

## Reduction of incidence and relapse or recrudescence cases of malaria in the western region of the Brazilian Amazon

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### Abstract

**Introduction:** Malaria is one of the major parasitic diseases in the State of Rondônia, located in the western Brazilian Amazon. The basic treatment scheme for this disease is chloroquine and primaquine. This study evaluated the epidemiological profile of malaria in Rondônia between 2008 and 2012.

**Methodology:** The epidemiological data were provided by the Health Surveillance Agency from the State of Rondônia, and socioeconomic indicators were obtained from the Brazilian Institute of Geography and Statistics, Department of Informatics of the Unified Health System, and from the National Institute for Space Research. The analyzed variables included year of diagnosis, gender, age group, main activity performed in the 15 days previous to the diagnosis, parasite species, level of parasitemia, number of relapse/recrudescence cases, and socioeconomic and environmental data for Rondônia.

**Results:** A total of 238,626 cases of malaria were recorded in Rondônia during the study period. Of this total, 65.6% were men and the most prevalent age group was 20–39 years. *Plasmodium vivax* was the most common parasite (89.8%), followed by *Plasmodium falciparum* (9.4%). An average of 30.9% of the individuals who were tested presented with relapse/recrudescence malaria. The API value was highest in 2008 and lowest in 2012, corresponding to 42.3 cases and 19.2 cases per 1,000 inhabitants, respectively.

**Conclusions:** A 58% reduction in the number of malaria cases and a 36.2% reduction in the number of relapse/recrudescence malaria cases were observed, due to increases in the economy, improvements in the health system, and reduction of deforestation in this region.

**Key words:** Amazon; malaria; epidemiological surveillance.

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### Introduction

Malaria, one of the major tropical parasitic diseases, affects approximately 500 million people and causes one million deaths per year. Updated data indicates that there has been an important reduction of annual deaths due to malaria in a period of 10 years, from 2000 to 2011 [1]. The treatment is relatively simple; the basic scheme for *Plasmodium vivax* (the most common species in Brazil) is chloroquine for three days plus primaquine for seven days or fourteen days [2]. In Africa, approximately one million deaths have been caused by the disease [3]. In recent years, malaria has resurged in temperate regions, including Greece, the Korean peninsula, and Australia, all of which previously had no cases [4-6].

In the Americas, the transmission of malaria occurs in 21 countries, in which 203 million people live in areas of high infection risk. In 2002, Brazil recorded 40.5% of the 960,000 cases reported in the Americas [7]. In 2003, 407,995 cases were recorded in the Legal Amazon Region, which led to 10,291 hospitalizations (2.5% of the total number of cases); 82 of these cases were fatal, which represented a lethality rate of 0.02% [8]. In 2011, the district of Porto Velho in Rondônia was the second district with the highest number of cases in the Americas, behind only the district of Sifontes, Venezuela [1]. Cases of malaria reported in other regions of Brazil frequently originated in the Amazon region or other malaria-endemic countries [7,9].

In Brazil, 99.6% of all registered malaria cases are found in the territory occupied by the Amazonian states [10,11]. In the Legal Amazon Region, 106 of a total of 594 municipalities are characterized as being high-risk areas for malaria. The dynamics of transmission vary with the involvement of several factors, including human and vector groupings [12]. For example, the risk of infection is lower within Amazonian capitals than in the outskirts of these cities, such as in the periphery of Manaus and Porto Velho, where significant transmission can occur [7].

The problems with malaria in the State of Rondônia date back to the 18th century with the exploitation of rubber. At the end of the 1980s, the State of Rondônia, which concentrated approximately 40,000 miners working in rafts on the Madeira River and in the town of Ariquemes, was given the title of malaria capital of the world [13]. The current distribution of malaria in the State of Rondônia is quite heterogeneous and includes high incidence areas, such as towns and districts traversed by the Madeira, Jamari, Candeias, and Machado Rivers, which concentrate approximately 50% of the State's population and encompass the towns of Porto Velho and Ariquemes [14].

In addition to analyzing disease control measures, this study evaluated the current epidemiological profile of malaria in the State of Rondônia to raise hypotheses to explain this disease's incidence and the reduction of relapse/recrudescence cases over the past five years.

## Methodology

This was an observational study about the prevalence of malaria in the State of Rondônia. Data provided by the Health Surveillance Agency from the State of Rondônia and from the Epidemiological Surveillance Information System were analyzed.

The collected data were from patients whose diagnoses were made by the Unified Health System between 2008 and 2012. The analyzed variables included year of diagnosis, gender, age group, main activity performed in the 15 days prior to the diagnosis, parasite species, level of parasitemia, and relapse/recrudescence cases (socioeconomic and environmental data for Rondônia). TABWIN software ([www.datasus.gov.br/tabwin](http://www.datasus.gov.br/tabwin)) was used in the analysis of the spatial distribution of malaria cases in the State.

Socioeconomic and environmental data from the State of Rondônia, obtained from the Brazilian Institute of Geography and Statistics (IBGE), Department of Informatics of the Unified Health

System (DATASUS), and National Institute for Space Research (INPE), were analyzed.

The software used for statistical analysis were Microsoft Excel 2010 and BioEstat 5.3. The calculation of incidence was based on 1,000 inhabitants.

## Results

A total of 238,626 cases of malaria were diagnosed in the State of Rondônia in individuals 0–101 years of age between 2008 and 2012. Of these, 156,415 (65.6%) were men and 81,847 (34.4%) were women. The age range with the greatest number of cases was 20–39 years, representing 41.8% (98,939) of all cases. Pregnant women represented 1,911 of all cases (0.8%) (Table 1). The annual parasite index (API; number of malaria cases divided by the population at risk) was higher in 2008 and decreased in 2012 (from 42.5 cases to 19.2 cases per 1,000 inhabitants, respectively). The northern region of the state also showed a reduction in the number of cases, from 19.6 cases to 18.2 cases per 1,000 inhabitants in 2008 and 2012, respectively (Figure 1). The average API in Rondônia during the study period was 30.9 cases per 1,000 inhabitants with a standard deviation of 9.2. All years under study were classified as being at medium risk according to the API.

The following municipalities in the State of Rondônia presented the highest API rates (cases per 1,000 inhabitants) in 2008–2012: Candeias de Jamari, 209.6; Rio Crespo, 176.7; Cujubim, 111.9; Machadinho d'Oeste, 94.1; and Itapuã do Oeste, 82.8 (Figure 2).

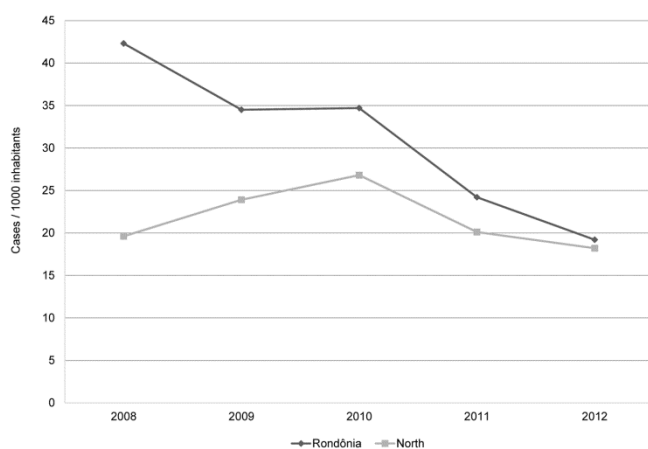
Agriculture was the most common activity performed in the 15 days prior to the diagnosis (62,856 cases; 26%), followed by domestic activity (32,879 cases; 13.7%). *Plasmodium vivax* was the malaria parasite usually found in Rondônia and was responsible for 213,713 (89.8%) of all reported cases. Conversely, malaria caused by *P. falciparum* was detected in 22,468 cases (9.4%) between 2008 and 2012. The parasitemia ranked in crossings showed 87,589 cases and 501–10,000 parasites per mm<sup>3</sup>, representing 36% of the recorded cases of parasitemia, which was most abundant in the State of Rondônia (Table 1). An average of 30.9% of all patients who underwent the malaria control test via the thick drop method presented parasitemia and were relapse/recrudescence cases (Table 2).

**Table 1.** Age group, main activity performed in the 15 days prior to the diagnosis, and parasite species in Rondônia, 2008–2012

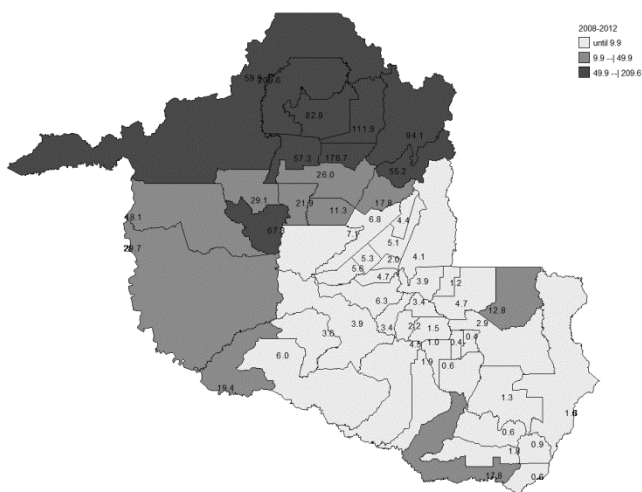
Variables	Number	Percentage
<b>Age group</b>		
0–9	30,015	12.6
10–19	50,597	21.3
20–39	98,939	41.8
40–59	50,076	21.0
≥ 60 or more	7,889	3.3
Ignored*	746	0.3
<b>Main activity in the 15 days prior to diagnosis</b>		
	<b>No.</b>	<b>%</b>
Agriculture	62,856	49.4
Domestic	32,870	25.8
Gold prospecting	10,133	7.9
Tourism	7,532	5.9
Hunting/fishing	3,348	2.7
Road construction	3,010	2.4
Other	7,552	5.9
Unknown*	57,121	44.8
<b>Type</b>		
<i>Plasmodium vivax</i>	213,713	89.8
<i>Plasmodium falciparum</i>	22,469	9.4
<i>P. vivax</i> + <i>P. falciparum</i>	1,683	0.7
<i>Plasmodium malariae</i>	34	0.01
Unknown*	398	0.1

\*Absence of data in the system due to improperly completed notification forms. Source: SINAN W and SINAN NET.

**Figure 1.** Annual parasite index (API) of cases per year of malaria in Rondônia and comparison with the northern region of Brazil, 2008–2012. Source: SINAN W and SINAN NET



**Figure 2.** Average annual parasite index (API) per 1,000 inhabitants in the municipalities of Rondônia province, 2008–2012. Source: SINAN W and SINAN NET



**Table 2.** Number of registered cases, number and percentage of patients who underwent the control exam, and parasite species responsible for recurring/re-emerging cases detected by performing the control exam in Rondônia, 2008–2012

Year	Number of registered cases	Control exam**		Recurring/re-emerging		<i>P. vivax</i>		<i>P. falciparum</i>		<i>P. vivax</i> + <i>P. falciparum</i>	
		N	%	N	%	N	%	N	%	N	%
2008	63,192	42,450	67.2	13,385	31.5	11,358	84.5	1,901	14.2	126	1.3
2009	51,936	33,763	65	10,569	31.3	9,215	87.2	1,297	12.3	57	0.5
2010	54,262	33,830	62.3	10,716	31.6	9,562	89.2	1,106	10.3	48	0.5
2011	38,208	11,653	30.5	3,386	29.1	3,147	92.4	225	6.6	14	1
2012	30,665	3,797	12.4	765	20.1	720	94.1	38	4.9	7	1
<b>Total</b>	<b>238,262</b>	<b>125,493</b>	<b>52.7*</b>	<b>38,821</b>	<b>30.9*</b>	<b>34,002</b>	<b>87.6*</b>	<b>4,567</b>	<b>11.8*</b>	<b>252</b>	<b>0.6*</b>

\*Percentage in relation to number.

\*\*Control exam for recurring cases performed through the thick drop test conducted at 30 and 60 days after diagnosis and the start of treatment.

Source: SINAN W and SINAN NET.

The Human Development Index (HDI) in Rondônia was 0.537 in 2000 and 0.690 in 2010 [15]. Between 2002 and 2010, an increase of 24.4% in formal employment indices was reported in metropolitan cities in Brazil [16]. Thus, according to DATASUS [17], the percentage of individuals in the State with low income was 53.9% in 2000 and 35.4% in 2010, a decrease of 34.4%. The deforestation index also decreased in the State of Rondônia, from 27,772 km<sup>2</sup>/year in 2004, to 7,646 km<sup>2</sup>/year in 2010 [18].

## Discussion

Malaria is one of the tropical diseases that most affect human health in the Amazon, lessening sufferers' ability to work and worsening their quality of life, which has a negative impact on the State of Rondônia and the Amazon region as a whole [7,19].

Factors contributing to the occurrence of malaria in the State of Rondônia include environmental changes caused by human activities that favor the proliferation of *Anopheles darlingi*, malaria's main vector [20,21]. Rodrigues *et al.* [14] studied the spatial distribution of malaria in Brazil between 1994 and 2005 and observed two significant time points in the evolution of the number of cases: the first from 1994 to 2000, in which a drastic reduction of 59.5% was observed; and the second from 2001 to 2005, in which an increase of 105.7% was observed. According to Barata *et al.* [22], the State of Rondônia presented an API of 128/1,000 inhabitants in 1990. According to Camargo *et al.* [23], an API of 292/1,000 inhabitants was observed in a riverside population in the State of Rondônia in 1998. In this study, the reduction in the numbers of malaria cases in 2008–2012 is evident (58%), which corroborates the results reported by Rodrigues *et al.* [14].

In addition, the reduction in the number of cases in Rondônia followed the pattern observed in the

northern region after 2010. The improvements in the financial and social conditions of the population of Rondônia that have occurred over the past 10 years might have influenced the disease outcomes; increased HDI, decreased numbers of low-income individuals, and increased incidence of formal employment [17] represent improvements in the population's quality of life and a reduced rate of exposure to infection risks. Moreover, reduced levels of deforestation [18], which led to a reduction in activities related to plant exploration, mining, and gold prospecting, represent decreased invasions into the mosquito's natural habitats and a subsequently reduced risk of exposure to malaria [24].

Our results showed that the municipalities in the northern region of the State have higher API rates than do other regions; the municipality of Candeias do Jamari in particular has the highest average API and has been described as an area of high endemicity in other studies [25,26]. The northern region of the State has the municipalities traversed by the Madeira River and its tributaries in addition to a large contingency of streams. The high rates of incidence in this region can be explained by the fact that these streams present favorable conditions for disease maintenance, where the inhabitants are asymptomatic carriers of the parasite [27-29].

According to data from the Health Surveillance Secretary [30], in the Legal Amazon Region, 70% of malaria cases are related to *P. vivax* infection, 29% to *P. falciparum*, and 1% to *Plasmodium malariae*. In Rondônia, the percentage of cases of infections with *P. falciparum* is lower, while that of *P. vivax* is slightly higher than that of the Amazon region as a whole; *P. vivax* infections account for 89.8% of the cases, *P. falciparum* for 9.4%, and *P. malariae* for 0.01%. According to Marques *et al.* [31], the prevalence of infection with *P. falciparum* in Rondônia was 59% in

1988, 34% in 1992, and 25% in 1996. Rodrigues *et al.* [14] indicated a tendency toward reduced numbers of cases of infection caused by *P. falciparum* throughout Brazil, which may be due to the introduction of halofantrine and artesunate in the treatment of malaria.

Couto *et al.* [32] noted that 71.7% of cases were found in men and 28.3% were found in women in a study of malaria in the State of São Paulo. Salcedo *et al.* [26] also noted a higher incidence of cases in the male population in a malaria study conducted on a farm in Rondônia in 1991–1996. We observed similar results, with 34.4% of the cases occurring in women and possibly correlated with domestic activities, which were reported in 25.8% of the cases in this study; this suggests that transmission may have occurred in these cases around or inside homes. Couto *et al.* [32] observed that the majority of cases occurred in the age range of 20–39 years; we observed similar results, as 63.1% of our patients were within this age group, which is also involved in more intense economic activity.

Marques *et al.* [33] observed that 75% of infected patients in their study performed some kind of leisure activity and that 25% worked. According to the study conducted by Gil *et al.* [34], malaria cases in the northern and northeastern regions of the State of Rondônia were mainly related to agro-industrial activities. In this study, the most common activity carried out in the recent months in Rondônia was agricultural in nature (49.4%). In addition, 0.8% of the patients were pregnant women. Despite this low percentage, pregnant women with malaria should be considered a high-risk group because the disease makes these women more susceptible to the severe forms of the disease [35], which can cause premature birth, low birth weight, anemia, and even abortion [36–39].

In Rondônia, patients with a confirmed diagnosis of malaria who are receiving treatment must undergo a control exam within 30 and 60 days after diagnosis [40]. The control exam is done through a thick smear stained with Giemsa, which is considered the gold standard test for the diagnosis of malaria [41,42]. In this study, only 52.7% of the patients underwent this exam within 30 and 60 days following diagnosis and the start of treatment, indicating a deficiency in case follow-up, which can result in re-infection. In 2008, 31.5% of patients who underwent the control exam within 30 and 60 days after diagnosis presented with relapse/recrudescence of the disease. In 2012, this number dropped to 20.1%, a decrease of 36.2% that can be explained by improvements in the care

provided to these patients and decreased non-adherence to treatment due to the use of primaquine for 7 rather than 14 days [43].

Regardless of the reduction in control exams within 30 and 60 days after diagnosis, the number of relapse/recrudescence cases decreased from 31.5% in 2008 to 20.1% in 2012. Despite this decrease over the past five years, this value remains high. The exact reasons for this high value are unknown; however, some considerations and hypotheses can be raised to explain that number. For example, certain therapeutic schemes might result in the prescription of inadequate doses and/or combinations according to patient weight [44,45]. According to Townell *et al.* [45], the effectiveness of the treatment against *P. vivax* can be impaired by an incorrect prescription of primaquine consisting of low doses and shorter treatment durations.

According to data from the Ministry of Health in 2013 [46], during the period of 2000–2011, a reduction of 78.3% in the number of malaria-related deaths was observed in the states of the Amazon region. Nevertheless, in states that do not belong to the Amazon region, a 37.5% increase in deaths was observed. This fact could be explained by the improved preparedness of healthcare professionals in the Amazon region because they are more familiar with the diagnosis of this disease, and therefore initiate early treatment.

This evaluation of malaria cases in 2008–2012 shows 58% fewer cases and 36.2% fewer relapse/recrudescence cases. These changes are associated with socioeconomic improvement in the population, decreased levels of deforestation in the State, and improved adherence to therapeutic schemes that include the use of primaquine reduced from 14 to 7 days. Despite this decrease, relapse/recrudescence cases must receive special attention from health professionals, because they may be related to treatment failure, including drug resistance, and because they represent reservoirs of the etiological agent, the protozoan, and sustain the disease transmission that is currently reflected in higher API values for *P. vivax* compared to *P. falciparum*. Regardless of the reduction in the number of cases, malaria remains a major endemic disease in the State of Rondônia.

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