Burden of Malaria on Egypt through Travelers Coming from Endemic Areas

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Abstract

Background: Malaria, the most common parasitic disease globally, is transmitted by Anopheles mosquitoes. With 229 million cases and 409,000 deaths in 2019, Africa is the most affected region, accounting for 94% of total cases and deaths. The disease is caused by five Plasmodium species: P. falciparum, P. vivax, P. ovale, P. malariae, and P. knowlesi. The increasing prevalence of P. vivax infections poses unique diagnostic and therapeutic challenges. Imported malaria cases into non-endemic regions and malaria-free countries are becoming a public health challenge. Egypt, known since ancient times, has successfully eliminated malaria but is currently preventing re-introduction. The last locally transmitted case was in 1998, but epidemiological evidence suggests a risk of resurgence in areas where malaria was eliminated but vectors still exist.

Keywords: Malaria

Introduction

Malaria is the most common parasitic disease in the world. The parasite is transmitted to the human host by mosquitoes of the genus Anopheles (1). The world witnessed 229 million malaria cases which resulted in 409,000 deaths in 2019 alone. Although malaria cases are reported from 87 countries globally, Africa bears the brunt of these infections and deaths as nearly 94% of total malaria cases and deaths occur in this continent, particularly in sub-Saharan Africa. Most of the Middle East Region countries are malaria-free as no indigenous cases of infection have been described in recent years (2).

Malaria in humans is caused by five Plasmodium species, namely P. falciparum, P. vivax, P. ovale, P. malariae, and P. knowlesi. Most malaria infections in Africa are caused by P. falciparum which is also more virulent and causes the majority of malaria-related mortality worldwide. However, increasing prevalence of P. vivax infections, particularly in the Indian sub-continent, poses unique diagnostic and therapeutic challenges (3).

Imported malaria cases into non-endemic regions and malaria-free countries are being increasingly recognized as a new public health challenge for the industrialized and other malaria non-endemic countries. Changes in the ecosystem and climate due to global warming have also increased the risk of vector-borne diseases such as malaria (1)

Malaria as a disease has been known in Egypt since ancient times. Malaria was endemic in almost all Governorates of the country but prevalence showed a marked decline by 1990, and regressed in most of the Governorates. Egypt was classified within group 2 of the EMR countries where malaria was firmly under control and aiming at eradication of the disease. During 2010–2013, Egypt successfully eliminated malaria (maintained zero indigenous

cases), but remained in the stage of prevention of re-introduction of malaria (4).

There have been no cases of locally-transmitted malarial in Egypt since June 14, 2014. Between late May to mid-June, 19 locally-acquired *P. vivax* malarial cases were identified in one village of the Aswan Govrnorate in Egypt (5).

In Egypt, malaria has been endemic in all governorates, including Fayoum, which was the last nidus of the disease. The prevalence showed a steady decrease by 1990, and the last locally transmitted case was in 1998. Also, available epidemiological evidence suggests that in areas where malaria was eliminated, but the vectors still exist, there is a risk of re-emergence of the disease. This particular situation applies to Fayoum governorate as it was the last focus of malaria, and the main mosquito vectors are still prevalent, therefore a potential for resurgence exists (6) (7).

Dynamics of Malaria in Africa

The key determinant of the dynamics of malaria transmission in Africa is the great efficiency of African vectors relative to those of other continents. This vector system is responsible for very high inoculation rates and is remarkably stable in a wide range of environmental conditions (8).

African vectors also appear to be relatively flexible in exploiting landscape changes brought about by anthropogenic activity estimates that together, Anopheles funestus, Anopheles gambiae, and Anopheles arabiensis account for 95% of all infective bites in the Afrotropical region. On a broad scale, we would expect the distribution of transmission to mirror that of these species. Other malaria vectors, including Anopheles melas nili, Anopheles moucheti, and the saltwater breeders Anopheles melas and Anopheles merus, are relatively inefficient but may have important effects at the local level (8).

In forested areas of Cameroon, for example, An. moucheti has been as efficient as Anopheles gambiae sensu stricto (s.s.); although its distribution is limited to the slow-running rivers of central Africa. Stable malaria has an inertia that tends to absorb environmental changes caused by human activities. However, that buffering capacity has its limits, even in Africa, and the degree of local environmental changes needed to effect the transition from stable to unstable malaria is uncertain (8).

Some heavily built-up areas near the center of Africa's large cities and mining areas with strictly enforced environmental health regulations have very little transmission. However, experience has shown that in most endemic areas, significant reductions in malaria transmission are difficult to achieve, whether by trying to eliminate breeding sites at the research lever in Tanga, Tanzania, or by reducing mosquitoes in West Africa, where less than one mosquito per house maintains endemicity (8).

The findings from bed net studies and Snow et al. (1997) suggest that even under conditions of persistent, stable, highly endemic malaria, environmental changes can change the frequency of febrile attacks or of the prevalent type of severe malaria while having little effect on parasitemia. This area needs much more research attention in terms of determinants, interventions, and clinical research (8).

The chief determinants of unstable malaria are the factors that vary the level of transmission, whereas the main determinant of stable holoendemic malaria in subSaharan Africa is human acquired immunity. The extremely efficient African vector mosquitoes, together with a favorably warm climate, lead to very high values of BCRR(Basic Case Reproduction Rate) and of the steady-state entomological inoculation rate (EIR), which is the mean number of mosquito bites infectious for malaria received by the average

inhabitant per unit of time (e.g., per year or per night) (9).

If transmission is considered in terms of BCRR, a value of 1 means that transmission is just at replacement level: for every individual infected with malaria who recovers or dies, another incident case appears. This situation is very unstable. If transmission decreases, the malaria ceases to renew itself in the human population and tends to die out. However, if the BCRR increases, so will malaria-except as limited by slowly acquired human immunity (9).

A BCRR value of 10 means that each case will give rise to 10 more, and the resulting exponential increase will lead to a large epidemic until either all the population is infected or the transmission falls as a result of changed environmental circumstances. When the BCRR remains high, the forces of immunity in the affected population will gradually regulate the spread of infection and the level of transmission (9).

This process is seen most clearly in Africa because the BCRR there is so high; it may exceed 1,000 in parts of the savannas of western and eastern Africa. Under these circumstances, the steady-state EIR (i.e., the risk to a nonimmune visitor) may exceed 300 infective bites per year. The features of this very high degree of endemicity must be understood if it's necessary to understand the likely effects of environmental change (including climate change) (9).

Climatic Determinants

Temperature

Environmental temperature affects the development and survival of malaria vectors and, perhaps more significantly, the duration of Plasmodium development within the invertebrate host. In simple terms, the duration of sporogony increases hyperbolically with decreasing environmental temperatures to a point at which parasite development ceases altogether (10).

This critical temperature varies by parasite species. For Plasmodium falsparum, the most abundant parasite in sub-Saharan Africa, laboratory studies have estimated it to be in the range of 16-19^{o}C in practice, transmission is commonly assumed to be limited to months in which the average temperature is above this threshold (10).

In Africa, these temperature limits commonly are reached only at high altitudes and at high latitudes. If a relatively conservative temperature threshold of 18^{o}C is assumed, then most of tropical Africa experiences temperatures suitable for malaria transmission at least 10 months per year however, extensive areas in which temperatures are suboptimal for six months or more are found in the high-altitude fringes of southern Africa (Botswana, Namibia, South Africa, Zambia, and Zimbabwe) and in highland fringe areas of Madagascar (11).

In these areas, the effects of low average temperatures may be compounded by those of frost. In Zimbabwe, for example, Leeson (1931) found that Anopheles gambiae sensu lato disappeared when minimum air temperatures fell below 5^{o}C (11).

The limits of vector distributions in South Africa also appear to be determined by those of frost. In regions near the equator, the effects of low temperatures are likely to be restricted to discrete highlands areas in Burundi, Democratic Republic of the Congo, Ethiopia, Kenya, Rwanda, Tanzania, and Uganda. The geographical transition from areas where suitable temperatures persist year-round to areas where temperatures are limiting for significant periods is often sharp (11).

It is often difficult to compare large-scale and small-scale effects, because environmental

changes may be described in different terms. The macroscale effects of climate are usually given in terms of temperature, precipitation, and humidity. Smaller-scale environmental changes include water and land resource changes, such as irrigation and deforestation. Comparability is improved if these changes are also described in terms of their effects on microclimate (11).

Rainfall

Although several studies have demonstrated an association between An. gambiae abundance and rainfall, a direct, predictable relationship does not exist. An. gambiae can breed prolifically in temporary, turbid water bodies such as hoof prints or rain puddles, whereas An. funestus prefers permanent water bodies. However, both temporary and permanent water bodies depend on adequate rainfall; therefore, there is good reason for using rainfall to indicate the probable presence of vectors, vector survival, and the potential for malaria transmission (13).

The highest amounts are found in coastal areas of Cameroon, Liberia, Madagascar, Nigeria, and Sierra Leone, but annual totals in excess of 1,000 millimeters are characteristic of much of the interior of the continent. The driest areas are southwest Africa (Botswana, Namibia, and South Africa), parts of the African Horn (Somalia and sections of Ethiopia and Kenya), and the northern Sahel. In these regions, the longevity of adult vectors is likely to be negatively affected by low humidity; relative humidity in excess of 60% is generally deemed necessary for effective malaria transmission. The effects of quite dramatic climatic events on the level of malaria transmission may depend on their timing (13).

Gambiae complex, nor is it ideal for funestus. The breeding habitats were likely to be created as the floods receded, but because the flooding was so extensive, breeding would not be very high until after the temperature had fallen to winter levels unsuitable for malaria transmission. Had the timing of the floods been different, the malaria hazard could have been far greater (14).

Thus, at the limiting temperatures for malaria transmission, the timing of rainfall hazards may be crucial, and the consequences may vary greatly by season. Increased rainfall in the arid zones will have a much greater effect on transmission. Near the equator, even though extra rainfall may augment mosquito breeding and potentially raise malaria transmission, malarial morbidity may be only modestly affected because of the already high levels of transmission and human immunity (14).

Burden of malaria on health in Africa

Mortality

There are three principal ways in which malaria can contribute to death in young children. First, an overwhelming acute infection, which frequently presents as seizures or coma (cerebral malaria), may kill a child directly and quickly. Second, repeated malaria infections contribute to the development of severe anemia, which substantially increases the risk of death. Third, low birth weight – frequently the consequence of malaria infection in pregnant women – is the major risk factor for death in the first month of life (15).

In addition, repeated malaria infections make young children more susceptible to other common childhood illnesses, such as diarrhea and respiratory infections, and thus contribute indirectly to mortality. The consensus view of recent studies and reviews is that malaria causes at least 20% of all deaths in children under 5 years of age in Africa.Although respiratory disease caused by a variety of infectious agents results in a similar proportion of deaths, P. falciparum is the most important single infectious agent causing death among

young children (15).

Morbidity and long-term disability

Children who survive malaria may suffer long-term consequences of the infection. Repeated episodes of fever and illness reduce appetite and restrict play, social interaction, and educational opportunities, thereby contributing to poor development. An estimated 2% of children who recover from malaria infections affecting the brain (cerebral malaria) suffer from learning impairments and disabilities due to brain damage, including epilepsy and spasticity (15).

Burden of malaria on African health systems

In all malaria-endemic countries in Africa, 25–40% (average 30%) of all outpatient clinic visits are for malaria (with most diagnosis made clinically). In these same countries, between 20% and 50% of all hospital admissions are a consequence of malaria. With high case-fatality rates due to late presentation, inadequate management, and unavailability or stock-outs of effective drugs, malaria is also a major contributor to deaths among hospital inpatients (16).

This high burden may in fact be partly a result of misdiagnoses, since many facilities lack laboratory capacity, and it is often difficult clinically to distinguish malaria from other infectious diseases. Nonetheless, malaria is responsible for a high proportion of public health expenditure on curative treatment, and substantial reductions in malaria incidence would free up available health resources and facilities and health workers' time, to tackle other health problems (12).

Burden of malaria on the poor

Poor people are at increased risk both of becoming infected with malaria and of becoming infected more frequently. Child mortality rates are known to be higher in poorer households and malaria is responsible for a substantial proportion of these deaths. In a demographic surveillance system in rural areas of the United Republic of Tanzania, under-5 mortality following acute fever (much of which would be expected to be due to malaria) was 39% higher in the poorest socioeconomic group than in the richest (17).

Malaria in Ancient Egypt

Malaria was endemic in ancient Egypt. Immunologic tests have been used to investigate the presence and incidence of malaria in ancient Egyptian mummies and confirmed the high prevalence of P. falciparum malaria in ancient Egypt. Assa et al., examined samples of Egyptian mummies belonging to the Anthropological and Ethnographic Museum of Turin, Italy and dated to 3200 B.C. (from Gebelen, near Assiut, Middle Egypt) to determine the presence of malaria antigens using an immunoenzymatic assay (Para Sight™ - F test) and found that the mummified remains were positive for P. falciparum in 42% of cases (n= 80). (18)

Bier et al. examined a 15–18 months old child mummy, belongs to the end of the Early Dynastic Period – beginning of the Old Kingdom that was discovered in Gebelein most likely in 1914 (presently housed in Turin's Museum of Anthropology) (19). Immunochromatographic and immune-histochemical analyses on skin and muscle samples were positive for P. falciparum and unidentified P. species. By using the polymerase chain reaction (PCR) technique, Nerlich et al. identified P. falciparum ancient DNA (aDNA) in samples of two Egyptian mummies (n= 91 examined samples) who died very young from ≈4,000 years ago and unearthed from a nameless tomb in Thebes (Luxor), thereby proving a specific infection by falciparum malaria in ancient Egypt. The authors stated that "We now

know for sure that malaria was endemic in ancient Egypt" (20).

Egypt in north Africa lies between latitudes 22° and 32°N, and longitudes 25° and 35°E at 1,001,450 square kilometers and with about 90 million inhabitants. Due to the aridity of its climate, the majority of people live along the narrow Nile Valley and Delta, i.e. about 99% of the population uses only about 5.5% of the total land area. Egypt is bordered by Libya to the west, the Sudan to the south, and the Gaza Strip and Israel to the east (21).

Apart from the Nile Valley, the majority of Egypt's landscape is deserts (the Western Dessert as part of the Libyan Desert and the Eastern Desert) which are sparsely inhabited and with several scattered oases namely: El Faiyoum, Siwa, El Gara, El Farafra, El Bahariya, and El Dakhla and El Kharga " New Valley". Ancient Egypt refers to the civilization of the lower Nile Valley between the First Cataract "south of Aswan" and the mouths of the Nile Delta, from circa 3300 B.C. until the conquest of Alexander the Great in 332 B.C (21).

Malaria in Modern Egypt

Malaria was highly endemic in almost all parts of the country. In 1960; infection rates reached up to 20 % in some localities. However, prevalence has shown a steady decrease in most of the Governorates by 1990, and focused mainly in El Faiyoum with sporadic cases from Siwa oasis and some parts of the Nile Delta. Based on the MOH reports to the World Health Organization (WHO), the disease had declined in most of the Governorates (22).

After this only 198 and 132 cases were reported during 1983 and 1990-1993, respectively with transmission was localized in El Faiyoum. In 1994 an increase in the cases was observed and in 1995 raised to 808 that necessitated an intensified multidisplinary control program. This resulted in decreasing the numbers of cases to 313 in 1997 and to only 13 in 1998. By the end of 1998 till now no local cases were reported In the subsequent years, all reported cases are imported (22).

Moreover, through parasitological surveys allover the country (May 1978 to April 1979), Hassan et al. (1983) identified 212 cases (106 P. vivax, 104 P. falciparum and 2 double infections) out of 19,850 individuals examined. All the cases were from El Faiyoum and Siwa. Dahesh et al. (2009) examined 9065 individuals in one village in El Faiyoum (September 1995 to December 1996) and identified 52 positive cases (2 P. vivax and 50 P. falciparum) (22).

Eleven native Anopheles species, are present in Egypt, these are: 1. Anopheles (An.) tenebrosus Dönitiz: is common and widely distributed in the Nile delta especially in the northern part, Nile valley, El Faiyoum and Suez Canal Zone; 2. An. (An.) algeriensis Theoblad: is localized only in Siwa oasis, 3. An. (Cellia) pharoensis Theoblad: is the most abundant and widely distributed species allover the country except Siwa oasis as this is not a rice cultivated area, the main breeding water for such species. However, in Sinai, it has a limited distribution; 4. An. (Cel.) sergentii Theoblad: is a desert species occurring in all oases of the Western Desert where it is the predominant species, common in El Faiyoum, more abundant in southern than in northern Sinai and rare in the Red Sea area and Nile Valley (23).

It is not present in the Nile Delta and Suez Canal Zone, although its past occurrence in the Canal Zone and in the Nile Delta on the border of the desert at Inshas, Sharqiya Governorate in east of Delta; 5.An. (Cel.) multicolor Cambouliu: is widely distributed throughout Egypt; 6. An. (Cel.) superpictus Grassi: is distributed in the south-western oases (El Bahariya, El Dakhla and El Kharga) and Sinai; 7. An. (Cel.) turkhudi Liston, 8. An. (Cel.) hispaniola Theoblad, 9. An. (Cel.) d'thali Patton and 10. An. (Cel.) rhodesiensis

rupicolus Lewis: all are restricted to Sinai, and 11. An. (Cel.) ainshamsi N. Sp. in inland salt swamps at Shukeir on the Suez Gulf. The species was formerly collected from the same area and identified as An. (Cel.) stephensi Liston (23).

Malaria was endemic in Egypt until the end of the last century, but the prevalence declined steadily and rapidly during the 1990s. Egypt was declared malaria free in 1998 and entered the WHO's prevention-of-reintroduction phase after sustaining at least three years of no autochthonous malaria transmission (24).

However, sporadic cases continued to occur, particularly in the Al-Fayoum Governorate in the northwestern part of Egypt due to a unique combination of hydrogeology, soil variables and the presence of a highly efficient mosquito vector. Malaria cases were also detected in Aswan Governorate, Egypt involving 21 confirmed cases during May–June 2014 and all cases were male subjects with history of travel to malaria-endemic Sudan. No indigenous malaria cases have been detected during the last several years and no malaria-related deaths have been recorded in Egypt during the period 2010–2019 (23).

The two major malaria species in patients coming from Africa are P. falciparum and P. vivax. Despite microscopic examination of Giemsa-stained blood films is considered the gold standard method for laboratory diagnosis of malaria, nPCR was a very good confirmatory diagnostic test with 100% specificity and sensitivity RDT is less specific and sensitive than nPCR, but it is rapid, simple, and lower in cost compared to nPCR. So it can be used for screening of blood in blood bank and screening of endemic areas to detect infected cases and carriers (23).

Malaria Vectors

Only An. pharoensis and An. sergentii are the proven vectors. An. pharoensis is mainly responsible for Plasmodium vivax transmission while, An. sergentii is responsible for P. falcipaum transmission in El Faiyoum. In addition, An. multicolor is suspected as a vector. An. pharoensis was found naturally infected with malaria parasite, more exophilic than endophilic, more exophagic than endophagic and zoophagic rather than anthropophagic (25).

Although it is the only vector in the Nile Delta, yet it is not so highly efficient. In spite of its great abundance and man biting rates during the favorable season, the percentage of epidemiologically dangerous aged females is low, i.e. those surviving to infective age under field condition for P. vivax and P. falciparum transmission were estimated to be 31.4% and 25.4% for the 2 Plasmodium species, respectively (26).

This may explain its low infectivity and degree of malaria transmission which is partly due to the short life span of the adults. Evidences such as the association of low sporozoite rate as 0.33% with high oocyst rate as 7.6% in Nile Delta and El Faiyoum indicate that females are short lived. This perhaps due to the climate in Egypt and it is thought that the varying ecological conditions mainly humidity affect the life of this species and thus influences its opportunities for malaria transmission (26).

Mosquitoes and Malaria Control

In ancient Egypt, few remedies against mosquitoes and other gnats are included in the Ebers Papyrus for examples: 1. Fresh palm wine would protect against gnats, 2. You can protect yourself against the gnats by planting an acacia tree, and 3. Fumigation of the house with incense and myrrh is recommended but was not affordable to many. Moreover, traditional herbal remedies have been used to treat malaria; the historian Herodotus (484–425 B.C.) wrote that the builders of the Egyptian pyramids were given large amount of

garlic, to protect them against malaria (27).

Conclusion:

Foreign-acquired malaria infections have elevated to a major concern for Egyptian travelers to African countries. To reduce the danger of catching the disease while traveling, high-risk groups should be made more aware of and given access to effective prophylactic measures against exposure to mosquito bites and malaria parasites. Increased capability for imported case detection is required to reduce the burden of fatal cases, severe malaria, as well as prevent secondary malaria transmission among Egyptians. RDTs have been found to be simple and effective for the rapid detection of malaria, which may encourage Egypt to put control measures against imported malaria into place.

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