

# Effect of Social and Clinical Conditions on Blood Pressure Variation in Angolans Hospitalized with Malaria

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## Abstract

**Introduction:** Malaria is the leading cause of death in Angola, followed by road accidents, and represents about 20% of hospitalizations in health facilities and about 35% of the demand for curative care. The objective of this study was to assess the effect of social and clinical conditions on the variation of blood pressure in hospitalized Angolans with malaria. **Materials and Methods:** The study was conducted as a cross sectional and quantitative approach. **Results:** Of the 333 patients followed, 28% of the patients were normotensive, 50% with moderate hypertension (HTN.1) and 20% with severe hypertension, in the first 48 hours of hospitalization. These data changed after 4 days, where in the last 48 hours before the end of the study, 33% of patients were normotensive, 56% were moderate hypertensive (HTN.2) and 11% were severe hypertensive and the average age of the patients was 27 years old (standard deviation = 9) and the female/male ratio was 153/180, mostly from urban areas in Luanda (76%) and moderate and severe hypertension was more frequent in students, unemployed and business people (72%). In the first 48 hours, the number of patients with low parasitemia was 42%, with moderate and high parasitemia was 58%. In the last 48 hours before the end of the study, patients with moderate and high parasitemia accounted for only 11% and patients with low parasitemia accounted for 89%, where patients treated with artemether were 90% of the study population and showed significant changes in pressure levels when compared with patients treated with artesunate (10%), the mortality rate was 6%, a large group of them remained hospitalized (63%) and 31% were discharged. **Conclusion:** In general, many patients with malaria had high blood pressure during hospital admission, and throughout the hospitalization period, in some cases, there was a significant reduction depending on social conditions, parasitemics, and medical and medication treatment.

**Keywords:** Angolan with malaria, blood pressure, social and clinical condition

## INTRODUCTION

Every year, the global number of new cases of malaria exceeds 200 million, with a child dying from this treatable disease every 2 min. More than 90% of the 400,000 annual deaths from malaria occur in Sub-Saharan Africa, where there are 10 African countries with an “urgent need for action” against malaria, including Nigeria, Democratic Republic of Congo, Uganda, Cote d’Ivoire, Mozambique, Niger, Burkina Faso, Mali, Tanzania and Angola, which together account for 67% of the world’s cases of malaria and 62% of deaths. The African continent represents 93% of global cases of the disease and 94% of global deaths from malaria.<sup>[1]</sup> Malaria is the leading cause of death in Angola, followed by road

accidents, and represents about 20% of hospitalizations in health facilities and about 35% of the demand for curative care. In 2018, Angola recorded 5.9 million cases of malaria and the mortality rate was around 40,000 more victims of the disease.<sup>[2]</sup>

Previous studies carried out in public hospitals in Angola show that malaria continues to cause death to many Angolans, the last of these studies, developed by our research team includes

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86 patients with malaria and showed that acute kidney injury (AKI) is a complication common in patients with malaria and may be associated with parasitemia levels, in addition to having a significant effect on the mortality and length of hospital stay of patients with malaria, especially in patients who have kidney damage in advanced stages; the moment has shown whether there is an effect of malaria on patients' blood pressure levels.<sup>[2,3]</sup> A study conducted in Cote d'Ivoire concluded that malaria parasitemia and hypertension (HTN) are prevalent comorbidities and apparently linked in African contexts, and this link may depend on the symptoms/latency of malaria parasitemia, where individuals with more latent/asymptomatic malaria parasitemia have a lower risk of HTN and those with more acute/symptomatic malaria parasitemia tend to increase blood pressure.<sup>[4]</sup>

Malaria is one of the many infectious diseases that have a high incidence in developing countries and appears to activate the inflammatory pathways, which are usually activated in other diseases and probably contribute to the burden of HTN through inflammation, which already happens with other diseases; There are studies that point out that the human leukocyte antigen (HLA), in particular the HLA - B and Class II alleles, are associated with the results of appearance in different different diseases in certain populations, among them the occurrence of *Plasmodium falciparum* malaria infection,<sup>[5,6]</sup> HIV infection, tuberculosis infection and others, which provides a new impetus for studies that provide substantial information for the control of these infections.<sup>[6]</sup> For the time being, most treatments of infectious diseases seek to eliminate that of the parasite and do not take into account the inflammatory responses, resulting from the adverse vascular consequences that are subsequently produced and the elucidation of these inflammatory pathways and their consequences that would open the way for adjuvant therapy trials.<sup>[6]</sup>

Some studies have shown that malaria is also associated with hypertensive disorders of pregnancy, such as gestational HTN and preeclampsia in young pregnant women and low birth weight, which have an effect on the higher incidence of HTN in adulthood. This was clearly demonstrated in a study conducted in Nigeria, where babies of mothers who suffered malaria during pregnancy had a higher incidence of increased blood pressure levels during the 1<sup>st</sup> year of life compared to other children.<sup>[7-9]</sup>

Some studies show that malaria is a disease that can cause a process of chronic inflammation and predisposes patients to cardiovascular disease in high-income countries, including a prospective study on 20,525 women health professionals in the USA, demonstrating that there was a linear relationship between baseline levels of reactive protein C and incidence of HTN.<sup>[10-12]</sup> There seems to be a relationship between inflammatory conditions and hypertension, especially in relation to levels of endothelial growth factors and levels of angiotensin-2 (Ang-2) which is a specific signaling ligand of vascular tyrosine kinase secreted by endothelial cells and

some cells smooth muscle, an essential condition for the development and stability of blood vessels, some studies that found that in children with severe malaria, the inflammatory and angiogenic states (Ang-2) were elevated.<sup>[13-16]</sup>

Some studies seek to demonstrate that the high prevalence of HTN in low- and middle-income countries contributes to higher rates of mortality from cardiovascular diseases, especially Africans, and some attribute it to urbanization and westernization of lifestyle to explain the high prevalence of HTN in the African population.<sup>[17-19]</sup> So far, there are no studies that explain why the high rates of hypertension observed in African countries, not even why people of African ethnic origin are better known for having a higher risk of high blood pressure and cardiovascular disease compared to Caucasians. , although this, it is known that malaria continues to prevail in these countries and contributes significantly to the high mortality rates, there are still some studies that raise the hypothesis that there is a possible link between the degree of malaria parasitemia and hypertension.<sup>[20,21]</sup>

There is very little scientific evidence that shows the factors to what extent blood pressure levels vary in patients monitored during hospitalization for malaria and antimalarial treatment, as well as whether there are social and clinical factors that may favor the association between malaria and HTN. The present study sought to assess the social and clinical factors that may contribute to the increase or reduction in blood pressure levels in patients admitted for malaria from their hospital admission to the hospital outcome.

## METHODOLOGY

The study was conducted as a cross-sectional and quantitative approach. The study was approved by the Human Research Ethics Committee of the Higher Institute of Health Sciences (Official Letter No. 755/GD/ISCISA/UAN/2018) and authorized by the Clinician Direction of Hospital Josina Machel-Maria Pia in Luanda (Official Letter No. 260/DPC/HJM/2018). All patients who agreed to participate in the study had to sign the free and informed consent form after being informed about the nature and objectives of the study.

## Patient recruitment

The sample was composed of 333 of 410 patients admitted and hospitalized for malaria to the Hospital Josina Machel-Maria Pia between December 2018 and January 2020, where a 99% confidence index was maintained with a margin of error of around 3%. Only those patients who met the selection criteria and agreed to participate in the study were included in the study. Additional information was collected through an open and closed question questionnaire for patients aged 16–50 years, and only patients who were hospitalized for more than 4 days were included in the study. All patients over the age of 55 years and those with a history of hypertensive disease, diabetes, chronic kidney disease, cerebral malaria, or other chronic disease that can affect blood pressure levels were excluded from the study to avoid confusing bias in the data analysis.

## Diagnosis of malaria and blood pressure

The diagnosis of malaria was performed by Josina Machel Hospital professionals using rapid malaria antigen test (SD-Bipline Malaria AG Pf/PAN) and confirmed with the technique of direct visualization of the parasite by Giemsa-stained peripheral blood thickening.<sup>[22]</sup> Patients who presented parasitemia  $\leq 40$  p/mm<sup>2</sup> were classified as low parasitemia, patients who presented parasitemia between 41 and 800 p/mm<sup>2</sup> were classified as moderate parasitemia, and patients who presented parasitemia above 800 p/mm<sup>2</sup> were classified as high parasitemia.<sup>[3,23]</sup> For the clinical data presented in the article, the average blood pressure data for each patient were obtained using three devices used simultaneously in each measurement of blood pressure, i.e., an electronic wrist sphygmomanometer, a mechanical sphygmomanometer with the support of a stethoscope, and a sphygmomanometer coupled to the cardiac vital signs device, and the mean value of blood pressure for each day of evaluation was added to the values of the three devices and the three daily evaluations. The mean blood pressure values that were presented in the results were obtained by adding the blood pressure values of the three daily assessments of the first 2 days (48 h) of hospitalization compared to the average values of blood pressure of the last 2 days of hospitalization; only patients who were hospitalized for more than 4 days were included in the study. Depending on blood pressure levels, patients were classified as having normal or normotensive blood pressure, when blood pressure values did not exceed the normal borderline pressure levels (normotensive: when systolic pressure is  $< 140$  mmHg and diastolic pressure  $< 90$  mmHg), Stages 1 and 2 or moderate HTN (moderate HTN: when the systolic pressure is between 140 and 179 mmHg and diastolic between 90 and 99 mmHg), hypertensive crisis or severe HTN (severe HTN: when the systolic pressure is above 179 mmHg and diastolic above 99 mmHg).<sup>[24]</sup>

## Statistical analysis

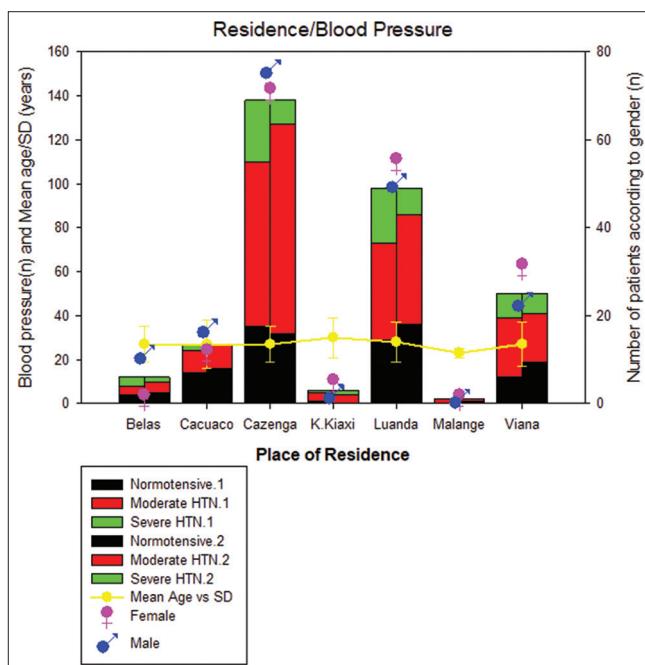
All descriptive statistic information, data, and clinical outcome data were entered into an SPSS V20 Database Statistical Program (IBM SPSS Statistics, USA Armonk, New York United States.) and analyzed for presentation of the study results, tables and graphs were prepared using the statistical program SigmaPlot 12 (SYSTAT Software, Inc. Systat Software Inc. (SSI), San Jose, California, United States of America).

## RESULTS

The general data of the study [Table 1] showed that in the first 48 h of admission, of the 333 patients followed in the present study, the normotensive ( $\leq 139/\leq 90$  mmHg) represented about 28% (95/33), patients with HTN Stages 1 and 2 or moderate HTN.1 (140–179/90–99 mmHg) represented about 50% (166/333), and patients with hypertensive crisis or severe HTN.1 ( $\geq 180/\geq 100$  mmHg) represented about 22% (72/333); these data changed in the last 48 h before the

end of the study where normotensive individuals accounted for approximately 33% (109/333), patients with HTN in Stages 1 and 2 or moderate HTN.2 accounted for 56% (188/333), and patients with hypertensive crisis or severe HTN.2 accounted for approximately 11% (36/333) of the entire studied population. The average age of the general population was 27 years (standard deviation [SD] = 9) and the ratio between female/male was 153/180. These data also demonstrated that on the 1<sup>st</sup> day, all groups of patients distributed by age group had parasitemia above 800 plasmodium/mm<sup>2</sup>, which means that they had high parasitemia at hospital admission where the average parasitemia of all patients was around 1450 p/mm<sup>2</sup>; these results were altered at the end of the study as no group of patients by age group had high parasitemia, and the overall average parasitemia was 150 p/mm<sup>2</sup>.

The pressure condition of the patients, according to the place of residence [Figure 1], was found that the majority of patients came from the municipality of Cazenga, representing about 41% (138/333), and in this group of patients, in the first 48 h of follow-up, about 54% (75/138) of the patients had moderate HTN.1 or HTN in Stages 1 and 2 and about 20% (28/138) of them presented with hypertensive crisis or severe HTN.1, while these data changed in 48 h before the end of the study, where patients with HTN in Stages 1 and 2 or moderate HTN.2 accounted for approximately 69% (95/138) and with hypertensive crisis or severe HTN.2 accounted for approximately 8% (11/138), where the average age was



**Figure 1:** Place of residence and blood pressure. (Belas): The data presented in the graph were described according to the reference of the patients, according to the locality in which they lived, which may be neighborhoods, towns and communes and others that were later organized according to the municipalities of the Luanda province (Belas, Cacuaco, Cazenga, Kilamba Kiasi, Luanda and Viana), which is the capital of the country and other provinces of Angola (Malanje)

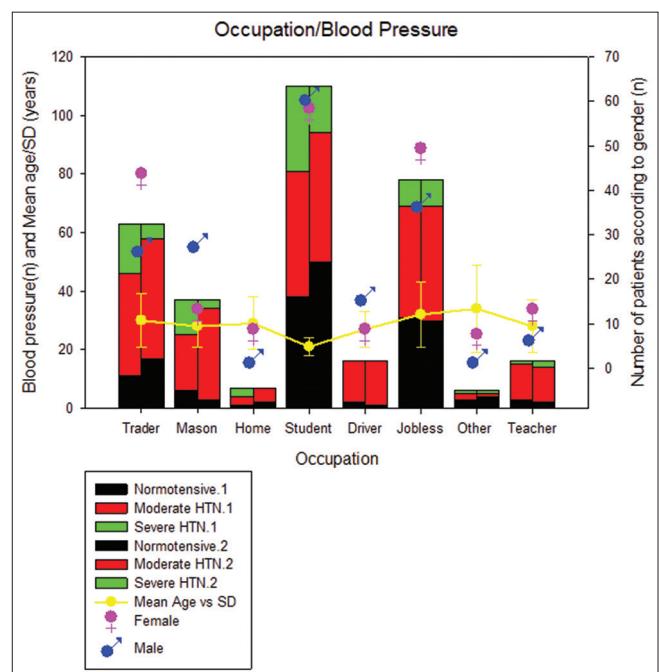
**Table 1: General patient data grouped by age group**

Age groups	Blood pressure classification 48 h after admission, n			Sub-total, n	Blood pressure classification 48 h before the end of the study, n			Sub-total, n	Gender, female/male, n	Average age, mean (SD)
	Normotensive 1	Moderate HTN 1	Severe HTN 1		Normotensive 2	Moderate HTN 2	Severe HTN 2			
	≤139/≤89	≤179/≤99	≥180/≥100		≤139/≤89	≤179/≤99	≥180/≥100			
Mean of BP	112/66	145/94	196/134		113/68	141/90	184/122			
15-20	1	3	-	4	4	-	-	4	2/2	14 (1.5)
21-25	26	22	12	60	31	23	6	60	21/39	19 (0.9)
26-30	23	51	36	110	26	64	20	110	61/49	23 (1.5)
31-35	22	43	8	73	14	55	4	73	35/38	27 (1.3)
36-40	9	15	10	34	12	20	2	34	13/21	34 (1.5)
41-45	5	22	3	30	11	18	1	30	10/20	37 (1.2)
46-50	9	10	3	22	11	8	3	22	11/11	49 (1.6)
Total	95	166	72	333	109	188	36	333	153/180	27 (9)

BP: Blood pressure, HTN: Hypertension, SP/DP: Systolic pressure/diastolic pressure, SD: Standard deviation, P/mm<sup>2</sup>: Parasitemia by mm<sup>2</sup>

27 years (SD = 8) and the female/male ratio was 62/76. Patients from the Luanda municipality, representing about 29% (98/333) of the patients studied, and in this group of patients, during the first 48 h of follow-up, about 45% (44/98) of the patients were with moderate HTN.1 or in HTN in Stages 1 and 2 and about 26% (25/98) of them presented with hypertensive crisis or severe HTN.1, while these data changed in the 48 h before the end of the study, where patients with HTN Stages 1 and 2 or moderate HTN.2 represented about 51% (50/98) and with hypertensive crisis or severe HTN.2 represented about 12% (12/98), where the average age was 28 years (SD = 9) and the female/male ratio was 48/50. Patients from the municipality of Viana represented about 15% (50/333) of the studied patients, and in the first 48 h of follow-up, about 57% (27/50) of them were in moderate HTN.1 or HTN in Stages 1 and 2 and about 21% (11/50) of them presented with hypertensive crisis or severe HTN.1, while these data changed in the 48 h before the end of the study, where patients with HTN in Stages 1 and 2 or moderate HTN.2 represented about 44% (22/50) and with hypertensive crisis or severe HTN.2 accounted for about 18% (9/50), where the average age was 27 years old (SD = 10) and the female/male ratio was 27/23.

When assessing the occupancy of the studied patients [Figure 2], the data showed that the majority of the studied population was students who represented about 33% (110/333), and in this group of patients, the average blood pressure values in the 48 h after hospital admission showed that about 39% (43/110) presented with HTN Stages 1 and 2 or moderate HTN.1 and 26% (29/110) presented with hypertensive crisis or severe HTN.1, while these data changed in the 48 h before the end of the study, where the mean blood pressure showed that the number of patients with HTN in Stages 1 and 2 or moderate HTN.2 increased to about 40% (44/110) and that of hypertensive crisis or severe HTN.2 decreased to about 14% (16/110), where the average age was 21 years old (SD = 3) and the female/male ratio was 49/61. The



**Figure 2:** Occupation with blood pressure. (Trader): those who sell products on the street. (Mason): they worked in different areas of civil construction. (Home): they worked as housekeepers or domestic servants. (Student): they were just students and did not perform any other remunerative activity. (Driver): they worked as a driver in private or public cars. (Jobless): they did not perform any remunerative activity and were unemployed. (Other): they performed several other remunerative activities on their own. (Teacher): they were teachers and taught in public or private schools

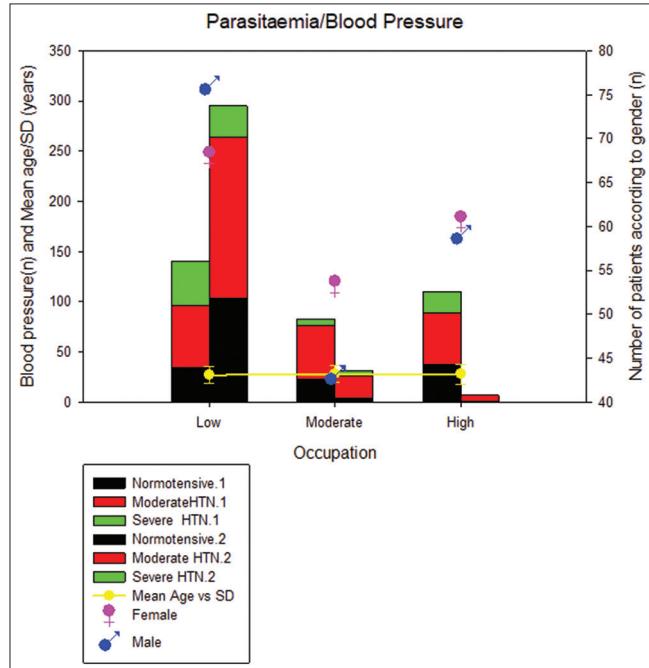
unemployed were the second largest group of patients with malaria, representing 23% (78/333) of the population studied, in the first 48 hours, 49% (38/78) of them were hypertension in stages 1 and 2 or moderate HTN.1 and about 11% (9/78) of them had hypertensive crisis or severe HTN.1, while these data changed until the 48 h before the end of the study where HTN in Stage 1 and 2 or moderate HTN.2 patients represented

50% (39/78) and patients with hypertensive crisis or severe HTN.2 remained at about 11% (9/78), where the average age was 33 years (SD = 11) and the female/male ratio was 41/37. Traders formed the third largest group of patients studied, representing 19% (63/333) of the studied population, of which about 56% (35/63) had HTN in Stage 1 and 2 or moderate HTN.1 and about 30% (17/63) had hypertensive crisis or severe HTN.1, while these data changed in the 48 h before the end of the study where patients with HTN in Stages 1 and 2 or moderate HTN.2 represented about 65% (51/63) and with hypertensive crisis or severe HTN.2 represented about 8% (5/63), where the average age was 30 years (SD = 9) and the female/male ratio was 36/27.

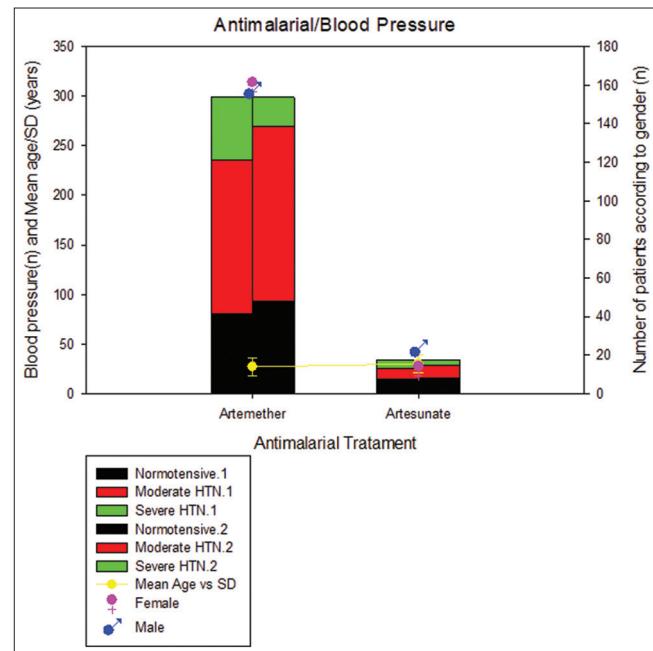
When assessing how the degree of parasitemia affected the pressure condition of the patients [Figure 3], it was observed that in the first 48 h, most patients with low parasitemia ( $\leq 40$  p/mm $^3$ ) represented about 42% (140/333) of all patients studied, where the average age was 27 years (SD = 8) and the female/male ratio was 62/76, while in this follow-up group, about 44% (62/140) of them were with moderate HTN.1 or HTN in Stages 1 and 2 and about 31% (44/140) of them had hypertensive crisis or severe HTN.1; however, these data changed in the 48 h before the end of the study, where patients with low parasitemia already accounted for approximately 89% (295/333) of all patients studied, and in this group, patients with HTN in Stages 1 and 2 or moderate HTN.2 represented about 54% (160/295) and with hypertensive crisis or severe HTN.2 represented about 10% (31/295). Patients with moderate parasitemia ( $\geq 41$ –800 p/mm $^3$ )

represented about 25% (83/333) of the studied patients, where the average age was 28 years (SD = 8) and the female/male ratio was 40/43 and in this group patients, about 64% (53/83) of them were with moderate HTN.1 or HTN in Stages 1 and 2 and about 8% (7/83) of them had hypertensive crisis or severe HTN.1; however, these data changed in the 48 h before the end of the study, where patients with moderate parasitemia represented only about 9% (31/333) of all patients studied and patients in this group with HTN in Stages 1 and 2 or moderate HTN.2 passed represented about 71% (22/31) and with hypertensive crisis or severe HTN.2 represented about 16% (5/31). In the first 48 h, patients with high parasitemia ( $\geq 801$  p/mm $^3$ ) represented about 33% (110/333) of the patients studied, where the average age was 28 years (SD = 10) and the female/male ratio was 52/58, and of these, about 46% (51/110) were with moderate HTN.1 or HTN in Stages 1 and 2 and about 19% (21/110) presented with hypertensive crisis or severe HTN.1; however, these data changed in the 48 h before the end of the study, where patients with high parasitemia represented only about 2% (7/333) of all patients followed and patients with HTN in Stages 1 and 2 or moderate HTN.2 passed represented around 87% (6/7) and without any cases of hypertensive crisis or severe HTN.2.

When it was assessed how antimalarial treatment affected the pressure condition of patients [Figure 4], it was found that most patients were treated with artemether, since about 90% (299/333) of the studied patients were treated with this drug, among these patients, in the first 48 hours, about 52% (156/299) had moderate HTN.1 or hypertension in phases 1 and



**Figure 3:** Parasitaemia and blood pressure. (Low parasitaemia): patients hospitalized for  $<24$  h and who presented parasitaemia lower than 41 p/mm $^3$ . (Moderate parasitaemia): Patients hospitalized for  $<24$  h who had parasitaemia  $>40$  p/mm $^3$  and  $\leq 800$  p/mm $^3$ . (High parasitaemia): Patients hospitalized for  $<24$  h and who presented parasitaemia  $>800$  p/mm $^3$



**Figure 4:** Antimalarial treatment and blood pressure. (Artemether): Patients who were hospitalized for more than 4 days and underwent anti-malarial treatment solely and exclusively with artemether. (Artesunate): patients who were hospitalized for more than 4 days and underwent anti-malarial treatment solely and exclusively with artemether

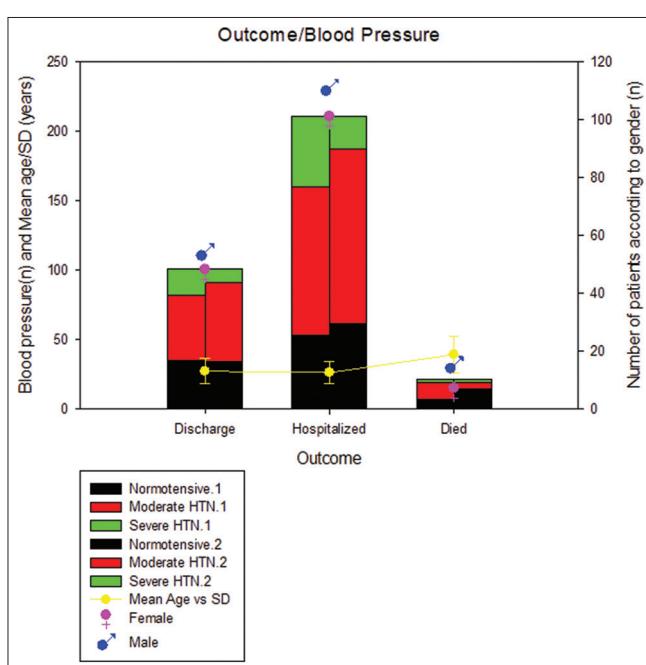
2 and about 21% (44/140) had a hypertensive crisis or severe HTN.1, these data changed in the 48 h before the end of the study, where patients with HTN Stages 1 and 2 or moderate HTN.2 accounted for approximately 59% (176/299) and hypertensive crisis or severe HTN.2 accounted for only about 10% (142/299), where the average age was 29 years (SD = 9) and the female/male ratio was 142/157. Only a small group of patients studied were treated with artesunate, representing about 10% (34/333) of the patients followed, and in this group of patients in the first 48 h of follow-up, about 29% (29/10) of them were with moderate HTN.1 or HTN in Stages 1 and 2 and about 26% (9/34) of them presented with hypertensive crisis or severe HTN.1, while these data changed slightly in the 48 h before the end of the study, where patients with HTN in Stages 1 and 2 or moderate HTN.2 accounted for about 35% (12/34) and hypertensive crisis or severe HTN.2 accounted for about 18% (6/34), where the average age was 30 years (SD = 9) and the female/male ratio was 11/23.

When we verified how the degree of parasitemia affected the patients' outcomes [Figure 5], it was found that about 30% (101/333) were discharged from the hospital, this group of patients in the first 48 h of entry was represented by about 35% (35/101) of patients who were normotensive. 1, about 47% (47/101) of patients with moderate HTN.1 or HTN in Stages 1 and 2, and about 19% (19/101) of patients with hypertensive crisis or severe HTN.1, whereas these data changed in the 48 h before the end of the study, a period in which normotensive. 2 patients accounted for approximately

34% (34/101), patients with HTN in Stages 1 and 2 or moderate HTN.2 accounted for approximately 57% (57/101), and patients with hypertensive crisis or severe HTN.2 accounted for about 10% (10/101), where the average age was 27 years (SD = 9) and the female/male ratio was 47/54, with an average blood pressure of 112/66 mmHg. Patients who remained in the hospital represented about 63% (211/333) of the patients studied, and in this group, patients in the first 48 h of follow-up, about 25% (53/211) of them were normotensive. 1, about 51% (107/211) presented with moderate HTN.1 or HTN Stages 1 and 2, and about 24% (51/211) of them presented with hypertensive crisis or severe HTN.1, whereas these data changed in the 48 h before the end of the study, i.e., normotensive. 1 patients represented about 29% (61/211), patients with HTN in Stages 1 and 2 or moderate HTN.2 represented about 60% (126/211), and patients with hypertensive crisis or severe HTN.2 represented about 11% (24/211), where the average age was 26 years (SD = 8) and the female/male ratio was 100/111, with an average blood pressure of 145/94 mmHg. Patients who died caused about 6% (12/333) of the studied patients, and in the first 48 h after admission, about 33% (7/21) of them were normotensive. 1, about 57% (12/21) of them presented with moderate HTN.1 or HTN Stages 1 and 2, and about 10% (2/21) of them presented with hypertensive crisis or severe HTN.1; however, these data changed in the 48 h before the end of the study, normotensive. 1 patients accounted for about 66% (14/21), patients with HTN Stages 1 and 2 or moderate HTN.2 passed represented about 24% (5/21), and patients with hypertensive crisis or severe HTN.2 continued to account for 10% (2/21), where the average age was 39 years (SD = 13) and the female/male ratio was 6/15, with an average blood pressure of 196/134 mmHg.

## DISCUSSION

The study showed that many patients hospitalized with malaria develop moderate or severe hypertension, patients in this condition accounted for 72% (238/333) of the population followed in this study in the first 42 hours of hospitalization, this condition was slightly reduced to about 67% (224/333) after 4 days of hospitalization and treatment with antimalarials and other co-adjuvant drugs, the most interesting was the fact that initially patients with severe HTN.1 decreased from 22% (72/333) observed in the first two days, for 11% (36/333) of severe HTN.2 observed in the last 48 hours (third and fourth day) before the end of the study, which represented a reduction of almost 50% in the number of patients. The results mentioned are similar to the results of a study carried out in Cote d'Ivoire, where the authors concluded that the results of their study suggested that malaria and blood pressure may influence each other or share a genetic history in a complex way,<sup>[25]</sup> and the study conducted in Nigeria, where the authors found that of the 300 malaria-positive patients, 60 (20%) of them were hypertensive;<sup>[26]</sup> although the results of the Nigeria study are lower than those found in the present study, this percentage was only about patients with severe HTN.



**Figure 5:** Outcome and blood pressure. (Discharge): patients who, after the days of follow-up, were discharged for improving their clinical condition after malaria infection. (Hospitalized): patients who, after the days of follow-up, remained hospitalized because they still did not show improvement in their clinical condition after malaria infection. (Died): patients who died during the follow-up period

In the present study, the general population had a relatively young average age, where the average age was 27 years (SD = 9) and the number of female patients was relatively lower than the male (153/180) and mostly from regions urban areas of Luanda (254/333), which is the capital of Angola where the lifestyle of the population is extremely agitated with the highest cost of living in the country, with high levels of traffic congestion, lack of basic sanitation, many locations with a lack of water and electricity, difficulties in accessing education and health, and many other social problems that provide a stressful lifestyle [Figure 1]. These data are similar to those observed in the study carried out in Nigeria, where the highest prevalence (83.9%) based on age was found in patients between 18 and 29 years, and of the 450 study participants, 265 (58.9%) were from males and 185 (41.1%) females and there was a high prevalence of malaria among unemployed patients (79.3%) which was consistent with the previous reports from other African countries.<sup>[26]</sup>

In this study, it was found that in patients hospitalized for malaria, moderate and severe HTN occurred more in students (110), unemployed (78), and traders (63), who together accounted for about 72% (241/333) of the total population studied and moderate and severe HTN seemed more persistent among unemployed patients, a phenomenon that we could not explain since it was the only group of patients with this problem where there were almost no changes in the mean pressure values measured in the first 48 h after hospital admission in comparison the last 48 h before the end of the study [Figure 2], demonstrating that malaria is more common among people of low socioeconomic status, who generally live in precarious housing conditions that increase their exposure to infection.<sup>[26]</sup> The data from the present study corroborate the hypothesis that there is a relationship between malaria and high blood pressure, which has been strongly supported by observations of the increasing incidence of HTN in malaria-endemic, low- and middle-income countries with poor socioeconomic conditions, particularly in Sub-Saharan African countries,<sup>[27]</sup> such as Angola.

The study showed [Figure 3] that, in the first 48 h, the number of patients with low parasitemia represented about 42% (140/333) of all patients followed in the study, where about 38% (62/166) of these patients with low parasitemia presented patients with moderate HTN.1 and about 61% (44/72) patients with severe HTN.1, patients with moderate and high parasitemia represented approximately 58% (193/333) of the studied patients, where approximately 62% (104/166) were patients with moderate HTN.1 and 39% (28/72) were patients with severe HTN.1; this percentage changed in the last 48 h before the end of the study, where the patients with moderate and high parasitemia represent only 11% (38/333) of all patients followed in the study, and of these 15% (28/188) were patients who presented moderate HTN.2 and 14% (5/36) were patients who presented severe HTN.2, with this reduction the number of patients with low parasitemia now represents 89% (295/333) of the studied patients, where patients with

moderate HTN.2 represented about 9% (16/188) and with severe HTN.2, representing about 86% (31/36). These results showed that as the patients went from high to moderate or low parasitemia during the treatment period, there was also a significant reduction in the number of patients with severe HTA that went from 72 to 36, thus increasing the number of patients with moderate HTN, which went from 166 to 188 and normotensive patients who went from 95 to 109, this data is similar to a study carried out in Germany, where the authors realized that HTN, cardiovascular diseases, dyslipidemia, malignancy, alcoholism, and chronic infections (infection, HIV) were individual diseases associated with severe malaria in the univariate analysis.<sup>[28]</sup> However, the data from the present study differ somewhat from the study carried out in Cote d'Ivoire which found that the prevalence of HTN was higher among negative participants for malaria parasitemia (24%) than positive participants for malaria parasitemia (14%), but pre-HTN was no difference due to malaria parasitemia status (both 33%).<sup>[25]</sup>

It was found in the study that only 299 patients treated with artemether showed significant changes in blood pressure levels, since the number of normotensive patients went from 80 to 93, patients with moderate HTN left from 156 to 176, and patients with severe HTN reduced from 63 to 30, demonstrating that this drug can have a positive effect on reducing blood pressure levels in patients hospitalized for malaria; however, this 34 patients treated with artesunate did not show significant changes in the reduction of patients with malaria, since normotensive patients left from 16 to 15, patients with moderate HTN went from 10 to 12, and patients with severe HTN went from 9 to 6 [Figure 4]. The results contrast somewhat with the study of patients with severe falciparum malaria in the United States, where artesunate should become the treatment of choice for severe falciparum malaria in adults, and differ slightly with another study carried out at the same hospital in patients with malaria, where quinine and artesunate were used mainly in patients who developed AKI, while artemether was used mainly in patients who did not develop AKI, and on the other hand, the quinine and artemether combination was used mainly in patients who presented AKI, while the quinine and artesunate combination was used mainly in patients who did not present AKI.<sup>[3,29]</sup>

The study showed a mortality rate of about 6% (21/333), and it was noticed that in this group of patients, there was no change in patients with severe HTN that remained around 20% (2/21) throughout the follow-up, but patients with moderate HTN decreased from 12 to 5 and normotensive patients increased from 7 to 14 between the first 48 h of hospital admission and 48 h before the end of the study. It was noticed that patients who remained hospitalized were those who presented some variation in blood pressure levels, since the number of patients with moderate HTN increased from 107 to 126 and patients with severe HTN reduced from 51 to 24, while in patients who they were discharged from the hospital, it showed variations in the number of patients with moderate HTN, which went

from 47 to 57 and with severe HTN decreased from 19 to 10. Mortality in this study was lower than the study developed in 2016, in the same hospital where mortality accounted for 9% (8/88) and the possibility of hospital discharge was higher in patients with low parasitemia and without AKI, the increase in hospital stay was higher among patients with high or hyperparasitemia and mortality was observed mainly in patients with high parasitemia with AKI and patients with hyper parasitemia with AKI.<sup>[3]</sup>

### Limitation of the study

A limitation of this study was the fact that many patients included in the study could be hypertensive before admission and they were unaware of their clinical condition, since the inclusion criteria allowed to reduce this bias that could be a factor of confusion; however, the fact that the study was developed in a young population and that significant changes in the blood pressure values of patients occurred even without any antihypertensive treatment may signal that this margin of error can be minimal and does not affect the validity of the study.

### CONCLUSION

In general, many patients with malaria had high blood pressure during hospital admission, and throughout the hospitalization period in some cases, there was a significant reduction depending on social conditions, parasitemics, and medical and medication treatment; it is necessary to improve the medical and medication approach in patient care with malaria to reduce the impact of parasitemia on blood pressure levels in these patients, especially in artesunate-treated patients who do not appear to help reduce blood pressure levels in patients, although this was not noticeable in the study, if blood pressure levels increase the chance of death from malaria.

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### Conflicts of interest

There are no conflicts of interest.

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