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Imported Malaria among Moroccan Military Personnel who have stayed in the Democratic Republic of Congo and Côte d'Ivoire

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Abstract

Malaria is a febrile and haemolyzing erythrocytopathy caused by the presence, development and multiplication of the Plasmodium genus protozoa in red blood cells, transmitted to humans by the bite of the female anopheles mosquito. It is a threat to travelers in general and in particular to military personnel from non-endemic countries and traveling to tropical regions.

We tried to analyze the epidemiological, diagnostic, therapeutic and preventive characteristics of imported malaria, through a series of 81 cases of Moroccan soldiers who stayed in the Democratic Republic of Congo (DRC) and Ivory Cost (IC).

The mean age was 33, 3 years, all male. 26 cases stayed in the DRC and 55 in the IC. We recorded one case of malaria in 2011, twenty-seven cases in 2012, twelve in 2013, eighteen in 2014, and twenty three cases in 2015. The average time between the return from the endemic area and the onset of symptoms was 175 days. Fever was present in all cases and neurological disorders in one case. *Plasmodium ovale* was found in 55.5% of cases (n=45) followed by *P. falcipaum* in 39.5% (n=32). P. malariae was found in 3.4% of cases (n=3). The association *P. falcipaum* + *P. ovale* was observed only once (n=1). The average parasite rate was 0.69%, and it ranged from 0.01 to 8%. We regretted a single case of death due to *P. ovale* infection. Patients who were in the DRC used mefloquine in chemoprophylaxis, and those in IC used doxycycline until 2013, and then they converted to mefloquine.

The Increase in the number of malaria cases imported from IC since 2012 appears to be due to the change of the place of deployment of half the Moroccan battalion deployed in the country. However, the increase in the number of cases from the DRC remains unexplained. Climatic factors or operational constraints could be the cause of their larger exposure to Anopheles risk.

Keywords: Army; Democratic Republic of Congo; Imported malaria; Ivory Cost; Morocco;

Introduction

Malaria is a febrile and haemolytic erythrocytopathy due to the presence, development and multiplication in the red blood cells of humans (or animals) of a protozoan transmitted by the infective bite of a female anopheles [1].

Four plasmodial species are responsible for this parasitosis in humans: *P. falciparum*, *P. vivax, P. ovale* and *P. malariae*. Recently a fifth species, *P. knowlesi* (responsible for monkey malaria), has been found as a human infection in a few Southeast Asian countries [2,3]. Vulnerable populations are mainly infants, immunocompromised and pregnant women living in endemic areas, and travelers from non-endemic countries to malarious areas.

Every year 25 to 30 million travelers from non-tropical countries visit malaria-endemic areas with about 30,000 cases of malaria associated with these trips [5]. In addition, recent decades have witnessed a steady increase in cases of imported malaria in non-endemic countries, despite the reported decrease in the number of malaria cases in recent years worldwide. Moreover, the latest data from Europe and America have shown an increase in the number of cases of imported malaria and American statistics have estimated this rise to 14% in 2010. This same trend was observed in Morocco 364 cases were recorded in 2012, 312 cases in 2011, and only 218 cases in 2010 and 145 cases in 2009 [6]. Most of the patients were occasional Moroccan travelers to sub-Saharan Africa, workers, traders, expatriates and migrants living in Morocco after returning to their country of origin and especially soldiers on a peacekeeping mission. [7].

Through this work, we have tried to study the epidemiological, clinical and biological characteristics of import malaria among soldiers who have stayed in the Democratic Republic of Congo (DRC) or Côte d'Ivoire (CI) who present malaria confirmed by a biological diagnosis.

Patients and Methods

This is a prospective study that was conducted in the parasitology department of the Moulay Ismail Military Hospital in Meknes during a period extending from 01/01/2011 to 31/12/2015.

As part of the implementation of UN Security Council Resolutions 1279 of 30 November 1999 and 1528 of 27 February 2004, two Moroccan contingents of 848 in the DRC and 726

men in CI have been called upon to participate in operations peacekeeping in these countries.

In the DRC, 51 soldiers were deployed in the city of Bunia (1275m above sea level) located in the north-east of the country and 780 men were in Dungu (393m above sea level) located further north. In CI, a battalion of 726 men (6 companies each comprising about 120 people) was deployed. Half of this battalion (3 companies) did not change their deployment location between 2011 and 2015. The remaining three companies that were in Bouaké, Divo and San Pedro in 2011 were relocated at the beginning of 2012 to new sites: Tai, Guiglo and Toulépleu where they were transiently sheltered in tents until the beginning of 2013 corresponding to the completion of prefabricated housing.

Before leaving on mission, all soldiers received a health education with an awareness of the various health risks related to the tropical environment including malaria.

Chemoprophylaxis started 10 days before departure for mefloquine and the day of departure for doxycycline.

This study was conducted in all military patients who stayed in CI or DRC admitted for malaria. The positive diagnosis was retained on the presence of Plasmodium haematozoa on the thick blood film and smear. Not included in the study were Moroccan military personnel who stayed in other sub-Saharan African countries, civilian patients and those from sub-Saharan Africa.

The demographic data (age, sex), epidemiological data (plasmodial species, endemic country, parasitaemia, chemoprophylaxis and its compliance), clinical data (the delay between the return and the appearance of the first symptoms, antecedents of malaria, the clinical signs) and biological (hemoglobin and platelet levels) were collected.

Results

In total we found 81 cases of malaria among soldiers returning from the DRC and the IC. 77% of cases (n=55) stayed in CI and 23% of cases (n=26) in the DRC. Only one case was recorded in 2011, twenty-seven cases in 2012, twelve cases in 2013, eighteen cases in 2014 and twenty-three cases in 2015 (Table 1). The proportion of cases with malaria in 2012 was significantly higher than those reported in 2011 (p <0.001), 2013 (p=0.003), and 2014 (p <0.001). The mean age of the patients was 33.3 ± 7.5 years (23 to 49 years). They were all male, and completed duration of 6 months regardless of the place of stay (Table 1).

Table 1: Annual distribution of cases by place of residence

Année	CI	RDC	Total
2011	0	1	1
2012	17	10	27
2013	7	5	12
2014	11	7	18
2015	20	3	23
Total	55	26	81

Fever was the common symptom and was present in 100% of patients (n=81). 93.8% of cases (n=76) had headaches and only one case of neurological disorders required hospitalization in the intensive care unit (Table 2).

Table 2: Clinical signs observed in our malaria cases

Clinical Signs	Number of Cases	Percentage (%)
Fever	81	100
Headache	76	93.8
Digestive disorders	34	41.9
Respiratory disorders	9	11.1
Neurological disorders	1	1.2

The most frequently found species was P. ovale identified in 55.5% of cases (n=45) followed by P. falciparum in 39.5% (n=32). P. malariae was found in 3.4% of cases (n=3). The association *P. falciparum + P. ovale* was observed only once (n=1).

In 2012, *P. falciparum* was predominant and accounted for 70.4% of cases (n=19) while *P. ovale* accounted for only 22.2% of cases (n=6). In 2014 and 2015, however, *P. ovale* was more prominent and was observed in 77.7% of cases (n=14) in 2014 and 87% of cases (n=20) in 2015; *P. falciparum* accounted for only 16% (n=3) in 2014 and 13% (n=3) in 2015(figure1, Table 3). P. ovale was more frequently imported in 2014 and 2015 than in 2012 (p <0.001).

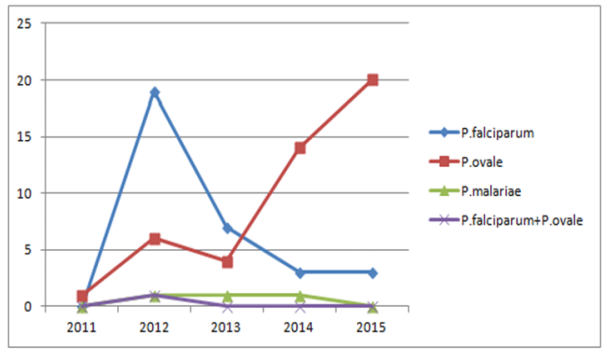

Figure 1: Evolution of the annual distribution of the Plasmodium species

Table 3: Annual distribution of the species

Species	2011	2012	2013	2014	2015	Total
P. falciparum	0	19	7	3	3	32
P. ovale	1	6	4	14	20	45
P. malariae	0	1	1	1	0	3
P. falciparum + P. ovale	0	1	0	0	0	1
Total	1	27	12	18	23	81

The mean parasitaemia rate was 0.69% and the values ranged from 0.01% to 8%. The maximum parasitaemia rate was 8% for *P. falciparum* and 2% for *P. ovale.*

Biologically, anemia was observed in 26% of cases (n=21) and thrombocytopenia in 84% of cases (n=68). The chemoprophylaxis was done by taking a weekly 250 mg tablet of mefloquine for the cases who stayed in the DRC and a daily dose of a 100 mg tablet of doxycycline for those who were in CI. Since 2013, they have also started taking mefloquine. All the soldiers reported a good observance of this prophylaxis during the stay. Mefloquine was continued for three weeks after return and doxycycline for four weeks. Only two cases reported non-taking doxycycline after their return. The rate of good adherence was overall 97.5% (n=79).

Discussion

In the history of armies, malaria has weighed heavily on the fate of several military campaigns around the world, posing a real threat to the troops [8-10].

P. ovale infection was predominant in this study, found in 55.5% of cases, more than what was found in the Tunisian series of Ajili, et al. (27%) and the two French series of Mayet, et al. (6.6%) and Migliani, et al. (2%) [11-13].

The second most common species in our study was *P. falciparum* in 39.5%. However, this species was the most frequent in 3 series of French soldiers who exercised in CI: that of Samy J, et al., Mayet, et al. and Migliani, et al. with respective frequencies of 84%, 83.3% and 78.9%. This species was also the majority (60%) in the Tunisian series of Ajili, et al. corresponding to soldiers having stayed in CI, DRC and Rwanda [11-14].

The rate of infection with *P. malariae* among our cases (3.4%) remains comparable to that of French series of Mayet, et al. (6.6%) and Migliani, et al. (8%). However, for *P. vivax* no case of infection due to this species has been found, contrary to what has been reported in soldiers who have stayed in CI by Ajili F, et al. who identified 10% of cases, Mayet, et al. who found 2.8% of cases and Migliani, et al. who noted this species in 1.8% of cases. The latter authors hypothesized a diagnostic error or a *P. vivax* infection contracted well before during a stay in French Guiana because this species would be absent in CI [11, 15].

The two-species mixed infection rate found among our cases was somewhat similar to that found in the Migliani, et al. (2.7%). During 2014 and 2015, we found an increase in *P. ovale* cases and a decrease in *P. falciparum* cases. An emergence of *P. ovale* infection has also been reported in French soldiers who have been living in CI since 2005, while the overall incidence of malaria among these troops has decreased significantly between 2005 and 2012. The authors advanced the hypothesis of a high exposure to infection by this species or a decrease in the effectiveness of chemoprophylaxis by doxycycline on *P. ovale* [16].

In CI, in 2012 half of the Moroccan battalion operating in this country was moved south where malaria transmission is permanent this could also explain the higher number of cases observed in our series since this year (Figure1, Table 1).

On the other hand, for the cases coming from the DRC, the increase of the number of cases in 2012, 2013, 2014 compared to 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 heavy rainfall during these years compared to the year 2011, or the operational conditions that led the military to expose themselves more to anopheline bites by more frequent exercises of guards and / or night patrols. Our descriptive study was based solely on cases that consulted at the military hospital located in Meknes, six other military hospitals located in the cities of Rabat, Marrakech, Agadir, Guelmim, Laayoune and Dakhla have also hosted other cases of import malaria from IC and DRC during this study period. A case study of these hospitals, or even better, field studies in sub-Saharan Africa could provide a more accurate picture of malaria in our military.

After an insect bite, at least 7 days of incubation are required for clinical manifestations to occur. In our study the average time between returning from home and the onset of symptoms was 175 days, similar to that found in the study by Samy J, et al. which were 182 days old. On the other hand, the study by Mayet A, et al. reported a much shorter 21 day delay. This delay varied by species, it was shorter for *P. falciparum* (68.7 days) and longer for *P. ovale* (227.1 days) [12,14]. The latter species may be the cause of malarial attack even several years after return because delayed hepatic schizogony may occur by the resumption of sporozoite evolution that has been quiescent in liver cells (hypnozoites). This can lead to the release of merozoites in the blood several months after the mosquito bite, thus explaining the late relapses observed for this species. It should be noted that vigilance must be observed several weeks or even months after the mission. Van Den Enden, et al. identified 48 cases of imported P. ovale malaria treated between January 1987 and November 1991, 40 cases (83%) occurring more than one month after leaving the endemic area. 23 cases (48%) regularly took chemoprophylaxis [17].

Malaria agent infection in humans is manifested by several clinical presentations ranging from the simplest to the most severe depending on the species of the patient, the field and the age of the patient.

Like the Tunisian series reported by Ajili F, et al. fever was present in 100% of our cases. In the French series of Samy J, et al. it was found in 96.8% of cases. This underscores the importance of this clinical sign, which is associated with a notion of stay in an endemic zone, must evoke a malarial access [14]. Our patients had headache in 93.8% of cases, much more frequently than what was observed in the French series of Samy J, et al. who found this symptom in only 15.6% of cases. Digestive disorders were also much more frequently observed in our series compared to that reported by Samy et al. 41.9% versus 21.8% [14].

Severe adult malaria is defined by the presence of *P. falciparum* parasitaemia and one or more of the clinical or laboratory manifestations defined by OMS in 1990 and revised in 2000. In our study, four cases of *P. falciparum* infection exhibited a sign of biological severity (parasitemia greater than 4%), one of which had neurological disturbances in addition, and its condition required hospitalization in the intensive care unit. He received intensive care in addition to the ant malarial treatment. The biological diagnosis of malaria is an emergency, defined by

the presence of asexual forms of Plasmodium on microscopic examination.

In addition to the clinical signs (fever) and the notion of stay in endemic areas, some biological signs, especially hematological, may be suggestive of malaria. In our series anemia was observed in 26% of our patients, which was consistent with other studies where it was present in 25 to 45% of cases [18]. Thrombocytopenia was quite common and was observed in 84% of our cases. This haematological sign appears to have a high positive predictive value in the diagnosis of malaria [19].

The specific biological diagnosis of malaria is made by the direct search of the parasite, its antigens or its nucleic acids (DNA or RNA). The serological diagnosis is more rarely indicated and is not adapted to the urgency seen the delay of appearance of the antibodies. The two techniques conventionally used to affirm the diagnosis of malaria are the thick blood film and the blood smear [20].

P. falciparum infects erythrocytes of all ages, parasitemia can be high, and it has reached 8% in our series. On the other hand, oval P. infecting mainly young red blood cells usually presents with weak parasitaemias. The maximum observed in our series was 2%. In the series reported by de Leval, et al. the mean parasitaemia rate was 0.17% [16]. As for P. malariae, it infects aged red blood cells, it also presents with parasitaemia generally weak as for our three cases.

About 10% of imported malaria cases have severe malaria due almost exclusively to *P. falciparum* with a mortality rate of about 1%. Other species are only fatal in 0.05% of cases [21].

Before 2013, the Moroccan military in CI used doxycycline 100 mg per day in chemoprophylaxis. This drug has the advantage of being relatively well tolerated. In a study conducted in 2003, 72% of French soldiers deployed in IC reported an absence of adverse effects related to this drug [14]. However, adherence to daily dosing during the stay and for 4 weeks after leaving the endemic area remains critical. It has been estimated, according to the studies, between 54.7% and 63.4% [22].

Since 2013, the Moroccan battalion deployed in CI has converted to mefloquine prophylaxis regime like the contingent in the DRC that still used this molecule. Weekly use of this medication will make it easier to take. However, its troublesome side effects could limit adherence to this prophylaxis.

According to our patients, the compliance with chemoprophylaxis was of the order of 97.5% which remains much higher than those reported in the literature. This suggests to us that this adherence collected by a questionnaire has been overvalued. This mode of assessment has several disadvantages including forgetting the date and time of drug intake especially for a retrospective questionnaire and an over-notification of a correct diet to conceal its failure. This has been elucidated in French soldiers who stayed in IC, by a study comparing plasma concentrations of doxycycline dosed with those expected from a questionnaire [11].

A 1997 Swiss study of 100 patients who traveled to sub-Saharan Africa showed a percentage of mefloquine chemoprophylaxis adherence of 32.1% by the electronic method contrasting with that revealed by a questionnaire that was of the order of 48% [23].

For optimal prophylaxis, there must be an association of all means of control, both against the insect and against the parasite. Military personnel from non-endemic countries traveling to tropical countries at risk of malaria should be protected through the use of means to avoid insect bites: insecticide-treated mosquito nets, application of skin repellents, clothing with long sleeves. However, these measures do not completely prevent insect bites during nocturnal activities, so chemoprophylaxis is essential.Many studies have been conducted to determine the various individual and collective factors that may influence adhesion to these prophylactic measures. Among civilian travelers, some studies suggest that women and older people are more compliant [23-25].

A longitudinal French study by Machault, et al. of a cohort of 1,189 soldiers serving on a short-term mission (approximately 4 months) in sub-Saharan Africa found that non-officer personnel over 30 years of age had poor compliance with these prophylactic measures, probably because of a false sense of urgency. invulnerability to malaria infection, especially if the disease has escaped during any previous missions [23]. However, the study carried out by Ressenguier N, et al. still among French soldiers who served in sub-Saharan Africa during a short mission did not find this association of the age and rank of the military with the degree of compliance of chemoprophylaxis. However, the non-morning behavior of soldiers who woke late and went to bed late was associated with poor compliance with this chemoprophylaxis. The latter would be risk-taking, non-conforming and lacking perseverance. In this study only 46.2% of the military correctly followed their chemoprophylaxis. Adherence to chemoprophylaxis ranged from 9.6 to 76.6%, according to the companies [25].

In our study, the change of assignment sites of half of the Moroccan battalion in CI could be at the origin of the high number of cases of malaria imported from this country. Ceci est d'autant plus que ces militaires étaient abrités transitoirement dans des tentes en attendant l'achèvement de construction d'habitats préfabriqués. La mise en œuvre de moyens de protection contre les piqûres d'insectes serait difficile sous les tentes moins étanches contrairement aux logements préfabriqués munis de grilles métalliques aux niveaux des fenêtres.

Conclusion

The increase in the number of malaria cases imported into the armies observed in our series shows that this pathology remains a serious health problem for soldiers on peacekeeping missions in sub-Saharan Africa. The fight against this parasitosis must be done by repeated sensitizations before departure in endemic areas and in the field. It must also be based on an estimate of the level of on-site transmission by observation of breeding sites, the

proximity or not to a malarious population and especially the assessment of the incidence of the disease within the troops. The evaluation of the degree of compliance of the various means of prophylaxis as well as the detection of possible obstacles (patrols and night guards) that can prevent this observance are important to consider. Taking them into account will help to control their impact on the incidence of the disease.

Contributions of the Authors

Sara Kouara wrote the article, Abderrahim Abbadi and Rabii Bahraouy did the statistical analysis, and Mohammed Errami supervised the work. All authors have read and approved the final manuscript.

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