

MALARIA SITUATION IN EGYPT THE LAST THREE YEARS: RETROSPECTIVE STUDY IN AN EGYPTIAN FEVER HOSPITAL

By

MAHFOUZ AHMAD AL-AGROUDI¹, GABR METWALLY SAYED AHMAD²,
KONDO MOHAMED KONDO³ and TOSSON A. MORSY⁴

Military Medical Academy Cairo11291¹, Department of Community Medicine, Faculty of Medicine, Al Azhar University², Land Forces Medical Officer In-charge, Tanzania People's Defence Forces³ and Department of Parasitology, Faculty of Medicine, Ain Shams University, Cairo 11566⁴, Egypt

Abstract

Malaria is a protozoan parasite caused by the genus *Plasmodium* with five human species: *P. ovale*, *P. vivax*, *P. malariae*, *P. knowlesi*, and *P. falciparum*. The last is the most dangerous and commonest in Africa. This retrospective study evaluated the situation of malaria in the last 3 years in an Egyptian Fever Hospital. The studied reviewed a total of 100 malaria patients medical sheets, their past and present history including (sign and symptoms, mode of trans-mission, diagnosis, complication, treatment and follow-up and prevention. The results showed all patients were youth returning back from Central Africa, (41), Darfur, (38), DR Congo, (11), Nigeria, (3) to Chad (2) and one from to each of Rwanda, Djibouti, Yemen, Kenya, &/or Tanzania. The infective malaria species were *P. falciparum* (83 cases), *P. vivax* (10 cases), *P. ovale* (one case) and mixed infections (six cases). Stained blood films gave 100% positivity and Rapid diagnostic test failed in 4%. All patients were successfully treated except two.

Key words: Egypt, Malaria, Retrospective study, Last three years, Fever hospital

Introduction

Malaria is one of the life-threatening diseases caused by parasites that are transmitted to humans through the bites of infected female *Anopheles* mosquitos (WHO, 2018). There are five parasite species (*P. falciparum*, *P. ovale*, *P. vivax*, *P. malariae* and *P. knowlesi*) which cause malaria, with two of them; *P. falciparum* and *P. vivax* posing the greatest threat to humans. *P. falciparum* is the most prevalent malaria parasite in Africa and accounted for 99% of malaria cases in sub-Saharan Africa in 2016 (WHO, 2017), and responsible for the most malaria deaths globally (WHO, 2018). However, *P. vivax* was the commonest one outside of sub-Saharan Africa, and in 2016 caused 64% of the cases in the WHO Region of the Americas and more than 30% of the cases in the WHO South-East Asia Region (CDC, 2018). The WHO reported that in 2016 nearly half of the world's population was at risk of malaria, with 91 countries and areas having ongoing malaria transmission (WHO, 2015). The most cases of malaria deaths occurred in sub-Saharan Africa, with the WHO regions of South-East Asia, the Eastern Me-

diterranean, the Western Pacific and the Americas also at risk (Cox-Singh, 2008).

HIV and malaria infections often coexist in many parts of the world, particularly in sub-Saharan Africa as HIV increased malaria infection risk and development of clinical malaria. Conversely, malaria increases HIV replication (Karp and Auwaerter, 2007).

In Egypt, Beier *et al.* (1987) reported mosquitoes in two neighbouring villages of Al Fayoum Governorate, Egypt, were sampled from April to December 1983 to determine host-feeding patterns. A total of 1,751 blood meals from nine mosquito species were analysed by the modified precipitin technique, and estimates of host availability were made by census in both villages. The species composition and feeding habits differed in the 3 habitats sampled: inside houses, inside animal sheds, and outdoors. The outdoor collection yielded *Culex pipiens*, *Cx. antennatus*, *Cx. univittatus*, *Aedes caspius*, and *Anopheles pharoensis*, at least 92% of all blood meals were human, bovine, or equine, and a few individuals of each species, except *Ae. caspius* that fed on birds. *Uranotaenia unguiculata* was the only species feed on rep-

tiles; no samples from this species reacted with mammal or bird antisera. Most blood meals from 8 species collected inside houses were from humans. In sheds, blood meals of six species were primarily from other large mammals. Forage ratios calculated for the 4 most abundant species from the outdoor collections, based on the proportion of humans, bovines, ovine, and equines in each village, were low for humans and high for ovine and equines. *An. sergenti* an important vector was reported in Al Fayoum (Morsy *et al.*, 1995). Bassiouny *et al.* (1999) in Al Fayoum over a year longitudinal study found that *An. sergenti* was the commonest species followed by *An. multicolor* and least was *An. pharoensis*. They concluded that only the monthly temperature but neither relative humidity nor wind speed had a significant effect on larvae abundance, and that *P. falciparum* transmission season extended to more than eight months per year. The last malaria focus was in Al-Fayoum Governorate became free but, with few annual imported cases since the year 1998. The outbreak of *P. falciparum* and *P. vivax* in the southern part at Aswan Governorate at May 2014 strongly supported the fact that malaria is re-emerging (Kenawy, 2015). But, Zaher *et al.* (2007) reported 16 malaria cases in Almaza Military Fever Hospital. They were nine Egyptian Pilgrims with *P. falciparum* and seven cases locally acquired *P. vivax* (October 2003 to July 2004), and treated successfully by chloroquine. El-Bahnasawy *et al.* (2010) in a Military Fever Hospital reported 36 patients of whom 20 diagnosed as malarial patients, who were recruited from Peace Keeping Mission Forces in Africa and 16 cases presented with pro-longed fever from different Egyptian areas. Fuller *et al.* (2012) stated that *An. arabiensis* is an opportunistic feeder and efficient vector of *P. falciparum* in Africa and might invade areas outside its normal range, separated by expanses of barren desert. They added that while gaps between potential habitat patches remained large in the Green Nile scenario,

models revealed large areas of future habitat facilitates invasion of *An. arabiensis* from Sudan to Egypt.

There were many factors contributed to the re-emergence of malaria, as infection of local Anopheline spp. by the imported cases, continuous movement of populations between Aswan and Sudan as well as the influx of large population from Africa and Asia to Egypt for educational and religious purposes. Another risk factor was *An. sergenti* in the oasis as vector or desert malaria vector due to its distribution across the Saharan belt in northern Africa into the Middle East countries with ability to cope with extreme climate condition (Sinka *et al.*, 2010), Also, environmental changes brought by the water-sources development projects as Toshka (Shoukry and Morsy, 2011). El Bahnasawy *et al.* (2011a) recorded *An. multicolor*, *An. sergentii* and *An. algeriensis* in Toshka District, and added that the endemic chloroquine resistant *P. falciparum* on the Egyptian-Sudanese Border pave the way for malignant malaria invasion to Egypt. El Bahnasawy *et al.* (2014) stated that travelling to different climates, cultures and environment abroad exposed to risk tropical infectious diseases. They added that a rural health nursing was considered a subspecialty within public health nursing, albeit one that required the nurse to be a generalist, and applied an educational program on selected infectious disease disasters, and vectors encountered at the Egyptian Sudanese borders.

Wassim (2014) reported by secondary structure and sequence of ITS2-rDNA *An. pharoensis* proven vector all over Egypt, especially in the Delta, *An. sergenti* a primary vector in the Western Desert Oases, *An. multicolor* in Al-Fayoum, *An. stephensi* in the Red Sea Coast, and *An. superpictus* in Sinai. Dahesh and Mostafa (2015) re-evaluated malaria in Al Fayoum reported that 14/2044 (0.68%) were passive males who attended to Malaria Units after their return from Sudan. Microscopically nine (64.2%) of them were positive, three *P. falciparum* (33.3%) and

six *P. vivax* (66.7%). Only one *vivax* was of low density while others were of high density class. Those with highest imported cases lived in Abu Shanap, Aboxa and Kafr Aboud. In Al Nazla, *An. sergeni* and *An. multicolor* larvae were detected. Kandeel *et al.* (2016) reported an outbreak of 21 *P. vivax* cases during May-June 2014. Health authorities carried out early detection and prompt treatment of cases, vector control, and public education. Twenty cases (95.2%) were in El-Sheikh Mostafa Village, Edfu District, Aswan. Cases were house-to-house visits with one *P. falciparum*. All the patients were successfully treated.

The study assessed retrospective malaria situation in an Egyptian Specialized Fever Hospital from April 2015 up to April 2018 to clarify the imported malaria to Egypt.

Subjects and Methods

This was a retrospective study of 100 malaria patients. research designs included

Table 1: Socio-demographic of malaria patients as reported in their medical files.

Characteristics	Variants	Number	Percentage
Ages in years	20-24	47	47
	25-29	23	23
	30-34	15	15
	35-39	9	9
	≥40	6	6
Local residence	Grater Cairo	15	15
	Giza Governorate	8	8
	Menoufia Governorate	12	12
	Sharkia Governorate	8	8
	Upper Egypt Governorates	57	57
Travel to endemic area	Yes	100	100
Stay abroad area	≤ 6months	76	76
	≥ 6months	12	12
	Missed data	12	12

Table 2: Endemic country visited by patients

Endemic country	Frequency	Percentage
Central Africa	41	41
Chad	2	2
Darfur	38	38
Djibouti	1	1
DR Congo	11	11
Kenya	1	1
Nigeria	3	3
Rwanda	1	1
Tanzania	1	1
Yemeni	1	1
Total	100	100

technical, operational, administrative and statistical analysis. the hospital was well equipped and furnished with the different specialists, consultants, nursing staff teams as well as ex-pert lab. technicians

Data included: a- Socio-demographic characters (name, age, status, social economic), b- Medical history (travel abroad, sign and symptoms, diagnosis, treatment, and follow-up).

Ethical considerations: Before data collection all approval ethical clearance was obtained. Besides, all the applicable international, natio-nal, and/or institutional guidelines for the care and treating patients were followed.

Statistical analysis: Data were computerised and analysed using SPSS package version 22 (SPSS, 2007).

Results

The results are shown in tables (1, 2 &3) and figures (1, 2, 3, 4, 5, 6 & 7)

Table 3: Treatment at admission, discharge and follow-up.

Items	Variants	Number	%
Treatment at admission	Coartem (Artemether-lumefantrine)	73	73
	Quinine (oral tablet) + Doxycycline	4	4
	Quinine (Injection) + Doxycycline	1	1
	Artemether (IM injection) Doxycycline	6	6
	Artesun (IV) + Doxycycline	6	6
Treatment Post discharge	Primaquine	3	3
	Doxycycline	83	83
	Not treatment	14	14
Prognosis	Cured	98	98
	Died	2	2
Relapse	Yes	9	9
	No	91	91

P. falciparum is the commonest causative agent in most malaria endemic area; mixed species neither identified in DR Congo nor other countries. Different in causative agent was not significant ($p= 0.380$). *P. falciparum* was the main species in all malaria endemic area visited.

Discussion

In the present study, the patients were males with ages between 20 to 24 years (47%), which was larger than other groups; between 25 to 29 (23%), 30 to 34 (15%), 35 to 39 (9%) and above 40 years was (6%). All visited endemic areas for less than 6 month (76%), more than 6 month (12%) or missed data (12%). The identified species of malaria were *P. falciparum* (83%), *P. vivax* (10%), *P. ovale* (1%) and mixed infection (6%). El-Bahnasawy *et al.* (2010) reported that in Military Fever Hospital among 36 patients recruited from Peace Keeping Mission Forces in Africa, 20 were malaria patients, and 16 with prolonged fever from different Egyptian areas.

In the present study, the visited countries were Central Africa (41%) patients, Darfur (38%), Congo (11%), Nigeria (3%), Chad (2%) and only 1% was from each of Rwanda, Djibouti, Yemen, Kenya and Tanzania. Zaher *et al.* (2007) in Egypt reported 16 malaria cases of which 9 were Egyptian Pilgrims with *P. falciparum*. Al-Kuwari (2009) in Qatar studied annual incidence of imported malaria in from 1997 to 2006 and epidemiological features from 2004 to 2006. He added that all 438 *P. vivax* malaria cases

were immigrant youth males from India, Pakistan, and Sudan. He concluded that imported malaria increased in the past 2 years after a long period of constant reduction, and the people most affected were adult male migrants from endemic countries. Kouarra *et al.* (2018) in Morocco reported that 364 cases were recorded in 2012, 312 cases in 2011 and only 218 cases in 2010 and 145 cases in 2009. Most of the Moroccan patients were travellers to sub-Saharan Africa, workers, traders, expatriates or soldiers on a peace keeping mission. Memish *et al.* (2014) in Saudi Arabia reported that 318 malaria cases were in 4 years, of which only 3.6% of cases were less than 10 years of age, including 2 cases below 5 years. Non-Saudis were 95% and Pakistanis, Nigerians, and Indians accounted for 62.0%. The agents were *P. falciparum* (67%), *P. vivax* (32%) and *P. ovale* (1.6%).

In the present study, the *P. falciparum* (83%) was among patients who stayed for less than six months in endemic areas, but mixed species (6%) were among those stayed less than 6 months and those stay more than 6 month *P. falciparum* was identified highest was 91.7% lowest was mixed 8.3%. Nevertheless, the staying time in endemic areas does not relate with the malaria species. The airport malaria was well recognized on the continent, and physicians were aware of its existence in those who have not travelled abroad but live or work near the international airports (Whitfield *et al.*, 1984). Guerra (2008) reported that the global area

at risk of stable *P. falciparum* malaria was quantified in 29.7 million km², distributed into Africa (18.2 million km², 61.1%), Americas (6.0 million km², 20.3%) and Central and South East Asia regions (5.5 million km², 18.6%). Of the 2.37 billion people exposed to *P. falciparum* transmission worldwide, 0.98 billion live in unstable risk areas, whereas 1.383 billion live in stable risk areas, distributed into Africa (0.657 billion, 47.5%), Americas (0.041 billion, 2.9%) and Central and South East Asia (0.686 billion, 49.6%). Children are the most represented category, accounting for 32% of the population at risk in Americas and in Central and South East Asia. CDC (2018) reported that malignant *P. falciparum* predominate worldwide in tropical and subtropical areas, especially in Africa. *Falciparum* can cause severe malaria because it multiplies rapidly in the blood, and can thus cause severe blood loss (anaemia), and the infected parasites could clog small blood vessels in brain causing cerebral fatal malaria. Feintuch *et al.* (2016) reported that in 2013, there were about 198million cases worldwide, with an estimated 584,000 deaths occurring mostly in sub-Saharan African children. CM is a severe and rare form of *Plasmodium falciparum* infection and is associated with high rates of mortality and neurological morbidity, despite antimalarial treatment. A greater understanding of the pathophysiology of CM would allow the development of adjunctive therapies to improve clinical outcomes. A hallmark of CM is cerebral microvasculature sequestration of *P. falciparum* infected the red blood cells (iRBCs), which resulted in the vasculopathy in some patients. These data gave a global analysis of the host pathways associated with CM and newly identify an association of activated neutrophils with brain iRBC sequestration. Products of activated neutrophils could alter endothelial cell receptors and coagulation to facilitate the iRBC adherence.

P. vivax is found mostly in Asia, Latin America, and in some parts of Africa. *P. vi-*

vax (and *P. ovale*) has dormant liver stages (hypnozoites) that can activate and invade the blood (relapse) several months or years after the infecting mosquito bite. *P. ovale* is in Africa (especially West Africa) and the islands of the western Pacific with the biological and morphological similarity to *P. vivax* (Adekunle *et al.*, 2015). However, the antigens of the Duffy Blood Group System, in addition to involvement in transfusion incompatibility and hemolytic disease of the newborn, are of great medical importance due to their association with the invasion of RBCs by *P. vivax*, and are receptors for the chemokine family involved in the regulation of inflammatory processes (Klein and Anstee, 2005). CDC (2008) listed the regions with risk for the malaria transmission, the presence of the antimalarial drug resistance, and recommended chemoprophylaxis were reported

In the present study, staying duration in endemic country was 58.3% of those patients in Darfur for more than 6 months had malaria. 1% of each of them travelled to Djibouti, Yemen, Kenya and Tanzania for unknown duration had malaria attack. El-Kady *et al.* (2017) found that the last malaria focus in Al Fayoum was of cases coming back mainly from Sudan.

In the present study, 70% of subjects were admitted 2 to 7 days, only 13% were admitted ICU, 38% reported high temperature, none had shaking-chills, 42 suffered from high fever, but none was hypoglycaemic. Hepatomegaly and/or splenomegaly were found in 9% of cases. Saleh *et al.* (2016) reported that malaria proved to be a serious *Anopheles* borne disease that causes symptoms like the flu, as a high fever, chills, and muscle pain also, anaemia, bloody stools, coma, convulsion, fever, headache, jaundice, nausea, sweating and vomiting. Symptoms tend to come and go in cycles. Apart from *Anopheles* vector, malaria could be transmitted nosocomial, blood transfusion or needle-stick injury. They added that some types of malaria may cause more serious damage

problems to heart, lungs, kidneys, or brain, which can be deadly. The primary factors contributing to the resurgence of malaria are appearance of drug resistant strains, insecticide-resistant strains of mosquito and lack of licensed malaria vaccines of proven efficacy. People can get malaria if they come into contact with infected blood as blood transfusion or needle-stick injury also nosocomial and congenital malaria was reported (Abdel-Motagaly *et al.*, 2017).

In the present study, all patients' blood films were positive, but by rapid test 96% were positive and 4% negative, and 51% were detected by screening. The causative agents were *P. falciparum* 83%, *P. vivax*, 10%, *P. ovale* 1% and mixed infections 6% cases. Meanwhile, one must take into considerations the encountered of zoonotic babesiosis, which ring form always misdiagnosed with *P. falciparum* were reported not only in Egypt but many regional countries (El-Bahnasawy *et al.*, 2011b).

Strickland (2000) reported that the serologic tests were relatively species-specific but when a zoonotic *Babesia microti* antigen was assayed for a patient infected with another *Babesia* species or *Plasmodium* species reacted minimally, if at all. Ayalew *et al.* (2014) stated that microscopic diagnosis of Giemsa stained thick and/or thin blood films by skilled microscopy remained to be the standard laboratory method for the malaria diagnosis, but, the detection and identification of the malaria parasites required a well-trained laboratory personnel.

Hansen *et al.* (2015) concluded that RDTs remained cost-effective across a range of drug costs and if microscopy was used for a range of diagnostic services. Mahende *et al.* (2016) reported that despite microscopic examination had low sensitivity and limited availability, but still the gold standard for diagnosis of malaria.

In the present study, Coartem[®] (Artemether-lumefantrine) was given to 73 patients, Quinine[®] (oral tablet) & Doxycycline[®] to 4 patients, Quinine (Injection) & Doxycycline

to one patient, Artemether[®] (IM) Doxycycline to 6 patients, Artesun[®] (IV) & Doxycycline to 6 patients. Connolly *et al.* (2004) reported the best therapy for imported malaria was polytherapy (75%) such as the Artesunate plus Sulphadoxine plus Pyrimethamine (Artescope) while monotherapy as Mefloquine was effective in three patients (15%). El-Bahnasawy *et al.* (2010) in Egypt treated all malaria (mainly *vivax*) patients were either by single drug (Alexaquine or Mefloquine) or by combined treatment (Amate, Pyrimethamine & Sulphadoxine) and the patients were followed up both clinically and parasitological to assess treatment. If parasitaemia still persisted, the drug was repeated or the patient was shifted to another treatment. Chu and White' (2016) reported that relapses contributed to malaria and morbidity in *P. vivax* and *P. ovale* infections, and primaquine was indicated for optimal treatment and elimination of *P. vivax* malaria. Dondorp *et al.* (2015) found that artesunate substantially reduced mortality in African children with severe malaria. They added that data, together with the meta-analysis of all trials comparing artesunate and quinine, strongly recommended that the parenteral artesunate must replace quinine as the treatment of choice for severe malignant malaria worldwide. Al-Agroudi *et al.* (2017) reported that antimalarial prophylaxis taken for by travellers to endemic area could delay appearance of malaria symptoms by weeks or months, long after they had left the endemic area. This can happen mainly with *P. vivax* and *P. ovale*, both produce dormant liver stage (hypnozoites) parasites, which may reactivate and cause malaria months after the infective mosquito bite.

WHO (2018b) recommended artemisinin-based combination therapies (ACTs) for the treatment of uncomplicated malaria caused by *P. falciparum*. By combining 2 active ingredients with different action mechanisms, the ACTs are the most effective antimalarial drugs available today. WHO currently recommended the 5 ACTs to be used against *P.*

falciparum malaria and that the choice of ACT should be based on the results of therapeutic efficacy studies against local strains of *P. falciparum* malaria. The WHO added that in low transmission areas, a single low dose of primaquine should be added to the antimalarial treatment in order to reduce transmission of the infection. Testing for the glucose-6-phosphate dehydrogenase (G6PD) deficiency is not required, as a single low dose of primaquine is both effective in the blocking transmission and unlikely to cause risk toxicity in individuals with any of the G6PD-deficiency variants. However, Melt-Pro G6PD assay proved useful as a diagnostic or screening tool for G6PD deficiency in clinical settings (Xia *et al*, 2016).

Regarding prognosis 98% cured and only 2% died. No doubt, *P. falciparum* is a life threatening species can cause death within 24 hrs, those 98% got early diagnosis and proper treatment and those 2% either delay treatment or did not get proper treatment.

In the present study, over years (2016, 2017 & 2018) malaria cases varied with a peak in year 2017. Hashim *et al*. (2017) in Egypt reported that the imported malaria with Egyptians, which totalled 25 patients were the predominance of *P. falciparum* (15 cases).

Conclusion

Although there is no true active malaria transmission in Egypt, imported cases still poses a significant health problem with the presence of *Anopheles* vectors. All patients had a history of travel to endemic area, Central Africa, Darfur (Sudan), Democratic Republic of Congo and other places for Peace Keeping Operations. They were all youth and 76% stayed in endemic area for less than 6 months. 70% of subjects were admitted in hospital for 2 to 7 days. Moreover, 100% of blood films of cases were positive but only 96% were malaria positive by rapid diagnostic test.

All the revised malaria patients' files during the period of study were imported malaria infection with travellers back to Egypt.

The study also would help Tanzanian authorities about imported malaria with soldiers, business men and/or visitors to endemic areas, also, from Democratic Republic of Congo and Tanzania interacts with each other. Risk of malaria transmission depends on a variety of factors including the geographic region visited and traveller type.

Recommendations

1. All travellers to endemic countries must be given a health education about malaria, pathogenicity, preventive measures and proper chemoprophylaxis especially for military persons on Peace Keeping Forces Missions.
 2. Close supervision by the Commanders and Medical Personnel from individual, section, Platoon, Company up to Battalion level in relation to use of preventive measures from sleeping places to other areas of operation, and environmental sanitation in collaboration with field sanitation team.
 3. Effective use of unit field sanitation team to train unit personnel in use of Individual Preventive Medicine Measures (PMM) as well as Unit Preventive Measures in general.
 4. *P. falciparum* symptoms are more severe and include behavioural changes, confusion, seizures, anaemia, respiratory failure, kidney failure, coma and shock. If not properly treated immediately, malignant malaria can lead to death.
 5. Pregnant women & children < 5 years should not travel whenever possible to chloroquine-resistant malignant malaria areas. Risk of stillbirth, spontaneous abortion, and other adverse pregnancy outcomes is increasing in the setting of malaria, and pregnant travellers should be advised to defer travel until after delivery whenever feasible.
 - 6- *Anopheles* eggs, larvae and pupae are confined within more or less small aquatic habitats and cannot readily escape control measures. Adults are flying in and outdoors.
- Consequently, periodical surveillance of the *Anopheles* immature stages is a must. They should be controlled by using environmental friendly insecticides. This is not only for the *Anopheles*-vectors, but also for

all other mosquitoes borne infectious diseases.

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Explanation of figures

Fig. 1: Malaria endemic area visited, Fig. 2: Presented malaria symptoms

Fig. 3: Signs presented by malaria patients

Fig. 4: Malaria diagnosis by rapid test and blood film

Fig. 5: Species diagnosed by blood film

Fig. 6: Malaria cases % reported from April 2016 to April 2018.

Fig. 7: Malaria species in different malaria endemic area.

Fig. 8: Africa map showed the different visited countries

