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Malaria in the Military Fever Hospital

Protocol of Thesis Submitted in Partial Fulfillment for Master Degree in Tropical Medicine

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List of Abbreviations

Abbrev	Meaning
NIH	National Institute of Health
WHO	World Health Organization
CDC	Centre of Disease Control
APC	Antigen presenting cell
APL	Altered peptide ligand
INOS	Inducible nitric oxide synthase
ADCC	Antibody Dependent Cytolysis
CTC	Cytotoxic lymphocyte
IFN	Interferon
NEET	N,N-diethyl-m-toluamide
ITNs	Insecticide-treated bed nets
GIS	Geographic information system
HRP	Histidine-rich protein
PLDH	Parasite-specific lactate dehydrogenase
WBC	White blood cells
RBC	Red blood cells
RDT	Rapid diagnostic tests
CSP	Circumsporozoite protein
TRAP	Thrombosporodin related adhensive protein
MSP	Merozoite specific proteins
AMA	Apical membrane antigen
RESA	Ring infected erythrocyte surface antigen
PFEMP	P. falciparum erythrocyte membrane protein
ARF	Acute renal failure

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Introduction

Malaria is a disease caused by a parasite that lives part of its life in humans and part in mosquitoes. It remains one of the killers of human population worldwide, threatening the lives of more than one-third of the world's population. Malaria thrives in the tropical areas of Asia, Africa, and South and Central America, where it strikes millions of people. Sadly, as many as 2.7 million of its victims, mostly infants and children, die yearly ***(NIH, 2002).***

In humans, malaria infection is caused by one or more of four species of intracellular protozoan parasite. Plasmodium falciparum, P. vivax, P. ovale, and P. malariae differ in geographical distribution, microscopic appearance, clinical features (periodicity of infection, potential for severe disease, and ability to cause relapses), and potential for development of resistance to antimalarial drugs ***(Bloland, 2001)***.

Infection with malaria parasites may result in a wide variety of symptoms, ranging from absent or very mild symptoms to severe disease and even death. Malaria disease can be categorized as uncomplicated or severe (complicated). In general, malaria is a curable disease if diagnosed and treated promptly and correctly ***(CDC, 2004)***.

Determination of a patient's clinical history and symptoms is an acceptable basis for the management of malaria disease. Although the signs and symptoms, such as fever, chills, headache and anorexia, are generally non-specific, some signs and symptoms, especially in combination, have diagnostic value in specific epidemiological and operational situations. However, it is not possible to apply any one set of clinical criteria to the diagnosis of all types of malaria in all patients populations ***(WHO Recommendations Working Document, 2005)***.

Laboratory diagnosis of malaria can be made through microscopic examination of thick and thin blood smears. Thick blood smears are more sensitive in detecting malaria parasites because the blood is more concentrated allowing for a greater volume of blood to be examined; however, thick smears are more difficult to read. Blood films need to be read immediately; off-hours, qualified personnel who can perform this function should be on-call. A negative blood smear makes the diagnosis of malaria unlikely. However, because non-immune individuals may be symptomatic at very low parasite densities that initially may be undetectable by blood smear, blood smears should be repeated every 12-24 hours for a total of 48-72 hours ***(Shah et al., 2004).***

Antimalarial drug resistance is defined as the ability of a parasite strain to survive and/or multiply despite the administration and absorption of a drug given in doses equal or higher than those usually recommended, but within the limits of tolerance of the patient. It is the result of spontaneously occurring mutation ***(Bruce et al., 1986; Bloland, 2001)***.

In P. vivax and P. ovale infections, patients having recovered from the first episode of illness may suffer several additional attacks (relapses) after months or even years without symptoms. Results occur because P. vivax and P. ovale have dormant liver stage parasite (hypnozoites) that may be reactivated. Treatment to reduce the chance of such relapses is available and should follow treatment of the first attack ***(CDC, 2004)***.

In Egypt, malaria transmission primarily occurs during the warmer months (usually from June through October). Risk exists in focal rural areas of AlFayoum Governorate. Possible risk exists in the Nile River Delta, along Suez Canal, the northern Red Sea coast. Urban areas include Alexandria and Cairo which are at risk ***(MEDIC, 1997)***.

Aim of the Work

The aim of this work was to evaluate the real state of malaria as a cause of fever among patients admitted to the Military fever hospital as well as to identify the predominant types of plasmodia causing malaria in Egypt. Also, to trace the source of malarial risk in Egypt and evaluate the diagnostic and management procedures.

Introduction to Malaria

I. *Introduction:*

The malaria parasite is a prevalent human pathogen with at least 300 million cases of malaria each year globally and more than a million deaths. The social and economic burden of malaria in endemic countries is immense. Already a disease of the poor, malaria further contributes to economic woes by debilitating people afflicted with the disease and imposing significant financial costs on affected people and governments ***(WHO, 2003).*** An estimated US$12 billion in economic revenue is lost annually in Africa because of malaria ***(The World Bank, 2001).***

Malaria is one of the most prevalent human infections worldwide. Over 40% of the world's population live in malaria-endemic areas ***(WHO, 1994).***

Exact numbers are unknown, but an estimated 300 to 500 million cases and 1.5 to 2.7 million deaths occur each year ***(WHO, 1994)***.

Ninety percent of deaths occur in sub-Saharan Africa, the majority involving children less than 5 years of age. Malaria disproportionately affects the poor, in whom higher morbidity and mortality can be largely attributed to lack of access to

effective treatment; 60% of malaria deaths worldwide occur in the poorest 20% of the population ***(The World Bank, 2001).***

II. *Epidemiology:*

A. The Causative Organisms:

Plasmodia species are the parasites responsible for malaria. Only 4 of the over 100 species of plasmodia are infectious to humans. The majority of cases and almost all deaths are caused by *Plasmodium falciparum*. *Plasmodium vivax, Plasmodium ovale* and *Plasmodium malariae* cause less severe disease ***(Kain et al., 2001; Kain et al., 1998)***.

B. Mode of Transmission:

The parasite is transmitted by night-biting *Anopheles* mosquitoes. Domestically acquired malaria can occur but is rare. Such cases include "runway" or "airport" malaria, in which local transmission of disease has been attributed to an infected mosquito that was transported on a long-haul flight ***(Conlon et al., 1990; Curtis and White, 1984)*** transmission by local mosquitoes that have acquired the infection from migrants or visitors ***(Zucker, 1996)*** transfusion-acquired infection ***(Slinger et al., 2003)*** and congenital infection ***(Malaria surveillance, 2001).***

C. **Precipitating Factors:**

Warm climates with high humidity and abundant rain create favourable conditions for mosquitoes by increasing breeding areas and prolonging survival, thereby facilitating transmission ***(Pouniotis et al., 2004)***.

D. **Susceptibility:**

In addition to children, pregnant women (particularly primigravidae) and nonimmune people (e.g., travellers, foreign workers) are at highest risk of severe disease. However, all age groups may be at risk of severe disease during malaria epidemics, which occur either when changes in the physical environment (caused by climatic variation, agricultural projects or mining, for example) increase the capacity of mosquitoes to transmit the disease or when population displacements (natural disasters, war) expose nonimmune populations to infection ***(Kain et al., 2001).***

E. **Geographical Distribution:**

Malaria is present to varying degrees in 105 countries **(Fig. 1)**, the majority of which contain drug-resistant strains. Over 90% of all malaria cases occur in Africa, and most are caused by *P. falciparum*. This species also predominates in Haiti and the Dominican Republic. In Mexico, Central and South America, the Mediterranean,