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Imported Malaria: Experience Of Avicenne Military Hospital of Marrakech-Morocco.

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ABSTRACT

Although malaria was eradicated in Morocco since 2005, it remains a concern for health authorities. Indeed, cases of malaria called "imported" are still observed and may involve life-threatening situations. This concerns travelers in general, and the military in particular from non-endemic countries and traveling to tropical regions. We tried through a series of 260 cases of imported malaria hospitalized in internal medicine and intensive care unit and external cases diagnosed in parasitology department of the military hospital of Marrakech between January 2002 and December 2016, to analyze the epidemiological, diagnostic, preventive and therapeutic characteristics of this parasitic disease and to review the latest national and international recommendations. It is about 218 soldiers and 42 civilians, predominantly male in 99.23%, with mean age of 32.65 years (20-60). The cases were imported especially from Ivory Coast (63.10%) and Democratic Republic of Congo (22.31%). Plasmodium falciparum was the most frequent parasite (46.92%) followed by Plasmodium ovale (34.23%). The severe malaria episodes were diagnosed in 5.39% of access (14 cases) with three evolving towards death. Given the current context of Morocco, its malariogenic power and the incessant number of cases of imported malaria, it is necessary to update the treatment protocols ensuring rapid and effective therapeutic care and anticipate the risk of re-emergence by the implementation prevention strategies based on chemoprophylaxis adapted according to the visited countries and raising awareness of travelers to strictly observe the prophylactic measures.

Keywords : Imported malaria ; Plasmodium falciparum;Diagnosis-Cerebral malaria-chemoprophylaxis-Morocco

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INTRODUCTION

Malaria is a global public health problem and is spreading to 91 countries, where almost half of the world's population is at risk of contracting the disease.

Moreover, the considerable development of tourism, business relations and humanitarian or military interventions leads to an increase in population displacements in a highly interconnected world.A

growing proportion of this traveling population opts for an "exotic" destination, Whatever the length of stay, this population comes into contact with the host environment, with a potential risk of developing short, medium or long term import pathologies.acute Malaria is one of them and places a heavy toll on travelers to tropical areas (1).

The diagnosis of P. falciparum or P. knowlesi malaria is an emergency since that can progress very rapidly to a serious and even fatal clinical situation (2)whence the need for adequate treatment once the diagnosis is confirmed. This critical situation prompted the World Health Organization (WHO) and the world's countries to pool their efforts to develop a global strategy to combat and eliminate malaria while ensuring universal access to prevention and strengthening the development of diagnostic tests and new therapeutics (3)

Indeed, in Morocco, more than 100 cases of malaria are recorded each year, the majority of which is due to P. falciparum. This figure is likely to increase given the massive displacements of Moroccans and Africans from and to Africa / Morocco for reasons of tourism, work, studies or others, The participation of the Royal Armed Forces (RAF) in many peacekeeping and conflict prevention operations in Africa and the realization of new projects for humanitarian and economic purpose through the conventions established by Morocco with other African countries.

This work aims to: To study the evolution of the incidence of import malaria during about fifteen years (from 2002 to 2016), describe the demographic, clinical and biological profile of hospitalized patients in the internal medicine department and resuscitation department at the Avicenne Military Hospital in Marrakech (A.M.H.) for import malaria, Evaluate the modalities of care, and focus on the latest recommendations for treatment and prevention.

MATERIALS AND METHOD

This is a study of the records of all patients who contracted malaria, diagnosed at the Department of Parasitology Mycology, followed in the Department of Internal Medicine and the Resuscitation Department of the (A.M.H.),This study is conducted over a period of 15 years, from January 1, 2002 to December 31, 2016.The patients included in our study were hospitalized in the department of internal medicine and / or in the intensive care unit of the HMA in Marrakech, having as main or secondary diagnosis import malaria in all its clinical forms.

The criteria for defining a case of imported malaria are: "Malaria contracted in a malarial endemic area and occurring in a malaria-free zone, with a clinical manifestation and parasitological evidence of the presence of plasmodium on the blood smear and thick blood smear In case of severe malaria, the severity criteria used for diagnosis are those defined by WHO in 2014 : Prostration; Disorder of Conscience, Glasgow score modified <10, Repeated generalized seizures (more than 1 in 24 hours),Respiratory distress ; Pulmonary edema : radiological definition, Shock (PAS <80 mmHg and peripheral signs of circulatory failure); Abnormal bleeding; Hemoglobinuria (dark red urine, hemoglobinuria with the strip); Renal insufficiency (creatinine> 265µmol / l and / or oliguria <400ml / day); Hypoglycaemia (blood glucose <2.2 mmol / l); Severe anemia (Hb<5g / dl or Ht<15%); Acidosis: carbonates <15 mmol / l ± pH <7.35; Hyperlactatemia:

plasma lactates> 5 mmol / l; Hyperparasitaemia ≥ 2% in the non-immune. ; Jaundice (clinical or totalbilirubinemia> 50 µmol / l);

The exclusion criteria are: The absence of proven infection to Plasmodium sp. The absence of proven infection with P.falciparum orP. knowlesi in case of severe malaria, Access treated with antimalarials without parasitological evidence,Asymptomaticpatients at the time of parasitological

examination.

The diagnosis is based on the detection of the parasite by microscopic examination of a thick and thin blood smear.

The data were collected from a pre-established operating record, from hospital records, medical records of hospitalized patients for imported malaria, the AMH register and parasitology records.

The information collected for each patient included: Demographic data; epidemiological; clinical; paraclinical; therapeutic; Evolution.

The statistical analysis describes and presents the frequencies for the qualitative variables as well as the averages for the quantitative variables. Data entry was done using SPSS 17 software. Quantitative variables were averaged.

RESULTS AND DISCUSSION

The annual incidence of imported malaria cases varies between 03 and 51 with an average of about 17 cases per year, The monthly distribution of registered cases shows a predominance during the months of May-June and December-January when we exceeded 20 case by month.Most patients in our series are male (258 men and 02women).

The average age is 32.65 years with extremes ranging from 20 to 59 years old. The percentages of patients of Moroccan origin and other origins are respectively 98.46% (256 Moroccans) and 1.54% (4 foreigners). Patient history: A patient with coronary stenosis for 10 years; Two comorbidities at risk for immunosuppression: one patient was followed for chronic viral hepatitis B and one diabetic patient ; one patient followed for gastric ulcer.

52 patients have already had at least one acute malaria; All our patients contracted the disease on the African continent in the sub-Saharan region d'Ivory coast (IC) and the Democratic Republic of Congo (DRC) represented the endemic areas where recorded the highest incidences(TABLE I).

218 patients were soldiers belonging to the Moroccan contingents in the sub-Saharan countries. In the other cases, they were occasional travelers in 39 cases (15%) (12 cases of tourist staying and 27 cases of business trip), 3 patients living in malaria-endemic areas found themselves in Morocco for training or occupation framework. The average length of stay in an endemic area was about 6 months with extremes ranging from 7 days to 4 years. 97 patients (37.30% of cases) did not take chemoprophylaxis medications and it was based on: Mefloquine in 83 patients (31.92%), Doxycycline in 61 patients (23.46%) and the association Atovaquone-Proguanil in 19 patients (7.30%) 122 patients (46.92%) reported having complied with the prescribed chemoprophylaxis protocol. The time to onset of symptoms is indicated in 181 patients (69.61%). It averaged 7.83 ± 10.27 days. Fever, chills and headache are the main reasons for consultation Digestive signs were noted in 28.07% of cases (73 cases) Splenomegaly was found in 10% of cases (26 patients), it was associated with hepatomegaly in 5.38% of cases (14 patients). Pains (myalgia, body aches, arthralgia and abdominal pain) were present in 37.69% of patients (98 cases) .15 of our patients (5.76%) were icteric (clinical jaundice and / or biologicalbilirubinemia> 50µmol / l) the urine was dark in 9 patients (or 3.46%) Moreover, the general signs were noted in 56.92% of cases (148 patients), namely asthenia 36.15% (or 94 patients), anorexia 23.84% (62 patients) and weight loss 5% (13 patients)(TABLE II). Biological exploration of our patients during hospitalization shows that 72.69% of cases (189 patients) had thrombocytopenia. Anemia was present in 35.00% of patients (91 cases). Leukopenia was observed in 22.30% (58 cases) of our patients whereas leukocytosis was only objectified in 15% of patients. sick (39 cases). The biological inflammatory

syndrome was present in the majority of patients (231 patients = 88.84% of cases). The disruption of the hepatic and renal assessment was respectively in 10.38% and 2.3% of patients (27 and 06 patients). In addition, we observed hyperglycemia in 15.38% of cases (40 patients) versus hypoglycaemia in 3.07% of patients (8 cases)(TABLE II).

The reference technique of the parasitological diagnosis of malaria used was based on the thin and thick peripheral blood smearsafter staining of May-Grünwald-Giemsa. It was sufficient to confirm the diagnosis of malaria, identify the species and determine parasitaemia. In our study, Plasmodium falciparum (Pf) was reported in 46.92% of cases (122 cases), Plasmodium ovale (Po) was identified in 34.23% of cases (89 cases), Plasmodium vivax (Pv) and Plasmodium malariae (Pm) were isolated in 10% (26 cases) and 3.84% (10 cases), respectively.

Parasitaemia was less than or equal to 1% in 200 patients (76.92% of cases), with extremes ranging from <0.1% to 20%. A parasitaemia level greater than or equal to 2% was found in 21 patients. It should be noted that parasitaemia was not reported in 39 patients. Since 2012, 173 Rapid Diagnostic Tests have been performed, they detected 169 infections among the 173 diagnosed by microscopy. The comparison of rapid diagnostic tests (RDTs) with the results of microscopic techniques of the 173 malaria cases diagnosed between 2012 and 2016 has a sensitivity of 98.27% and 97.69% for RDTs. Of the 260 cases recorded in our series, 246 (or 94.61%) were simple acute malaria , while 14 (5.39%) were severe malaria managed at the ICU resuscitation department. Patients were admitted to the intensive care unit either: Directly through the emergency department: 6 cases, After a stay in the internal medicine department, with an average duration of 5 days ± 4 days, the transition to intensive care corresponded to a secondary aggravation: 8 cases The predominant species of Plasmodium falciparum was Plasmodium, the only species isolated in 12 cases of severe malaria, whereas it was associated with Plasmodium ovale in two cases. Parasitaemia was high, averaging 12% ± 5. The analysis of the severity criteria of the WHO during the first 4 days of hospitalization in intensive care shows that each patient had at least the association of 4 severity criteria established by the WHO. Treatment with Artéméther-lumefantrine alone was prescribed in 123 patients (47.30%) and in combination with doxycycline in 4 patients (1.53% of cases). Quinine is used in 59 patients (22.7%): Only by injection in 37 patients (14.23%); Oral only in 13 patients (5%);In combination with doxycycline in 6 patients (2.30%); With a relay of Artemether-lumefantrine per os in 3 patients (1.15%).

Mefloquine was prescribed in 35 patients (13.46%) while 09 patients (3.46%) were treated with halofantrine. Treatment was not specified in 11.54% of cases (in 30 patients).

Adverse reactions were reported in 15 patients (5.77%), mainly nausea-vomiting-related digestive disorders (6 patients, 2.30%) and diarrhea (9 patients = 3.46%).) for oral treatment whereas only one case of intolerance for injectable quinine with vertigo, dyspnoea and hearing loss has been recorded. For patients in intensive care, some have presented complications directly related to malaria and others to the complications of resuscitation. Complications included in the WHO 2000 definition of severe malaria during access are: Coma: 1 case (0.38%); State of shock: 4 cases (1.53%) including one in the context of multi-visceral failure; acidosis: 2 cases (0.77%); acute respiratory distress syndrome: 1 case (0.38%); convulsion: 1cas (0.38%); hypoglycemia: 1 case (0.38%); acute renal failure: 1 case (0, 38%); The main complication associated with resuscitation was nosocomial pneumonia, mainly to gram-negative bacteria in 2 patients, ie 0.77% of cases (one case with Acinetobacterbaumanni and another case with Pseudomonas aeruginosa).

The evolution of external cases recorded in the register of the parasitology service was not reported (30 cases : 11.53%). But it was favorable in most cases 87.3% (or 227 patients) without any case of

recidivism. On the other hand, we deplored the death of three patients, a mortality rate of 1.3%. Deaths were related to multi-organ failure (DMV) (2 cases) and ARDS (one case).

DISCUSSION:

Since 2005, no indigenous case of malaria has been recorded [4] in our country. All cases notified from this date are cases imported from abroad. This achievement has enabled our country to be certified "malaria-free" by WHO in 2010.

The analysis of the annual incidence of malaria cases in our hospital shows on the one hand the decrease of the incidence in 2008 and 2010, which could be explained by a better observance of chemoprophylaxis. On the other hand, and as of 2012, the number of imported malaria cases has increased dramatically. The majority of cases were soldiers deployed mainly to the IC and the DRC. Half of the Moroccan battalion engaged in the United Nations operation in Côte d'Ivoire (UNOCI) changed the settlements in 2012. However, for cases coming from the DRC, the increase in the number of cases since 2012 compared with in the year 2011 remains unexplained, other factors not explored in our study could be at the origin of this peak of incidences, such as a high rainfall during these years compared to the year 2011, or operational conditions that caused the military to become more exposed to anopheline bites through more frequent night guard and / or night patrols. As for the monthly distribution, the imported cases are recorded throughout the year, with two small peaks in December - January and in May - June, succession of our military at the end of every six months as part of missions in malaria endemic areas.

The average age of our study series is 32.65 years old. Our population is a little younger than Bellazreg F. at FarhatHached-Sousse [5] and Lamblin A. at the Desgenettes Hospital in Lyon (about 115 cases) [6], with an average age of 35 years and 37 years, knowing that it is still a young and dynamic population, and therefore more exposed to travel, whether for studies, for work or for service military. All studies agree that sub-Saharan Africa is the most-at-risk region in the world [7]. As a result, the Ivory Coast and the Democratic Republic of Congo are the countries most visited by our military, and therefore the most incriminated in the plasmodial attack of our troops, especially that they are classified by the WHO. among the 19 countries accounting for 90% of malaria cases recorded in Africa [8]. The cause and duration of trips also vary according to author. For the most part, stays are rather short (1 to 2 months) for tourism, family visits for migrants and finally cooperation and humanitarian aid [9]. In our study, they are rather long and professional (Moroccan military missions abroad) whose stays last about six months. These results are similar to those observed in the study conducted at the Moulay Ismail military hospital in Meknes concerning 30 cases of imported malaria [10].

in our series, the use of care is slightly slower than in France where access to care is easier (but which remains in the norms), as well as the delay of the diagnosis, can be explained by our population of most of them soldiers, who prefer to join their families during their leave rather than consult for their health problems. Most of the malarious patients, before being transferred to the Avicenna Military Hospital in Marrakech, consulted a doctor in a garrison infirmary where the notion of malaria is not often mentioned in the first place, which contributes to the delay in diagnosis A Canadian study shows that there is a delay in diagnosis and initiation of treatment when patients present themselves to an inexperienced service in tropical medicine. [11] Almost all patients in our study were febrile (93.46%), which is consistent with the 100% of febrile cases of Tlamçani I, et al. [10] and the 83.4% of cases of El Wartiti MA et al [12]. In the study of Severov M. and Comolet 81.48% of cases [13] had chills against 84.61% of cases in our series. The presence of headache and fatigue are often present in patients. They were present in 60.38% of our patients

compared with the study of El Wartiti M. [12] et al. with 71.7% and 76% of cases according to the study by Tlamçani I, et al. [10] Data from the Pitié-Salpêtrière hospital study in 2004 showed that vomiting occurred in 19.7% of cases and diarrhea in 25.5% of cases [14]. What is consistent with our study, the most common digestive signs was vomiting with 22.69% of cases, followed by transit disorder with 18.46% and abdominal pain in 08.07% of cases. Thrombocytopenia accounted for 72.69% of cases in our study, confirming its frequency in this condition, while anemia was present in 35% of cases. According to the study by El Wartiti M. et al., Thrombocytopenia was seen in 73.2% of cases and anemia in 43.9% of haemolytic type cases due to the destruction of red blood cells. [12]

Plasmodium falciparum is the most frequently reported species in our study, accounting for 46.92% of cases (66.7%). According to the study by Tlamçani I. et al. (10) is 96, 15% According to the study by Bellazreg F. et al (5) followed by P. ovale with 34.23% of cases (from 23.3% according to the study made by Tlamçani I. et al. (10) is 3.84% According to the study by Bellazreg F. et al. (5)

P. falciparum infects erythrocytes of all ages, the parasitemia rate can be high, it reaches 20% in our series. On the other hand, P. ovale infecting especially young red blood cells presents itself with usually with weak parasitaemias, the maximum observed in our series was 2%. In the series reported by Tlamçani I. et al., The majority of patients (90%) has parasitemia ≤1%. It ranged from 0.01% to 8% with an average rate of 1%. [10] In our series, we found that parasitaemia was a few traces and reaches about 50%, as well as 76.92% of patients have parasitaemia ≤1%. Severe forms of imported malaria represent a rare reason for admission to intensive care of H.M.A. of Marrakech, with a frequency of less than one case per year over 15 years of study. severe malaria account for approximately 5.39% of malaria cases in our population. Over the 15 years covered by our study, the collapse of the halofantrine prescription is confirmed, while there is a rise in therapeutic combinations based on artemisinin derivatives according to the latest WHO recommendations. The reference treatment was CTA (COARTEM ®) administered in 127 patients = 48.85% of cases (as monotherapy or in combination with doxycycline) and 59 patients (22.7% of the cases were treated with quinine either in part of severe malaria or simple access associated with severe vomiting.

In our series, only 15.38% of the required checks were made. In addition, only 10.38% of cases benefited from a control at seventh day compared to 46% at the CHU de Bordeaux. The number of tests carried out should normally be higher in our series, since 88.46% of malarious patients were hospitalized, compared to only 70% in Bordeaux [15]. This lack of follow-up is due to the remoteness of the home units where the soldiers work compared to the HMA and the impossibility of keeping them hospitalized for a long time.

The evolution was favorable in 87.3% (227 patients) without any case of recurrence. However, there were 3 cases of death complicated by multi-organ failure (2 cases) and acute respiratory distress syndrome (1 case).

GUIDELINES :

The preventive health program should be of interest to different scales in order to ensure maximum effectiveness

-The travellers :

The need for simultaneous protection against mosquito bites and chemoprophylaxis should be emphasized. No lonely preventive measure provides total protection.

-The physician:

We propose to initiate individual and collective programmed consultations, to explain the principles and objectives of antimalarial chemoprophylaxis, to answer travelers' questions and to share the experiences of each one with respect to malaria. Travelers should be reassured about the existence of side effects, most often innocuous and transient, will not to stop taking chemoprophylaxis.

Insist on the mosquito net impregnated as night comfort system but also as a means of vector control.

-Hospital scale:

Update recommendations for travelers based on new developments in prophylaxis and chemoresistance.

Create a service of infectious and tropical diseases to ensure a fast and adapted care.

Restructure the emergency care laboratory in a quality control concept, which will ensure a minimum of ongoing training of staff in the recognition of haematozoa and the timeliness of the emergency.

The introduction of rapid diagnostic tests is therefore essential to ensure diagnostic and therapeutic support in the best off-hours conditions.

-At national scale :

Create a Malaria Research Center or a travel medicine center.

Improve the management of malaria in general practice, whether in the public or private sector through campaignsinformation to all health professionals.

Promote consultation in travel medicine prior to departure. This last recommendation is important because the risk of occurrence of imported malaria can be significantly reduced by the application of personal protection measures. Many studies have shown that the lack of advice when traveling to endemic areas, or advice s given by unsuitable health professionals, lead to incorrect prophylaxis.

Establish a system of "Moroccan Center for Disease Control and Prevention» to analyze, monitor and, see, limit the introduction of invasive vector species, with the aim of preventing the occurrence of emerging vector diseases in the country.

Table I : Number of cases according to country of contamination

country	Number	percentage
IVORY COST	164	63.10
D.R.C	58	22.31
EQUATORIAL GUINEA	6	2.30
CONGO	6	2.30
CAMEROON	2	0.77
MAURITIUS	2	0.77
SENEGAL	2	0.77

CENTRAL AFRICAN REPUBLIC	1	0.38
GHANA	1	0.38
BURKINA FASO	1	0.38
NIGERIA	1	0.38
MAURITANIA	1	0.38
MALI	1	0.38
UNSPECIFIED	14	5.4
TOTAL	260	100

Table II : Synthesis of clinical evidence of imported malaria cases

Clinical evidence	**Number of case**	**percentage**
Fever	243	93.46
Chills	220	84.61
headaches	157	60.38
vomiting	59	22.69
Transit Trouble	48	18.46
splenomegaly	26	10
Hépato splénomégaly	14	5.38
Pains • Diffuses •Arthralgia •Dolor abdominals •Myalgia	 98 35 26 21 10	 37,69 13,46 10,00 08,07 03,84
jaundice	15	5.76
Dark urine	9	3.46
Asthénia	94	36.16
Anorexia	62	23.84

emaciation	13	5

Table III : Synthesis of biological manifestations of imported malaria cases in our series

Biological criteria	**number**	**percentage**
anemia	91	35
thrombocytopenia	189	72.69
leukopenia	58	22.30
leukocytosis	39	15
CRP	231	88.84
hepatic balance disruptions (asat / alat)	27	10.38
renal balance disruptions (urea / creat)	06	2.3
hyperglycaemia	40	15.38
hypoglycaemia	8	3

CONCLUSION:

The increase in the number of cases of imported malaria reported in Morocco imposes rigorous surveillance to minimize the potential risk of its reintroduction into our country. This is carried out on the one hand by the screening and the systematic treatment of the parasitized subjects originating

or having stayed in the endemic zones as well as the updating of the therapeutic and chemoprophylactic protocols and on the other hand by the sensitization of Moroccan travelersinmalarious areas with prophylactic measures, in particular adequate chemoprophylaxis. Plasmodium falciparum malaria remains a fatal disease. We must therefore insist on the information of the travelers for a great rigor of the preventive measures and a good observance of chemoprophylaxis which can contribute to decrease the incidence, the prevalence and the mortality of this affection.

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