

## ORIGINAL ARTICLE

**Clinical-epidemiological aspects of severe malaria in patients at the Municipal Hospital of Cuimba, Angola****Aspectos clínico-epidemiológicos en pacientes con malaria grave del Hospital Municipal de Cuimba, Angola****Aspectos clínico-epidemiológicos da malária grave em pacientes do Hospital Municipal do Cuimba, Angola**

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**Introduction:** Plasmodium falciparum is responsible for more than 90 % of malaria worldwide. **Objective:** characterization of Clinical-epidemiological aspects of severe malaria in patients treated at the Municipal Hospital of Cuimba, Zaire, Angola. **Method:** an observational, descriptive, cross-sectional and retrospective study was conducted, during the period January - June 2023, in patients reported with severe malaria. The study involved 452 patients with positive malaria but only 97 of them, who presented a complication of severe malaria, were selected, as sample. The variables used were as follow: severe anemia, convulsions, hyperparasitemia, among others. **Results:** male sex was predominant, with an average age of 14.8% and 43.3% of patients under five years of age. Plasmodium falciparum was found in 59 patients (60.8%) with high parasitaemia prevalence. Manifestations of cerebral dysfunction in association with severe

anemia were found in the clinical picture of 31% of patients. The 40.2% of patients had no complications in admission period. Acute Respiratory Distress Syndrome was the most frequent complication (18.6%), and it was the leading cause of death in 12.4% of patients. Artesunate was used in 77.3% of patients. **Conclusions:** malaria is a health problem in Municipal Hospital of Cuimba, with a higher incidence in children under five years of age; Plasmodium falciparum infection prevailed in patients with severe anemia.

**Keywords:** malaria; severe malaria; Plasmodium falciparum; malaria complicated

**RESUMEN**

**Introducción:** el *Plasmodium falciparum* es el causante de más del 90 % de los casos de malaria en el mundo. **Objetivo:** describir aspectos clínico-epidemiológicos de pacientes con malaria grave, atendidos en el Hospital Municipal de Cuimba, provincia de Zaire, República de Angola. **Método:** estudio observacional, descriptivo, de corte transversal y retrospectivo, durante el periodo comprendido entre enero-junio de 2023, en pacientes con diagnóstico de malaria grave. El universo fue conformado por 452 pacientes positivos de malaria, la muestra quedó conformada por 97 pacientes que desarrollaron malaria grave. Se estudiaron variables asociadas como: anemia severa, convulsiones, hiperparasitemia, entre otras. **Resultados:** la media de edad fue de 14,8 años, el 43,3 % menor de cinco años, con predominio del sexo masculino (53,9 %). El *Plasmodium falciparum* estuvo presente en 59 casos (60,8 %), con elevadas tasas de parasitemia. Las manifestaciones de disfunción cerebral en asociación con la anemia severa resultaron estar en el cuadro clínico del 31 % de los pacientes. El 40,2 % de los enfermos no presentó complicaciones en su estadía hospitalaria. El síndrome de dificultad respiratoria aguda(18,6 %) fue la complicación más frecuente que sobrellevó al fallecimiento del 12,4 % de los pacientes. El artesunato fue usado en 77,3 % de los pacientes. **Conclusiones:** el paludismo representa un problema de salud en el Hospital Municipal de Cuimba, con mayor frecuencia en los menores de cinco años. Prevalece la infección por *Plasmodium falciparum* en pacientes con anemia severa.

**Palabras clave:** malaria; paludismo; malaria grave; *Plasmodium falciparum*; malaria complicada

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**RESUMO**

**Introdução:** o *Plasmodium falciparum* é responsável por mais de 90 % da malária em todo o mundo. **Objetivo:** caracterização dos aspectos clínico-epidemiológicos da malária grave em pacientes atendidos no Hospital Municipal de Cuimba, Zaire, Angola. **Método:** foi realizado um estudo observacional, descritivo, transversal e retrospectivo, durante o período de janeiro a junho de 2023, em doentes notificados com malária grave. O estudo envolveu um total de 452 doentes com malária positiva, mas apenas 97 deles, que apresentavam uma complicação de malária grave, foram selecionados como amostra. As variáveis utilizadas foram as seguintes: anemia grave, convulsões, hiperparasitemia, entre outras. **Resultados:** o sexo masculino foi predominante, com uma idade média de 14,8 anos e 43,3 % dos doentes com menos de cinco anos de idade. O *Plasmodium falciparum* foi encontrado em 59 doentes (60,8 %) com uma elevada prevalência de parasitemia. Manifestações de disfunção cerebral em associação com anemia grave foram encontradas no quadro clínico de 31% dos doentes. Os 40,2 % dos doentes não tiveram complicações no período de admissão. A Síndrome de Angústia Respiratória Aguda foi a complicação mais frequente (18,6%) e foi a principal causa de morte em 12,4% dos doentes. O artesunato foi utilizado em 77,3% dos doentes. **Conclusões:** a malária é um problema de saúde em Hospital Municipal de Cuimba, com uma maior incidência em crianças com menos de cinco anos de idade; a infecção por *Plasmodium falciparum* prevaleceu em pacientes com anemia grave.

**Palavras-chave:** malária; paludismo; malária grave; *Plasmodium falciparum*; malária complicada



## INTRODUCTION

Malaria is an infectious disease characterized by acute febrile illness with high temperatures, transmitted by the bite of the female mosquito of the genus *Anopheles*, where in humans it can be caused by five of these protozoa: *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*, *Plasmodium knowlesi* and *Plasmodium falciparum*.<sup>(1)</sup>

*Plasmodium falciparum* causes more than 90% of malaria cases worldwide. More than half of the world's population is exposed in endemic areas.<sup>(2)</sup> The World Health Organization (WHO) described the incidence of malaria cases of 59 per 1 000 inhabitants in 2021; from a target of 31 cases per 1 000, for a deviation of 48 percent; the mortality rate was set at 14.8 per 100 000 population at risk, the WHO requested target of 7.8.<sup>(3)</sup>

At the global forefront in terms of the incidence of this scourge is the continent of Africa, with an estimated 247 million confirmed cases of malaria, with 95 % of confirmed cases and 96 % of deaths worldwide.<sup>(4)</sup>

At the World Health Assembly held in 2015, an unprecedented milestone was reached in relation to malaria control at the global level through resolution WHA68.2, the Global Technical Strategy (GTS) against Malaria/Malaria 2016 - 2030.<sup>(4)</sup>

This strategy projected very ambitious lines of work from the reduction of rates and incidence, interrupting transmission, developing preventive vaccine projects in at least half of the signatory countries with high levels of malaria transmission in a directional sense with the Sustainable Development Goals (SDGs). In addition to creating a professional technical framework from the improvement of informational data capabilities, professional development, and based on guidelines to link the governments of the signatory countries, to achieve a governmental combination with health care entities.<sup>(5)</sup>

From the regional point of view, the province of Zaire, located in the northwest of the Republic of Angola, with borders with the Democratic Republic of Congo and bathed by the waters of the Pacific Ocean. Zaire is characterized as a malaria hyperendemic area,<sup>(7)</sup> in this province is the municipality of Cuimba, where the authors undertook the task of conducting this study.

In the regional context in question, the Republic of Angola has a population of more than 25 million inhabitants, of whom slightly less than half are under fifteen years of age, with high rates of malaria transmission and it is the leading cause of death in the country. However, there are encouraging figures for the control, spread and reduction of cases caused by *Plasmodium falciparum*.<sup>(6)</sup>

Having exposed all the background related to the subject, without neglecting to mention the scarce presence of similar research. This research is taking up with the aim of describing the epidemiological clinical aspects present in patients with severe malaria, attended at the Municipal Hospital of Cuimba, province of Zaire, Republic of Angola, during the period January-June 2023.



## METHOD

Database on clinical-epidemiological aspects in 97 patients with severe malaria at the Municipal Hospital of Cuimba, Angola, from an observational, descriptive, cross-sectional and retrospective study conducted in the period January-June 2023.

The study universe consisted of 452 malaria-positive patients who attended the on-call department of the Cuimba Municipal Hospital. The sample consisted of 97 patients who developed severe malaria, where the selection criteria used were all cases that presented a clinical picture of malaria accompanied by signs and/or symptoms of severity such as severe anemia, convulsions, hyperparasitemia, hyperthermia, renal failure, changes in consciousness, among others, as described in detail in the variables.

### Selection criteria

Patients with positive results of thick blood drop and rapid test for Plasmodium who provided all the necessary data to compile the database were included.

All patients with negative results of the sample for Plasmodium, all pregnant women, and those patients who did not have the data available to prepare the database for the elaboration of the research, as well as those who did not present a serious clinical condition and/or complications, which would condition their diagnosis, were excluded.

### Variables

Sociodemographic variables: age groups, sex and origin

Clinical and laboratory variables: cell count and cell count distribution of parasitemia values, type of infecting Plasmodium, clinical and laboratory manifestations according to Plasmodium serotype, treatment applied and complications.

The variable of severe malaria was defined according to the Manual of Diagnosis and Treatment of Malaria in Angola.<sup>(8)</sup> All those clinical presentations in which the patient, in the presence of a positive malaria test or even in the absence of testing possibilities, present one or more of the following manifestations:

- a) Changes in the state of consciousness: the patient is not conscious (assess the degree of coma according to the Glasgow scale < 8 or Blantyre < 3), or malaria with coma persisting for more than 30 minutes after a seizure.
- b) Manifestations of cerebral dysfunction (psychomotor agitation, delirium, incoherent speech, confusion, behavioral disturbance, stupor), multiple seizures (more than two episodes in 24 hours)
- c) Severe anemia (hematocrit < 15 % or Hb<5 g/dL)



- d) Hyperparasitemia ( $> 100000$  parasites/ $\mu\text{l}$  or more than 2.5 % of parasitized red blood cells in non-immune individuals) Hyperthermia ( $T > 41^\circ\text{C}$ ) Hypoglycemia ( $< 2.2 \text{ mmol/lo} < 40 \text{ mg/dl}$ ); hyperinsulinism, attention to pregnant women and children)
- e) Cold malaria (arterial hypotension, severe dehydration, septic shock)
- f) Acute respiratory distress syndrome/pulmonary edema (ARDS): radiologically confirmed or oxygen saturation  $< 92\%$  with  $\text{RF} > 30$  (crackling fevers on auscultation).
- g) Metabolic acidosis: base deficit  $> 8 \text{ mEq/L}$ , plasma bicarbonate concentration  $< 15 \text{ mmol/L}$ , venous lactate  $> 5 \text{ mmol/L}$
- h) Hyponatremia ( $< 136 \text{ mEq/L}$ )
- i) Renal failure: serum to plasma creatinine  $> 3 \text{ mg/dl}$  or urea  $> 20 \text{ mmol/L}$ . CIVD (coagulation disorders and major bleeding, including nosebleeds) recurrent or at venipuncture sites, hematemesis or melena)
- j) Hepatic dysfunction (jaundice)
- k) Hemoglobinuria
- l) Shock: systolic pressure  $< 70 \text{ mmHg}$  in children or  $< 80 \text{ mmHg}$  in adults with poor peripheral perfusion (cold extremities)<sup>(8)</sup>

The source of information used was secondary, the clinical histories and data from the registry book of the patients attended in the Pediatrics and Internal Medicine on-call departments. Subsequently, an Excel database with the study variables was created, and it was exported to the SPSS program; version 20.0, for information processing.

The results of the univariate analysis for the qualitative variables were expressed in absolute and relative frequencies (%) and the quantitative variables by measures of central tendency (mean, median, standard deviation).

The Scientific Direction of the Cuimba Municipal Hospital authorized the study, and the parents/protectors of the children signed the informed consent for the interview and collection of blood samples. The data were collected anonymously; the researcher team treated confidentially, under compliance with the Declaration of Helsinki and the Standards of Good Clinical Practice.

## RESULTS

Table 1 shows the sociodemographic statistics studied, where the researchers found that 43.3% (n=42) of the total number of cases in the sample were under 5 years of age; consequently, the mean age was 14.8 years, with a standard deviation of 19.4 years. The most affected sex was male with 53 (54.6%) cases of the total, 55.7% (n=54) coming from urbanized areas of the municipality.



**Table 1: Distribution of sociodemographic variables**

General characteristics	Values			
	No.	%	Media	Standard deviation
<b>Age groups</b>				
≤ 5 years old	42	43,3		
6 - 14 years	29	29,9	14,8	19,4
15 - 29 years	5	5,2		
30 - 49 years old	9	9,3		
≥ 50 years	12	12,3		
Total	97	100,0	6	
<b>Sex</b>				
Male	53	54,6		
Female	44	45,4		
Total	97	100,0		
<b>Origin</b>				
Urban	54	55,7		
Rural	43	44,3		
Total	97	100,0		

Source: medical records

According to the representation in Graph 1, the age groups studied is related with the Plasmodium protozoa found; the highest frequency was Plasmodium falciparum, with an incidence of 59 cases in the pediatric age group, coexisting with Plasmodium vivax, with a higher incidence in the 6 to 14 age group.

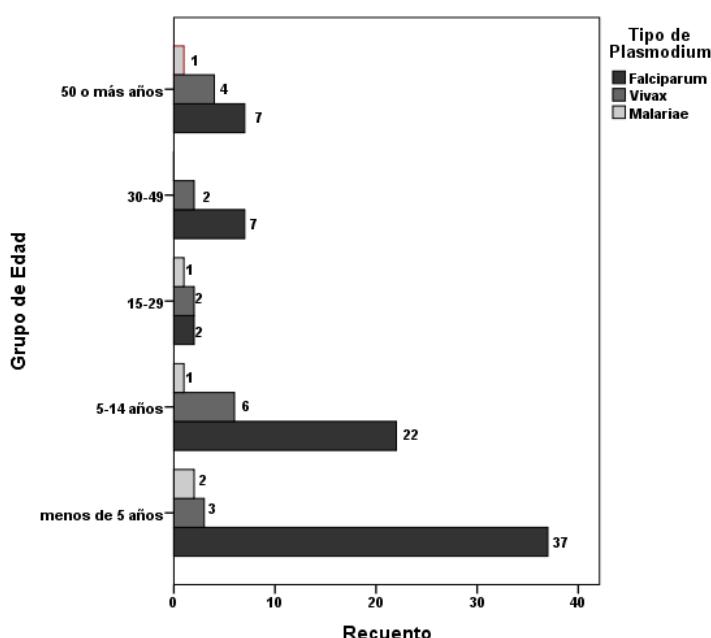
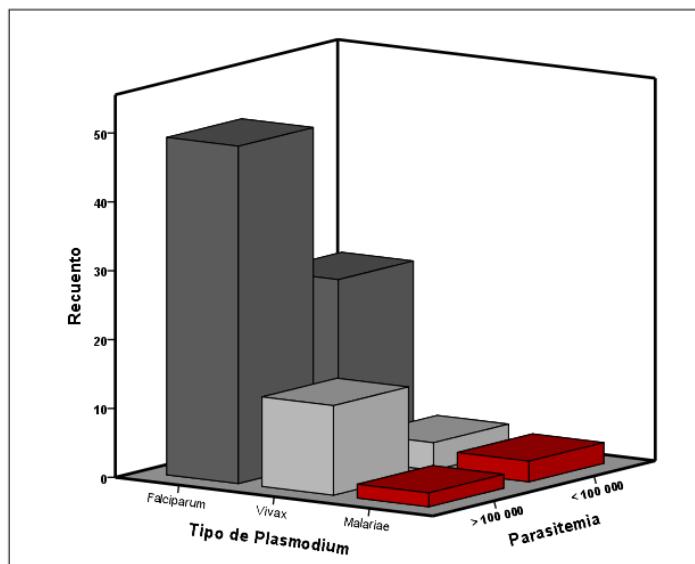
**Graph 1** Distribution of age groups with Plasmodium serotypes

Figure 2 represents the parasitemia values according to Plasmodium serotype; Plasmodium falciparum was present in more than 50 cases, with high parasitemia rates of more than 100,000 parasites per mm<sup>3</sup> in blood, in the thick drop laminar count.



**Graph 2** Cell count and cell count distribution of parasitemia values and Plasmodium type

Table 2 shows how the clinical manifestations are present with the different types of Plasmodium. The manifestations of cerebral dysfunction were the most common at hospitalization 25.8%, severe anemia, and hyperparasitemia 5.2% were manifested in Plasmodium vivax positive samples and in Plasmodium malariae samples severe anemia was in 2.1%.

**Table 2:** Distribution of clinical and laboratory manifestations according to Plasmodium serotype

Clinical manifestations	Laboratory data	Plasmodium type			Total
		Falciparum	Vivax	Malariae	
Alterations in the state of consciousness	Count	13,0	2,0	0	15,0
	% of total	13,4	2,1	0	15,5
Manifestations of brain dysfunction	Count	21,0	2,0	2	25,0
	% of total	21,6	2,1	2,1	25,8
Multiple seizures	Count	7,0	0	0	7,0
	% of total	7,2	0	0	7,2
Severe anemia	Count	13,0	5,0	2	20,0
	% of total	13,4	5,2	2,1	20,6
Hyperparasitemia	Count	11,0	5,0	0	16,0
	% of total	11,3	5,2	0	16,5
Hyperthermia	Count	2,0	0	1	3,0
	% of total	2,1	0	1,0	3,1
Hypoglycemia	Count	7,0	1,0	0	8,0
	% of total	7,2	1,0	0,0	8,2
Hepatic dysfunction (jaundice)	Count	1,0	2,0	0	3,0
	% of total	1,0	2,1	0	3,1

Source: medical records



Table 3 shows the distribution of patients according to the treatment used. It is worth noting that 40.2% did not present complications during their hospital stay, ARDS (18.6%) and cerebral malaria (17.5%) were the most frequent complications that led to the death of 12.4% of the study sample. The most commonly used antimalarial drug was artesunate in 75 (77.3 %) patients.

**Table 3:** Distribution according to treatment and complications

Complications	Lab data	Medications		
		Artesunate	Artemether	Quinine
ARDS	Count	13	4	1
	% of total	13,4	4,1	1,0
Cerebral malaria	Count	13	4	0
	% of total	13,4	4,1	0
Death	Count	10	1	1
	% of total	10,3	1,0	1,0
Liver and/or splenic damage	Count	6	1	0
	% of total	6,2	1,0	0
Renal damage	Count	4	0	0
	% of total	4,1	0	0
None	Count	29	7	3
	% of total	29,9	7,2	3,1

Source: medical records

## DISCUSSION

Malaria is a significant public health problem worldwide; there are alarming figures issued in the latest World Malaria Report 2022,<sup>(5)</sup> in the biennium 2020 - 2021 diagnosed cases of malaria were on the rise, with figures of 247 million cases.

During the years of the COVID-19 confrontation, health services in countries with high malaria incidence rates maintained control of the disease despite major economic upheavals. Nevertheless, the WHO African Region continues to have the highest malaria burden worldwide, with 95% (243 million) of the world's reported cases and 96% (593,000) of the world's deaths from malaria.<sup>(5)</sup>

Angola is one of the countries where malaria is endemic in all its provinces, with incidence rates of 254 cases/1000 population.<sup>(5)</sup>

Despite the progress achieved in recent years in the control and eradication of malaria, it is still the main cause of morbidity and mortality that mainly affects children under five years of age and pregnant women.<sup>(5)</sup> The present research found similar data according to the age group described in the malaria studies conducted in the years 2019 - 2020.



Acosta Torres JR,<sup>(1)</sup> conducted a cross-sectional clinical epidemiological study that included 3410 patients under 15 years of age, attended in the emergency department of the Provincial Hospital of Cabinda where the age group most at risk was children under five years of age, similar figures are expressed in this research.

Regionally, neighboring countries report interesting data, such is the case of the study by Kamalanga HC,et al.<sup>(9)</sup>. In their characterization of malaria cases in children under 15 years of age in 2018 at the Regional Hospital of Cela, Tete province/Moatize district in Mozambique which describes the lethality present in their sample which was 8, 12%, with no differences by sex and higher in children aged 0 - 4 years. These results coincide in relation to the most affected age group in the research conducted.

According to the Annual Report<sup>(10)</sup> of the Regional Director on WHO activities in the African region, the Angolan population is very young, 48% of the population is under 15 years of age, a demographic characteristic, and several studies<sup>(1,2,7,11)</sup> did not find strong associations with respect to sex. In this study, it is demonstrated that the affection in dependence of sex is variable but the patients are between one and five years of age and its incidence could be determined by several factors, environmental as well as demographic, which coincides with the information of several authors.<sup>(5-15)</sup>

As mentioned in the World Malaria Report 2022<sup>(5)</sup> 99.7% of malaria cases reported in the African Region of the WHO are caused by Plasmodium falciparum. It is also responsible for 50% of cases in South-East Asia and 71% of cases in the Eastern Mediterranean is the predominant agent in the present study and is consistent with the results of similar studies.<sup>(1,7,9,11,12,13)</sup>

The above-mentioned report warns about the spread of a mosquito species adapted to cities in Africa:<sup>(5)</sup> Anopheles Stephen that can transmit both Plasmodium falciparum and Plasmodium vivax parasites, which poses an added challenge to disease control efforts in Africa. This species can thrive in urban environments and is resistant to many of the insecticides used in public health.<sup>(5)</sup>

In the region under study in this study, there is no report on this species by the epidemiological surveillance entities in the province of Zaire, but it should be noted that there are already relevant alerts in the entire health network for its detection.

Cassy A. et al.<sup>(13)</sup> and Motombo, et al.<sup>(14)</sup> described in their studies in Mozambique and in the Democratic Republic of Congo, respectively, a combination of the most frequent symptoms and signs in patients with malaria showing the presence of fever/seizures/paleness, fever/hepatitis splenomegaly asthenia and fever/depression of consciousness/abdominal pain. These associations represent the highest risks for carrying a plasmodium infection, which should be taken into account to differentiate this diagnosis from other diseases such as hemolytic anemia or typhoid fever, common in this region.



Hyperparasitemia in association with severe anemia (46.90%), are aggravating factors present in large percentages of their study samples, these increase mortality as a complication of severe malaria. This research also showed that the combination of symptoms and signs is varied and presents the same patterns found in the literature with figures similar to regional studies conducted in the Sub-Saharan African region.<sup>(12,13,16)</sup>

A study by Favier, et al.<sup>(15)</sup> showed that anemia (62.5%) and manifestations of cerebral dysfunction (52.1%) are inherent in each region, as the study population is located in a hyperendemic area of Angola, very similar results and without major differences are expressed in this research.

Menendez-Capote R, Suarez O<sup>(18)</sup> refer in their study to certain factors such as age, ethnicity and parasite count can predict the possibility of a serious event. The immune status of patients and the species of parasite, as it is known that severe malaria is more frequently due to Plasmodium falciparum, but also Plasmodium vivax Plasmodium knowlesi produce severe and lethal forms. We were able to corroborate in this research that the cases with high levels of parasitemia present higher probabilities of complications that could be life threatening, hence the importance of the immediacy in the beginning of the antimalarial treatment according to the established protocol.

All patients were treated according to the protocol established by the Manual of diagnosis and treatment of Malaria in Angola, used at all levels of the Angolan National Health System<sup>(8)</sup> for the radical curative treatment of malaria with the use of antimalarial therapies with artemisinin derivatives (Artesunate/Artemether/ Dihydroartemisinin). These therapies have proved to be the most effective, the therapeutic response was excellent with the negativization of the thick drop, and they have reduced deaths and other complications in important numbers and have managed to delay the appearance of resistance by Plasmodium falciparum.

It is worth noting that many relapses are experienced repeatedly, and that this aspect deserves particular investigation since many studies<sup>(17,18)</sup> reflect its importance in avoiding severe and complicated forms of malaria.

## CONCLUSIONS

Malaria represents a health problem in the Municipal Hospital of Cuimba, with greater frequency in children under five years of age; Plasmodium falciparum infection prevailed in patients with severe anemia.



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The authors declare that there are no conflicts of interest.

**Author contributions:**

Marelys Ramírez Rabí: conceptualization, data curation, formal analysis, research, methodology, supervision, writing-original draft, writing revising and editing  
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 Ernesto Fernández Carrillo: data curation, formal analysis, research, methodology, writing-revision and editing  
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