and systems of the body. It is the most important parasitic infection in the world. Though the disease is known to mankind for a very long time, it still continues to be a major cause of death and disability in endemic countries, especially among pregnant women and young children.[1] Today, malaria has become a priority for the international health community and is now the focus of several new initiatives. It has been estimated that nearly 40% of the world's population are at risk of malaria.[2]

Malaria is caused by protozoan parasites belonging to the genus *Plasmodium*, of which *P. falciparum, P. ovale, P. vivax, and P. malariae* are responsible for human disease. Of these four species, *P. falciparum* is most common in sub-Saharan Africa and also the most deadly species.2,3

Transmission: Malaria is transmitted through sting of female Anopheles mosquitoes, which feed on human blood mostly at night. Though malaria can be transmitted by several species of female anopheline mosquitoes that differ in behaviour, *Anopheles gambiae*, which is widespread in Africa, is the most effective vector and it is difficult to control.[1] Furthermore, *P. vivax* and *P. ovale* form resting stages in the liver (hypnozoites) that, once reactivated, can cause a clinical relapse many months after the initial event.

Also, because *P vivax* can develop in mosquitoes at a lower temperature than can *P. falciparum*, its geographical range is wider.[2] The life cycle of malaria is divided into two stages which occur both in man and female anopheles mosquitoes. Once mosquito sucks human blood (which is needed for it to lay its eggs), the male and female gametocytes are taken along. Within the mosquito, the gametocytes fuse to form a zygote, which is further divided asexually several times to form sporozoites. Finally, the sporozoites migrate to the mosquito's salivary gland from where they are transmitted to another person following subsequent human blood meal. A brief representation of the life cycle of malaria is shown in the figure below.[2]



Epidemiology: The main determinants of epidemiology of malaria are the number (density), the human-biting habits, and the longevity of the anopheline mosquito vectors. Anophele gambiae occur in high densities, bites humans frequently, and are long-lived.[4] Today, malaria is considered a disease of tropical and sub-tropical regions of the world, having been successfully eliminated in many western countries.[1]

Pathogenesis and clinical features: The clinical features of malaria are extremely diverse and may range in severity from a mild headache to the development of acute pulmonary oedema in a moribund patient. However, the majority of attacks develop in a well-recognized pattern in which bouts of fever alternate with asymptomatic periods.[4,5] Incubation period (time between infection and the onset of clinical features) is shorter for patients with blood induced infections than sporozoites induced infections. In both conditions, the duration is influenced by the species of infecting parasite, by the degree of acquired immunity possessed by the patient and, probably, by the parasite dose.[6] The pathogenic changes related to malaria involve blood and blood forming system, spleen and the liver, though other secondary changes may also occur in all major organs, depending on the type and severity of the infection.[6]

Burden of malaria: Nature had recognized the phenomenal burden of malaria long before the application of economic principles in analysis of disease burden became evident. This is exemplified in the inherited disorder of sickle cell trait. In geographical regions where malaria is still endemic, nature rather allowed a potentially fatal mutation into the genetic pool than have humans unprotected from malaria. Sickle cell trait (heterozygous AS) protects individuals against malaria.[7]

Malaria is one of the top three killers among communicable diseases particularly in tropical Africa. In 2000, a WHO report stated that half of over 2400 million of the world's population at risk of malaria are in Africa.1 Malaria affects the health and wealth of nations and individuals alike. In Africa today, malaria is understood to be both a disease of poverty and a cause of poverty, and it is estimated to result in growth penalty of 1.3% per person per year in the region.[8,9,10] In some countries with a very high malaria incidence, the disease may account for as much as 40% of public health expenditure, 30-50% of inpatient admissions and up to 60% of outpatient visits.[11,12] Malaria hits hardest poor tropical and sub-tropical countries[3,12]

Medically, about 300-500 million clinical cases of malaria are said to occur every year, resulting in over 1 million deaths, particularly among under five year old children. Over 90% of global malaria burden occur in sub-Saharan Africa.[1,10] In Nigeria, malaria accounts for 50% of all outpatient visits, 10-30% of all hospital admissions13 Furthermore, it has been reported that malaria accounts for 25% of infant and 30% of childhood mortality.[13] Among pregnant women, malaria is estimated to cause as many as 10,000 deaths each year,[14] contributes to approximately 2 to 15% of maternal anaemia, 8 to 14% low birthweight infants (an important contributor to infant mortality), and 3 to 8 % of all infant deaths.[15,16] Malaria infection in pregnant women is largely asymptomatic in areas of greatest burden even though parasite can sequester in the placenta particularly in the primigravidae, thus contributing to low birth weight infants.[17,18] However, this condition is one of the few contributors to morbidity and mortality that is amenable to intervention once a woman becomes pregnant.[19] Furthermore, it is important to appreciate the fact that the impact of malaria extends far beyond the direct measures of morbidity and mortality. There are several reports linking malaria to reduction in school attendance and loss productivity.[20,21] Also, evidence suggests that the disease can impair intellectual development of a child.[22] Factors which have been identified as contributing to increasing burden of malaria in Africa include: drug and insecticide resistance, war and civil disturbances, environmental and climatic changes, travel and population increase.[23]

Intervention: Despite the huge burden of malaria in endemic countries, all hope is not lost. Several national and international organizations are committed to drastically reducing the burden or even completely eliminating the disease. For example, in an effort to combat the growing threat of malaria, the Roll Back Malaria (RBM) partnership was launched in 1998, with the goal of halving the burden of malaria by 2010. Combating malaria has been set as a high priority within the United Nations (UN) Millennium Development Goals.[25] Also, the African Region of the World Health Organization in its Strategic Framework for malaria prevention and control during pregnancy recommended a three-pronged approach for effective malaria intervention for pregnant women. These approaches include use of intermittent preventive therapy (IPT), insecticide treated bed nets (ITNs) and appropriate case management of malaria illness and anaemia.[17]

Intermittent preventive treatment in pregnancy (IPTp) involves providing pregnant women with two treatment doses of an effective anti-malarial drug during pregnancy, at predefined intervals after quickening (i.e. after 16 weeks gestation or first noted movement of the fetus).[17,26] In many African countries, sulphadoxine- ▶

pyrimethamine is the programmatic drug used for IPTp, and studies have shown that it is safe and efficacious in reducing adverse maternal and fetal outcomes[17,27,28] It is recommended that pregnant women should receive two doses of IPT, each at least one month apart, under directly observed therapy during regularly scheduled antenatal care visits in the clinic. [17,26,29]

Insecticide treated bed net (ITN) is another form of intervention for reducing the burden of malaria, particularly for young children and pregnant women. The recommendation is that to prevent mosquito sting especially at night, one should regularly sleep under ITNs. Insecticide treated bed nets protect pregnant women and children who sleep under them, thus reducing the adverse effects of malaria in these populations.[17,30,31]

The recommended first line anti-malarial drug in the treatment of acute uncomplicated falciparum malaria is artemisinin-based combination therapy (ACT).[13, 32] In Nigeria, artemether-lumefantrine (A-L, 20mg-120mg), and artesunate/amodiaquine (At-Aq) are recommended for children and adult non-pregnant patients. The dosage regimen for A-L, based on body weight, is: 5- <15 kg, one tablet per dose; 15-<25kg, two tablets per dose; 25-<35kg, three tablets per dose, and 35kg and more, four tablets per dose; given over three days (give the first dose, 8hrs later give a second dose, thereafter, give 12 hourly for the remaining 4 doses). At-Aq is given as 4mg/kg-10mg/kg over 3 consecutive days.[13] For pregnant patient, the Nigerian anti-malarial treatment guideline recommends oral quinine as first line drug for treatment of uncomplicated malaria at a dosage regimen of 10mg/kg, 8-12hr for 5-7days.[13]

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