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# Malaria overdiagnosis and subsequent overconsumption of antimalarial drugs in Angola: Consequences and effects on human health

Sylvie Manguin<sup>a,\*</sup>, Vincent Foumane<sup>b</sup>, Patrick Besnard<sup>c</sup>, Filomeno Fortes<sup>d</sup>, Pierre Carnevale<sup>e</sup>

<sup>a</sup> Institut de Recherche pour le Développement France (IRD), Laboratoire d'Immuno-Physiopathologie Moléculaire Comparée, UMR-MD3, Montpellier, France

<sup>b</sup> Organisation de Coordination pour la lutte contre les Endémies en Afrique Centrale (OCEAC), Yaoundé, Cameroon

<sup>c</sup> SUBSEA7, SONAMET Malaria Control Programme, Lobito, Angola

<sup>d</sup> National Malaria Control Programme, Luanda, Angola

e Portiragnes, France

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#### ABSTRACT

Microscopic blood smear examinations done in health centers of Angola demonstrated a large overdiagnosis of malaria cases with an average rate of errors as high as 85%. Overall 83% of patients who received Coartem<sup>\*</sup> had an inappropriate treatment. Overestimated malaria diagnosis was noticed even when specific symptoms were part of the clinical observation, antimalarial treatments being subsequently given. Then, malaria overdiagnosis has three main consequences, (i) the lack of data reliability is of great concern, impeding epidemiological records and evaluation of the actual influence of operations as scheduled by the National Malaria Control Programme; (ii) the large misuse of antimalarial drug can increase the selective pressure for resistant strain and can make a false consideration of drug resistant *P. falciparum* crisis; and (iii) the need of strengthening national health centers in term of human, with training in microscopy, and equipment resources to improve malaria diagnosis with a large scale use of rapid diagnostic tests associated with thick blood smears, backed up by a "quality control" developed by the national health authorities.

Monitoring of malaria cases was done in three Angolan health centers of Alto Liro (Lobito town) and neighbor villages of Cambambi and Asseque (Benguéla Province) to evaluate the real burden of malaria. Carriers of *Plasmodium* among patients of newly-borne to 14 years old, with or without fever, were analyzed and compared to presumptive malaria cases diagnosed in these health centers. Presumptive malaria cases were diagnosed six times more than the positive thick blood smears done on the same children. In Alto Liro health center, the percentage of diagnosis error reached 98%, while in Cambambi and Asseque it was of 79% and 78% respectively. The percentage of confirmed malaria cases was significantly higher during the dry (20.2%) than the rainy (13.2%) season. These observations in three peripheral health centers confirmed what has already been noticed in other malaria endemic regions, and highlight the need for an accurate evaluation of the Malaria control programme implemented in Angola.

#### 1. Introduction

Angola is currently facing an outbreak of malaria and in the last biannual letter (June 24, 2016) of the Chief of the Global Malaria Programme, Dr P. Alonso stated that "According to government reports, there has been a significant increase in the number of malaria cases and deaths in Luanda since late 2015. Hospital reports showed very high case fatality rates, mainly among older children and adults. Across the country, weak data collection systems are hampering a timely and effective response to malaria. The epidemic in Angola offers a stark reminder of the importance of strong surveillance to measure the extent of increases in disease burden and to ensure targeted interventions for those most in need".

It is well recognized that malaria cases reported from national surveillance systems vary in quality and quantity (Besnard et al., 2006; Besnard et al., 2009). This may have limited value in understanding the actual malaria burden, but may be useful for understanding trends in the relative burden of malaria in the public health sector.

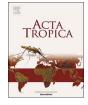
One of the key point is the actual reliability of data reported from health centers in a passive detection method due to 3 main points moreover the bias in recruitment:

\* Corresponding author.

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E-mail addresses: sylvie.manguin@ird.fr (S. Manguin), vfoumane@yahoo.fr (V. Foumane), patrick.besnard@subsea7.com (P. Besnard), filomenofortes@gmail.com (F. Fortes), pjcarnevale2001@yahoo.fr (P. Carnevale).

- 1) There is no pathognomonic symptoms of malaria "simple crisis" and the lack of reliability of clinical diagnosis (even if and when a clinical examination is done) has been long ago underlined (Baudon et al., 1988; Baudon et al., 1986);
- 2) There is a lack of technical equipment such as microscope which is critical to diagnose malaria (Baudon et al., 1988; Besnard et al., 2006; Rogier et al., 2001) and in countries where 50% or more children are asymptomatic carriers, parasite density could be of great help even with its limitations (Bouvier et al., 1997; Delley et al., 2000). To overcome this issue, WHO recommended a large scale use of Rapid Detection Tests (RDT) and actually "The WHO African Region has had the largest increase in levels of malaria diagnostic testing, from 36% of suspected malaria cases tested in 2005, to 41% in 2010 and 65% in 2014" (World Health Organization, 2015). But RDT has some well-known drawbacks and limitations such as false negative, no detection of low densities, no estimation of parasite densities, etc. Nevertheless they can be considered as interesting tools for malaria diagnosis at Peripheral Health Centre (PHC). Immunological method based on PCR are scientifically the best to detect parasite (Fancony et al., 2013) even at a very low density but they required some skills and equipment which can be implemented only at the Central level and not at the Peripheral one.
- 3) There is a usual behavior in several PHC to consider any fever as malaria and to implement Artemisinin-based combination therapy (ACT) without going any further. This attitude has 3 main consequences: (1) lack of reliability of malaria diagnosis ("overdiagnosis") and therefore of data dealing with actual malaria; (2) lack of diagnosis of other diseases that do not receive needed appropriate treatment and are not quoted in official statistics such as diseases that could blow up (recent dengue epidemics); (3) increase of selective pressure due to over scale use of ACT.

Although the Angolan Ministry of Health has put efforts these past 12 years to rebuild the health-care infrastructure, child (167/1,000) and maternal (460/100,000) mortality rates remain among the highest in the world (Luckett et al., 2016). Recent reports have shown that in Angola the available statistics for the burden of malaria are not reliable because of the poor case reporting system and the scarcity of nationally representative malaria surveys (Gosoniu et al., 2010; Luckett et al., 2016). For 2002, official numbers reported 1,4 million malaria cases with 11,344 deaths; in 2004, 3,2 million cases and two-thirds occurred in children > 5 years old (UNICEF, 2008). Then, in 2006–2007, a large scale Angola Malaria Indicator Survey was implemented at the national level to assess the prevalence of malaria and anemia among children > 5 years old. For 2013, a total of 2,3 million cases were officially reported with 5,714 deaths. According to recent surveys in Angola, malaria is by far the highest cause of morbidity and mortality and has an epidemic potential in five provinces (Gosoniu et al., 2010).

In the framework of the National Malaria Control Programme, which implemented several integrated measures, including case management based upon ACT and large scale distribution of long lasting impregnated nets (LLIN), a cross sectional study was done to monitor three public health centers and to compare their malaria diagnosis with crosscheck microscopy done in the laboratory of the Medical Department (MD) of the private SONAMET<sup>\*</sup> Company.

#### 2. Materials and methods

#### 2.1. Study setting and design

Between July 2010 and March 2011, at the request of the National Malaria Control Programme (NMCP), the Sonamet MCP team implemented a classical case-control study during the dry and rainy seasons in three health centers, one in Alto Liro (district of Lobito town) and two in neighboring villages, Cambambi and Asseque, located in the Table 1

Number of patients, presumptive and confirmed malaria cases with their proportions (%), and diagnosis error rate per health center.

Health Centers	Alto Liro	Cambambi	Asseque	Total
Patients	227	152	345	724
Presumptive cases %	156 68.7%	78 51.3%	339 98.3%	573 79.1%
Confirmed cases <sup>a</sup> % per Presumptive cases % per Patients	3 1.9% 1.3%	13 16.7% 8.6%	74 21.8% 21.4%	90 15.7% 12.4%
Rate of error (%)	98.1%	83.3%	78.2%	84.3%

<sup>a</sup> Thick blood smears.

Benguela Province. Carriers of Plasmodium, among 724 patients of newly-born to 14 years old, with or without fever, were analyzed (Table 1). Information on age, gender and temperature (front) were taken. Thick blood smears were systematically processed in order to estimate their parasite load by classical microscopy. Parasitological data were compared to the malaria diagnosis done in the health center according to clinical symptoms, and eventually parasitological observations, which was considered as "presumptive malaria". In these cases, antimalarial drugs were systematically given, free of charge, by the nurse of these health centers. Initially, the aim of the study was to evaluate the proportion of malaria cases among feverish patients, then to use this information for other health centers and improve the statistical data on malaria procured by Peripheral Health Centre. However, it quickly appeared that even the notion of "fever" was not reliable and could not be used as good discriminant factor of "cases" and "control" because we noticed records of "fever" with body temperature of 35 °C-36 °C (Carnevale, unpublished observation). Therefore, we changed and considered clinically diagnosed malaria (or "presumptive malaria") as cases and "other pathologies" as controls.

#### 2.2. Location

Three health centers were chosen for our study. One is in Alto Liro (12°21'S; 13°32'E) located on the upper part of Lobito, a town of 200,000 inhabitants. Vegetation is scarce and the landscape is dry. Until 2007, domestic water was kept permanently in tanks close to habitations, which were suitable breeding sites for Anopheles gambiae (Carnevale et al., 2015; Toto et al., 2011). The Alto Liro health center was selected by the NMCP for monitoring data, as it is well equipped with biological service and microscopes. Asseque (12°39'S; 13°27E) is a village of 8,000 inhabitants, close to Benguela town, in an agricultural area with numerous irrigation canals. The health center is well equipped with microscopes and solar panels given by Sonamet. Cambambi village (12°33'S; 13°32'E) is close to Asseque although located in a dryer area with fewer plantations and the health center has no microscope. In addition, some classical cross-sectional malaria surveys were done by MCP team among asymptomatic children of the same three locations to evaluate their P. falciparum prevalence for a comparison with the plasmodial prevalence and parasite load among patients of the health centers.

#### 2.3. Ethics statement

This study was conducted in accordance with the Edinburgh revision of the Helsinki Declaration and was approved by the National Malaria Control Program of the Ministry of Health of Angola, the ethical authority in charge of approving studies on malaria research in Angola. Download English Version:

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