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Malaria: Diagnosis and treatment in the context of elimination in Cape Verde

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Abstract

Malaria remains a public health worldwide, mainly in Africa. With the efforts in the fight against the disease in recent years, morbidity and mortality by malaria have been decreasing, and several countries aims for elimination of disease by 2010, being Cabo Verde eligible. Malaria data in Cabo Verde from recent years (2010-2016) demonstrate an unstable variation of cases in the country. In this study was analysed the capacity of the country in the diagnosis and treatment of malaria in the country. During the period a total of 37.811 malaria suspects cases was tested in the country in which 312 was positive to *Plasmodium falciparum*, being the main cases imported from different African countries. The country implemented the "test, track, treat initiative" where 100% of cases are confirmed by Rapid Diagnostic Test (RDT) and microscopy. The treatment is free and exclusive to the public health system and all patients are hospitalized to the complete treatment in according with the WHO policies. The health facilities are organized, with material and human resources trained to the correct diagnosis and treatment of malaria resulting in low mortality rate, being 2.24%. The country has made progress in controlling the disease, so it is one of the eligible for the elimination by 2020, counting on the support of national and international entities.

Keywords: Cabo Verde; Malaria Elimination; Diagnosis; Treatment;

Abbreviations

ACT: Artemisinin derivatives; AL: Artemether + Lumefantrine; DDT: dichlorodiphenyltrichloroethane; G6PD: Glucose-6-phosphate dehydrogenase; GDP: Gross Domestic Product; IRS: Indoor Residual Spraying; MoH: Ministry of the Health; NMCP: National Malaria Control Program; RDT: Rapid Diagnosis Test; WHO: World Health Organisation.

Introduction

Malaria remains a vector borne disease with more impact in the public health worldwide. In according with World Health Organisation (WHO), 91 countries remain notifying the disease and about 216 million cases occurred worldwide, with 90% in Africa. The mortality was estimated in 446.000 deaths, 91% in Africa and the vast majority of deaths (99%) are due to *Plasmodium falciparum*. Children under 5 years old are the most affected with 303.000 malaria deaths, equivalent to 70% of deaths [1].

In the last decade, the number malaria cases and countries reporting was decreased. Seventeen countries eliminated the disease between 2000-2015. (i.e. attained zero indigenous cases for 3 years or more) and three of these countries have been certified as malaria free by WHO in 2016 [2]. Being Paraguay, the last country certified free of malaria in June 2018 [3].

In Cabo Verde malaria was endemic in the late 1950s, with 5.000 to 15.000 cases per year and more than 200 malaria-related deaths. Early control efforts through Indoor Residual Spraying (IRS) with dichlorodiphenyltrichloroethane (DDT) and larval source management using both, chemical larviciding and larvivorous fish, have allowed the elimination of malaria the twice in the country. Then the disease was re-introduced twice afterward [4,5]. In the last years, malaria cases in the country had been unstable, affecting mainly adult men. Indeed, the country is characterized by a low malaria incidence with indigenous cases restricted to the islands of Santiago (mainly in the Capital city of Praia) and Boa vista and the imported cases, from the African continent, were more widespread across the country [6].

In according with low cases number of malaria and the policies

implementation, Cabo Verde is one the country eligible and aim to eliminate the disease in its territory by 2020 [4,7]. To achieve it, one of the essential domains is the adaptation of the WHO's latest evidence-based recommendations [8-10]. The policies and strategies adaptation to malaria elimination, in countries as Cabo Verde, with a low incidence of disease [6], becomes essential to enhance case detection and case management to find all suspected malaria cases, to test for confirmation all malaria infection, treat all cases according to national treatment policies to clear infections, characterize and classify infections by their most likely place of origin and report cases and actions taken to the national surveillance system.

In the National Strategic Plan for malaria elimination, 2014-2017 elaborated by the National Malaria Control Program (NMCP) [11], the strategies and interventions were defined to reduce the cases number to less of 01 cases by 1.000 inhabitants and zero death by malaria. For it, the Malaria Treatment Protocol [12] were updated, in according with the latest WHO recommendations in the diagnostic and treatment domains.

The correct malaria diagnosis in the country, permits to treat the patient early, administering the antimalarial drug to those who are actually infected with Plasmodium, exclude malaria from febrile pathologies from other causes, and triggering epidemiological, entomological and vector control surveillance to prevent the occurrence of new infections.

This paper provides the last data of malaria diagnostic and treatment in Cabo Verde, during the 7 years (2010-2016), analysing the diagnostic process, the number of testes available, the percentage of positive tests, the incidence evolution as well the treatment procedures of malaria in the country, in the context of elimination [12].

Methods

Study area

Cabo Verde is an archipelagic country of 10 islands and 22 municipalities, with 4.33Km2 and located about 540 Km from the west Africa coast. The Population in 2018 is estimated in 535.936 [13]. The archipelago is classified as a lower middle-income country with a Gross Domestic Product (GDP) per capita of 2,998 USD [14] (Figure 1)

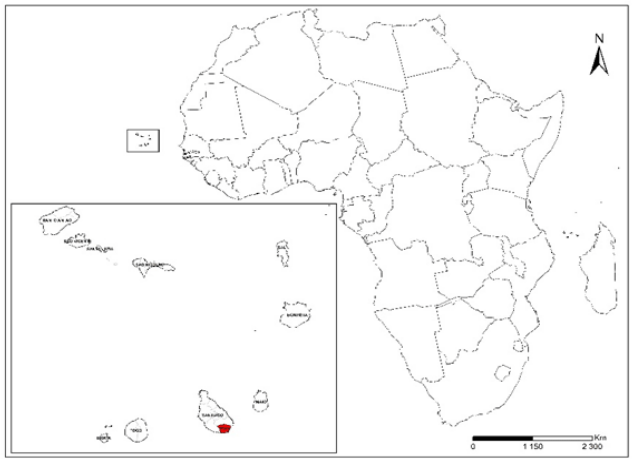

Figure 1: Location of the Cape Verde islands

In terms of health coverage, the health structures network consists of two national reference hospitals (Agostinha Neto in Praia, Santiago Island and Baptista de Sousa in Mindelo, São Vicente), four regional hospitals (in Santo Antão, Sal, Fogo and Santa Catarina, Santiago), 30 health centres, 34 health posts with nurses and 113 Basic Health Units with sanitary agents, in addition to the offices of the Health Delegation in Praia and Mindelo.

This administrative and care structure are coordinated at the central level by the National Direction of Health, responsible for coordinating the activities of the health departments and supervising the activities of the Regional Hospitals. Health Delegations coordinate the activities of the respective Health Centres, Health Posts and Basic Health Units and are responsible to communicate the health data to the central services.

Malaria data collect

Malaria in Cape Verde is a notifiable disease, where case reporting is immediate through a separate form and is also included in the weekly notification form for diseases with epidemic potential. The individual notification form includes personal information of the patient, address, information that allows to classify the disease in indigenous or imported, among other data. The data used in this study was obtained through the National Service of Surveillance and NMCP, both from the Ministry of the Health (MoH) and Social Security. Individual data of each patient with personal information, local of notification of malaria and classification of case, from 2010 to 2016, from all health structure in the country was used in this study.

The collect of Rapid Diagnosis Test (RDT) data and slides made at national level is made through the own forms, with information provided by each health structures with monthly data.

Data analysis

The data were recorded in a Microsoft Excel sheet and structured by islands and their respective municipalities. Analyse of malaria incidence in the country, defined as incidence rate was calculated as [number of positive species – specific clinical cases notified/total population of the country] × 1000. The number of tests by health structure was analysed and the percentage of positive tests determined. The treatment of cases, including the medicine by cases as studied, in according with the polices for malaria treatment in the country.

Results

In according with the protocol of malaria treatment in the country, in the cases of malaria suspect, the RDT and the microscopy with smear and the thick are used throughout the country for the detection of malaria cases. The microscopy allows to confirm the diagnosis as to the type of parasite as well as to have a permanent file of the infection.

During the period, 37.811 suspect cases of malaria was identified in the country and 100% was tested (Table 1). The majority of suspect cases was in 2016 and the high test positivity rate in 2010.

During the period of study, a total of 312 cases of malaria was reported in Cabo Verde. Being 129 indigenous and 183 imported from different countries in Africa (Figure 2). All the cases were due the P*lasmodium falciparum.*

Table 1: number of suspect cases of malaria in the country , the confirmed cases and the teste positivity rate by year in Cabo Verde.

YEARS	Nº of suspected cases	Nº Person tested	Nº cases confirmed	Test positivity rate	Nº of Complicated cases	Incidence rate (%)	Nº of Death	Lethality rate (%)
2016	9 433	9 433	75	0.80%	2	0,10	1,00	2.13
2015	2 744	2 744	27	0.98%	8	0,07	3,00	8.33
2014	5 439	5 439	46	0.85%	9	0,07	1,00	2.78
2013	5 872	5 872	45	0.77%	7	0,09	0,00	0
2012	5 285	5 285	36	0.68%	6	0,09	1,00	2.17
2011	4 757	4 757	36	0.76%	2	0,05	0,00	0
2010	4 281	4 281	47	1.10%	5	0,14	1,00	1.33
	37 811	**37 811**	**312**	**0.83%**	**39**		**7,00**	**2.24**

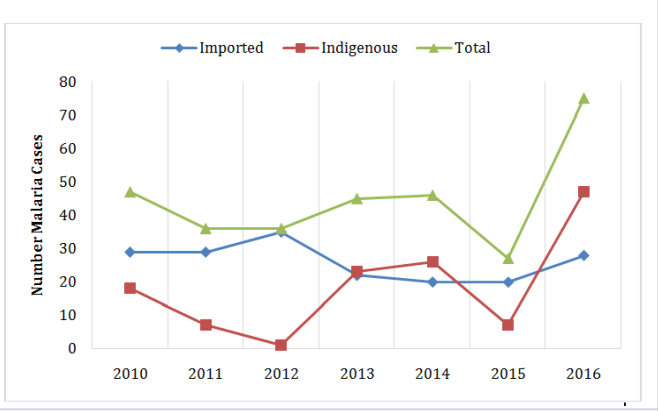

Figure 2: Variation of malaria cases reported in Cape Verde, 2010 - 2016

During the period the malaria cases had an instable variation. The number of imported cases was higher than indigenous cases in the first three years (2010 – 2012). In 2013 and 2014 the indigenous cases were higher (23 and 26 indigenous to 22 and 20, imported, respectively). In 2015 was registered more imported again 20 to 07 imported, and in 2016 the indigenous cases have increased again in comparison with the imported cases (47 and 28 respectively).

The number cases of severe malaria also varied from year to year, being 39 cases notified. The higher number was in 2012, with 9 cases and 2010 and 2015 with 2 severe cases respectively (table 1).

The incidence was variable between 0.05 in 2015 and 0.14 in 2016. And mortality from malaria and Cape Verde has been lowered, varying from 0 to 3, with the highest rate in the year 2011. Consequently, the lethality rate was higher in 2011.

All of these malaria cases reported in the country was treated in accordance with the national guidelines for the treatment of malaria in Cape Verde, based on WHO recommendations.

Discussion

Malaria diagnosis in Cabo Verde

The National Strategic Plan for Malaria Pre-Elimination view is "Cabo Verde a country without malaria". The mission is to make available to the population, the best recognized, effective and adequate interventions in the fight against malaria, the country's epidemiological profile for the elimination of the disease [12].

The priorities and guiding principles are part of the priorities of the National Health Policy [7], developed in the National Health Development Plan and articulates with the Sustainable development goals and according to the WHO guiding principles for the elimination of malaria [9,10, 15, 16].

The use of microscopy to parasitological confirmation of suspected malaria is considered the gold standard. Therefore, the diagnosis based on RDTs, which are quick and easy to perform, is becoming more attractive and recommended, especially in health structures at the peripheral level, where there are no conditions and capacity for the diagnosis using the microscope. The PfHRP2- and pLDH-based RDTs are the most commonly used. PfHRP2 RDTs appear to be more sensitive than pLDH RDTs, particularly at low parasite densities, areas [17], like Cabo Verde islands.

Malaria diagnosis in Cabo Verde follows the WHO recommendations. In according to which, the routine parasitological confirmation of cases is based on either blood films by microscopy or detection of parasite antigens with RDTs [16]. The RDT is used and allow an immediate diagnosis and the examination by microscopy is done in all structures with laboratory capable to that and the blade must be done in a laboratory with trained technicians for the confirmation. In the health structures without a laboratory the RDT are available and technicians are trained to prepare the smear and blood films to be sent to the nearest competent laboratory. The laboratory is responsible to the Identification of the species, the gametocytes

and to determine the parasite density. The treatment follow-up is ensured by municipal health delegation, through the microscopy [12].

In according with the national protocol the decision to choose the methods, rapid tests and / or microscopy depend on the health structures in terms of diagnostic capacity. Traditionally, the confirmatory diagnosis of malaria is made by microscopic examination of the blood, requiring adequate material and reagents, as well as well trained technicians to perform it, in order to detect and differentiate the species of Plasmodium [18].

In all health structures at national level RDT are available. Since the basic health units to regional and central hospitals, and the health posts and health centres. In structures with laboratories, namely central and regional hospitals or health delegations, microscopy is the gold strategy in the process of diagnosis and confirmation of all cases of malaria. In each health structure with laboratories, there are specific data collection sheets, which allows the collection of the quantification of the tests performed by sex, age, date of realization, as well as the differentiation of the number of RDTs and micros copies performed.

The RDT in use in the country is a Malaria HRP2/pLDH (Pf/PAN) Combo, with capacity to detect HRP2 (Pf) and pLDH and to diagnose all 4 main types of malaria (*P. falciparum, P. vivax, P. ovale* and *P. malaria*) infections. It permits also to distinguish between *P. falciparum* and other infections. This choice of this test follows the WHO recommendations, taking into account the globalization of the country and the possibility of introducing species from different areas of the world [11].

Finally, the highest challenge in malaria diagnosis in Cabo Verde, involves the implementation of a diagnostic quality control system and the implementation of molecular biology diagnostic techniques. The national laboratory network has been working in recent years to improve and implement the quality control system, with training of technicians and elaboration of a manual of quality control [19], so that the system has gradually been improving in this sense. With the recent inauguration of the medical entomology laboratory, in the National Institute of Health publishes with capacity and strand for molecular biology techniques, the first steps have been taken, regarding the training of technicians, and initiation of research in the field which will allow improve malaria diagnostic techniques in the country.

Malaria treatment and follow up in Cabo Verde

The main challenge to reduce and eliminate malaria in Cabo Verde implicates the implementation of the new recommendations and strategies as appropriate in the affected areas and populations. In the case of Cabo Verde, the two principal malaria focus in the last years, had been Praia, the capital of the country in Santiago and Boa vista islands [6]. Hence malaria elimination in the country will require a thorough understanding of transmission dynamics and a dedicated investment in key effective interventions [20].

As happens worldwide, including others African countries, Cabo Verde, despite the declining malaria, persist a significant uncertainty on its absolute magnitude. Cabo Verde had significant gains realized, in malaria control, it will be vital not to give complacency a foothold as happened in the past [4]. Changes in the environment, the parasite biology, the vector bieocology and human activities are essential aspects to have account in the elimination process [21,22].

Anti-malarial drugs, additionally to the insecticides have been used for many decades and will remain cornerstones in malaria elimination efforts. Although the clinical failure of the Artemisinine derivatives (ACTs), against falciparum malaria recently observed in the Greater Mekong Sub region [23,24], the ACTs are generally highly effective and well tolerated, especially in the sub-Saharan Africa, where it contributed substantially to reductions in global morbidity and mortality from malaria [10].

In Cabo Verde, some aspects are taken into account before starting the anti-malarial treatment. Namely, the plasmodium species confirmation by microscopy, the history of patients travels to countries where there are others plasmodium species. In addition to *P. falciparum*, the patient age and weight, history of previous episodes of malaria due to the increased risk of presenting the severe form, associated conditions, such as pregnancy, HIV infection, kidney failure, and other health problems that may condition treatment and the malaria severity due to the need for anti-malarial treatment with injectable medication [12].

All the children and adults (except pregnant in the first trimester) diagnosed with *P. falciparum* are treated with Artemeter + Lumefantrine (AL), according to the recommended dosage. A single dose of primaquine 0.25 mg / kg body weight is administered orally (maximum dose = 45mg) as early as the first day of treatment.

To the others plasmodium species, the treatment take account the parasitic forms in the blood and, in the case of *P. vivax* and *P. ovale*, it is also the hypnozoites present in the liver (called radical cure) thus preventing recrudescence and relapse. In this cases, AL or Artesunate + Amodiaquine are available in the country. However, all the malaria cases identified in the country during the period, indigenous and imported, had been by *P. falciparum* [6]. By eliminating the hypnozoites from *P. vivax* and *P. ovale*, the primaquine are also administered (0.25 mg / kg body weight per day) orally once daily for 14 days. There is a contraindication of primaquine, to the Children <6 months old, pregnancy, or Breastfeeding women, unless their babies are over 6 months of age and know that they do not have Glucose-6-phosphate dehydrogenase (G6PD) deficiency, respecting the WHO recommendation [10].

Treatment of severe malaria cases

The treatment of malaria severe in the country is in according to WHO guide [10]. In this cases, all severe cases, (adults or children, including pregnant women in any trimester of pregnancy, infants and breastfeeding women), are treated with intravenous or intramuscular artesunate for a minimum period of 24 hours [12].

Some are considerations are taken in this protocol. If after 24 hours of treatment the patient still does not tolerate the oral anti-malarial medication, continues with artesunate injectable of 24/24 hours until be able to take tablets. If the patient is never able to tolerate oral medication, the treatment will be used the artesunate injection for 7 days (1 dose per day, according to body weight). The single dose of primaquine should be given as soon as the patient tolerates oral medication. If after 24 hours of treatment the patient already tolerates the oral medication, injectable artesunate should be discontinued and an oral combination of ACTs for 3 days in addition to the single dose of primaquine (0.25 mg / kg) in the first day of oral tolerance, except in the pregnant woman and infants less than 6 months old. The primaquine was introduced in the country in 2017.

The Malaria Treatment Protocol, has in considerations others specials cases of malaria, as in pregnant and Pregnant women and children aged <6 months with severe malaria, HIV and Malaria Co-infection, Malaria in patients with sickle cell anaemia (Drepanocitoses), patients with the deficiency of G6PD, Children weighing <5 kg, Diabetics and nonimmune travellers to endemic areas [12], in according to new WHO indications [10].

All malaria cases are hospitalized in the central or regional hospital in the country. During 03 days in the simple cases or more days in according with the According to the needs of each severe case, to ensure complete and better case management. After the complete hospital treatment of the patients, they are referred to the health delegations, charged to the follow up the cases during the day 07, 14, 21, 28, 32 and 42 days.

After the case confirmation, the notification of malaria in immediate from the health structure to the central service in the Ministry of the health, namely the Epidemiological surveillance service and the National Malaria Control Program. The structure that notifies have 24-hour deadline to send the notification forms, as well as the response to the case, which implies a reactive response in the reactive search of cases in parity with the index case with RDT, vector control as well as aspects related to community awareness.

Substantial progress has been made in the control of malaria in Africa and Cabo Verde is one, of the is a reference in the fight against disease, with intensive efforts and investments and support of national and international partners. There are good health infrastructures in the country, the equitable and universal access to health services with trained technicians for the correct management of the cases, reflected in the low mortality rate by malaria in the country.

The past lessons from Malaria Control strategies in the country [10], the encouragement of WHO and other partners, as The Global Fund to Fight AIDS, Tuberculosis and Malaria, Roll Back Malaria, The African Leaders Malaria Alliance (ALMA), West African Health Organisation (WAHO) and others partners, efforts to ensure that the goal of malaria elimination in Cabo Verde in the coming years can be achieved.

To achieve malaria elimination in the country, further progress should be made, by enhancing uptake the strategies and new tools, especially in diagnosis in accounting the experience of others countries in the same context [25, 26]. These strategies will pass to a substantial human capacity well trained in many different diseases domains [23, 24].

Surveillance should not only aim to detect the last case, namely the strengthen of the system for monitoring and evaluation at national program including the "test, track, treat initiative" already implemented in the country, and the monitoring of therapeutic efficacy including the assessing clinical and parasitological outcomes. With the elimination programmes, epidemiological investigations in the country need to focus in the study of outbreaks in Santiago and Boa vista islands, to achieve the elimination in 2020.

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