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Severe Childhood Malaria in Two Health Districts of Cuvette-Congo

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Abstract

Introduction: Malaria is a public health problem. Severe forms of malaria are linked to high mortality. Objective: To establish the cartography of severe malaria in two health districts in Cuvette-Congo. **Methodology**: An analytical and cross-sectional study was conducted from January to September 2019 in two health districts of Cuvette-Congo. Children aged three months to 17 years diagnosed with severe malaria were included. The epidemiological, clinical and paraclinical variables were analyzed. The statistical tests used were Pearson's chi^2 and the corrected Yates test. **Results**: Out of 806 children hospitalized, 277 had severe malaria (34.4%). There were 144 boys and 133 girls, an average of 60.9 months old. Anemia n = 247 (89.2%), repeated seizures n = 66 (23.8%), were the signs of severity observed. The clinical forms were isolated (n = 237) in 85.6% and associated (n = 40) in 14.4%, including 210 (88.6%) anemic form and 27 (11.4%) neurological form. The death occurred in seven cases (2.5%). The predictors of death were coma, jaundice, hypoglycemia, thrombocytopenia, hepatomegaly, undernutrition, dehydration and delayed consultation. **Conclusion**: The large number of cases of severe malaria in Cuvette, often in children under five years old, requires that the national program for control of malaria be strengthened by insisting on a wide distribution of long-lasting insecticide-treated mosquito nets.

Keywords

Severe Malaria, Child, Cuvette-Congo

1. Introduction

An infectious disease caused by parasites of the plasmodium genus and transmitted by female mosquitoes belonging to the genus Anopheles, malaria remains

a major public health problem. It is an endemic that occurs predominantly in the tropical and subtropical poverty belt of the world [1] [2]. In its severe form, malaria is the fifth leading cause of death from infectious diseases in the world and the second in Africa [3].

According to the World Health Organization (WHO), 219 million people are infected, including 200 million in Africa, or 92%, and the number of deaths is estimated at 435,000, including 266,000 or 61% among children under five [4], the anemic, neurological and metabolic forms are the deadliest [5] [6]. The "Roll Back Malaria" initiative [7] and the Millennium Development Goals [8] have not achieved the expected goal. Thus, malaria remains one of the main causes of morbidity and mortality in Africa [9] as evidenced by recent hospital frequencies. This is the case in Mali where the frequency of severe malaria is 55.8% and the lethality 10% [10], in Niger 35% frequency and 3.6% death rate [11] and in the Democratic Republic of Congo (DRC) with frequencies of 18% to 67.8% and lethality of 4% [12].

In Congo, despite the generalization of the use of artemisinin-based therapeutic combinations, the distribution of mosquito nets impregnated with long-lasting insecticides, coupled with a free treatment regimen for children under five [13], the hospital frequency was evaluated in urban areas of Brazzaville at 11.2% with the lethality of 6.5% [14]. We carried out this first study in a department, in a rural area, in two health districts located 406 km from Brazzaville. The aim was to evaluate the epidemiological, clinical and evolutionary aspects of severe malaria in children and the objectives were to determine the prevalence of severe malaria in children, describe the nosological varieties, evaluate the evolutionary profile and identify the predictive factors of death.

2. Patients and Methods

This was an analytical and cross-sectional study that took place between January and September 2019, *i.e.* in nine months. The study setting was the pediatric services of the level III general hospital: Edith Lucie Bongo Ondimba (HGELBO), of the level II hospital: 31 Juillet general hospital of Owando, and of two basic hospitals: Maman Mouebara and Boundji, level I hospitals.

The department has an area of 48,250 km^2 with 222,613 inhabitants including 158,056 children. It has three health districts and health coverage is provided by two general hospitals, four base hospitals, 24 integrated health centers and 66 health posts. The reception capacity of the pediatric services, part of the study, is seven beds for the ELBO general hospital, 24 beds for the 31 Juillet general hospital in Owando, ten beds for the base hospital Maman Mouebara and 11 beds for the base hospital in Boundji.

The study population was children aged three months to 17 years hospitalized in the pediatric wards of the selected hospitals. Those whose discharge diagnosis included, among other, the item severe malaria, children whose parents consented, were included. Children treated as severe malaria without or with nega-

tive thick film were not included.

A consecutive census of the children was carried out and the data collected on a pre-established form. We used the SCHLESSELMAN formula taking into account the previous hospital prevalence reported in Brazzaville by Okoko [14]. Based on these criteria, 277 subjects were selected.

Before the start of the study, the objectives and the survey sheet were explained to the parents and/or adolescents. Informed consent was required and mandatory. A questioning was carried out in search of epidemiological data, a physical examination and a biological investigation included a microscopic examination of stained blood smears and depending on the clinical orientation: serum creatinine performed in seven cases (2.5%), glycaemia. blood gases, serum bilirubin assay were not performed.

Therapeutically, the etiological treatment consisted of the administration of Artesunate at a dose of 2.4 mg/kg in those over 20 kg and 3 mg/kg in those under 20 kg by intravenous (IV) or intramuscular injection. at H0, H12, H24 then once every 24 hours for five to seven days; Artemether 3.2 mg/kg on the 1st day and 1.6 mg/kg IV from D2 to D5; Quinine 8 kg/kg IVL every 8 hours. The other medications used depending on the clinical form were: Diazepam 0.5 mg/kg intra rectally, Phenobarbital 10 to 15 mg/kg/day IVL, blood transfusion taking into account Mollisson's formula quantity of blood to bring = 3 × weight (Desired hemoglobin − Hemoglobin of the patient) and when the hemoglobin level was not known, 15 - 20 ml/kg of erythrocyte pellet, Furosemide 1 - 2 mg/kg, glucose serum at 10% at a dose of 50 ml/kg.

The healing criteria were in all cases, apyrexia and negativation of GERH. The other criteria, depending on the clinical form, were recovery of consciousness, diuresis, and normalization of renal function and elements of the blood count.

The study variables were: age, profession, level of education and socio-economic status of parents, age and sex of the child; the consultation time, the antimalarial treatment received before hospitalization, the reason for hospitalization, the signs of examination, the nosological varieties, the comorbidity, the criteria of severity, the parasite density, the hemogram, the glycemia, the serum creatinine, the therapies administered and the evolutionary data.

The definition of severe malaria retained was that associating the presence of Plasmodium falciparum trophozoites in the blood after completion of the malaria parasites test with at least one of the WHO severity criteria [15]. Nutritional status was assessed using WHO norms and standards [16] and socioeconomic level assessed using the classification of Gayral-Taminh *et al.* [16]. An opinion from the ethics committee was obtained.

The data was entered and processed with SPSS version 20.0 software and the analysis was done with SPSS software and Microsoft Excel 2013.

The statistical tests used were Pearson's chi^2 and Yates' corrected test when a number (n) was less than 5. A margin of error of 5% was taken, meaning that a test showed a statistical link between two variables when the p-value (Pearson

value) was less than or equal to 0.05. The risk was measured using the odds ratio (OR).

3. Results

3.1. Descriptive Study

3.1.1. Epidemiological Data

A total of 806 children hospitalized, 277 (34.4%) were for severe malaria. The frequency was 2.9% (n = 8/81) at HGELBO; 43.7% (n = 121/204) at HG Owando, 11.9% (n = 33/105) at HB Boundji and 41.5% (115/416) at HB Mom Mouebara. The study population consisted of 144 (52%) boys and 133 (48%) girls, *i.e.* a sex ratio of 1.1. The mean age was 60.9 months ± 43.7 extreme (three months and 204 months). There were 56% (n = 155) children under 60 months, 33.9% (n = 94) whose age was between 60 and 120 months and 10.1% (n = 28) aged over of 120 months. They came from home n = 208 (75.1%), from an integrated health center n = 65 (23.5%) and from a doctor's office n = 4 (1.4%). The average age of the mothers was 33.3 years ± 7.8 extreme (16 and 55 years) versus 39.5 years ± 8.9 extreme (17 and 65 years) for the fathers. In 10 cases (3.6%), the mothers were under 20 years old versus two fathers (0.7%). On the other hand, 76 mothers (27.4%) were between 20 and 29 years old versus 35 fathers (12.6%), and 144 mothers (52%) were between 30 and 40 years old versus 131 (47.3%) for the fathers and over 40 n = 47 (17%) for mothers versus n = 109 fathers (39.4%). Mothers were educated in 234 (84.5%) versus 242 fathers (87.4%). The level of education was primary for 137 mothers (49.5%) versus 83 fathers (30%), secondary level for 94 mothers (33.9%) versus 154 fathers (55.6%), university for three (1.1%) versus five fathers (1.8%). The mothers were uneducated in 43 cases (15.5%) versus 35 fathers (12.6%). The work sector was the informal sector for 222 mothers (80.1%) and 200 for fathers (72.2%). In 10 cases (3.6%) the mothers were workers and the fathers in 46 cases (16.6%). The mothers were managers in five cases (1.8%), the fathers in 15 cases (5.4%). On the other hand, the status of no profession concerned 40 mothers (14.4%) and 16 fathers (5.8%). The parents had a low socioeconomic level in 201 cases (72.6%), average in 56 cases (20.2%), and good in 20 cases (7.2%).

The average consultation time was 3.8 days ± 2.7 extreme (1 and 30 days). It was less than two days in 5 cases (1.8%), between two and seven days in 239 (86.3%), and greater than seven days in 33 (11.9%).

The children slept under a mosquito net in all cases. Among them, 30 or 10.83% used an insecticide-treated mosquito net (MIILA). An antimalarial treatment was administered before hospitalization to 108 children (40.3%) consisting of quinine (n = 60 or 55.6%), Artemether (n = 7 or 6.5%), Artemether-lumefantrine (n = 40 *i.e.* 37%), artesunate (n = 1 *i.e.* 0.9%). It had been prescribed by a pediatrician (n = 7 or 6.5%), a general practitioner (n = 2 or 21.3%), and a paramedical staff (n = 39 or 36.1%). The drug was obtained over the counter n = in 39 cases (36.1%).

3.1.2. Clinical Data

The reason for hospitalization is recorded in Table 1.

3.1.3. Physical Examination Data

Dehydration was noted n = 4 (1.4%). They were eutrophic n = 263 (94.95%), malnourished n = 14 (5.1%). The examination signs are recorded in Table 2.

Table 1. Reason for hospitalization.

Reason for hospitalization	N	%
Fever	277	100
Pallor	247	89.2
Hypodynamia	236	85.2
Convulsions	66	23.8
Vomiting	25	9.0
Obnubilation	25	9.0
Respiratory distress	20	7.2
Prostration	15	5.4
Headache	10	3.6
Arthromyalgia	8	2.9
Diarrhea	4	1.4
Coma	4	1.4
Abdominal pain	3	1.1
Agitation	1	0.4

*A patient could have one or more symptoms.

Table 2. Clinical signs.

Signs	N	%
Pallor	247	89.2
Splenomegaly	70	25.3
Hepatomegaly	33	11.9
Jaundice	14	5.1
Crackles	11	3.9
Coma	4	1.4
Edema of the pelvic limbs	4	1.4
Bronchial rales	2	0.7
Altered diuresis	1	0.4

*A patient could have one or more symptoms.

3.1.4. Paraclinical Data

The mean thick film parasite density was 92262.4 p/ul ± 194184.7 extreme (32 and 1,000,000 p/µl), hyperparasitaemia in 20 cases (7.2%). Hypoglycaemia was noted in 9 cases (3.3%), with an average rate of 0.9 g/l ± 0.2 extremes (0.1 and 2.1 g/l). Serum creatinine was elevated in one case. The blood count showed anemia in 247 cases (89.2%) with an average hemoglobin level of 5.5 g/dl ± 2 extremes (2 and 5.5 g/dl), a hemoglobin level below 5 g/dl in 150 cases (60.7%) and an average platelet count of 236303.3 c/mm^3 ± 110,123 extremes (20,000 and 500,000 c/mm^3) including thrombocytopenia with a rate below 100,000 c/mm^3 in six cases (2.2%).

3.1.5. Severity Criteria

The severity criteria noted were anemia n = 247 (89.7%), repeated convulsions n = 66 (23.8%), obnubilation n = 25 (9.0%), hyperparasitaemia n = 20 (7.2%), prostration n = 15 (5.4%); jaundice n = 14 (5.1%); hypoglycaemia n = 9 (3.3%); a coma n = 4 (1.4%) and renal failure in one case (0.4%). It was an isolated form n = 237 (85.6%) including 210 (75.8%) anemic form and 27 (9.7%) neurological form and an associated form n = 40 (14.4%) including 20 (7.2%) neuro-anaemic forms; 10 (3.6%) neuro-anemic and icteric forms; n = 3 (1.1%) neurological and hypoglycaemic forms; n = 3 (1.1%) neuro-anemic and hypoglycaemic forms; n = 2 (0.7%) neuro-anaemic, hypoglycemic, and icteric forms; and one (0.4%) anemic and icteric form; neuro-anemic, hypoglycemic, jaundiced and Renal failure in one case each.

The anemic and neurological forms, the most frequent, were noted in children of mean age 61.1 months ± 23.5 extreme (three and 204 months) for the anemic forms versus 46.1 months ± 33.5 extreme (five and 132 months) for neurological forms. The children were under 59 months 61.1% (n = 128), between 60 and 120 months 29.2% (n = 62) and over 120 months 9.7% (n = 20) for the anemic forms versus less than 59 months 63.4% (n = 17), between 60 and 120 months 27.7% (n = 8) and more than 120 months 8.9% (n = 2) for neurological forms.

We found comorbidities in 16.6% (n = 46) of cases; pneumonia n = 23 (8.3%), meningitis n = 4 (1.4%), sickle cell disease n = 5 (1.8%), dehydration in 1.4% (n = 4) and undernutrition in 5.6% (n = 14).

3.1.6. Therapeutic Data

The treatment consisted of the administration of Artesunate n = 207 (74.7%), quinine base n = 58 (21%) and Artemether n = 12 (4.3%). The mean duration of treatment was 4.67 days ± 1.2 extreme (one and 10 days). The other medications were: a transfusion of packed red blood cells n = 245 (99.2%) and whole blood n = 2 (0.8), an anticonvulsant n = 66 (23.8%) including diazepam n = 60 (90.9%) and phenobarbital n = 6 (9.1%). A loop diuretic was used in one case.

3.1.7. Scalable Data

The average length of hospitalization was 5.5 days ± 2.2 extreme (one and 12

days). The evolution was favorable in 270 children (97.5%), one death was noted in seven children (2.5%) whose mean age was 55 months ± 45.1 (extreme 11 and 120 months). Causes of death were anemic shock in all cases.

3.2. Analytical Study

Predictive factors of death (Table 3)

Age (p = 0.783) and sex (p = 0.296) did not influence the occurrence of death, as well as comorbidities such as pneumonia, meningitis and sickle cell disease.

The predictive factors for death are: coma, hypoglycaemia, jaundice, hepatomegaly, thrombocytopenia, undernutrition and delay of consultation.

4. Discussion

4.1. Analysis of Methods

Severe malaria is a public health problem. Within the same country, its frequency varies from one region to another. In the urban area of Brazzaville, its frequency is known [14]. To determine the prevalence of severe malaria, to describe these nosological varieties, to evaluate the evolutionary profile and to identify the predictive factors of death, were the objectives of the study. This study has the advantage of being the first carried out in Congolese rural areas in districts with a high population density, but it nevertheless presents some pitfalls, including that relating to any hospital study and that relating to the obsolescence of the technical laboratory facilities.

Table 3. Predictors of death.

Variables	N	Death	%	OR	IC (95%)	p-value
Prostration	15	1	14.3	2.8	(0.3 - 25.1)	0.328
Convulsions	66	3	42.9	2.2	(0.4 - 10.2)	0.290
Hepatomegaly	33	4	57.1	9.5	(2.1 - 44.7)	0.0005
Undernutrition	14	3	42.9	13.7	(2.9 - 67.3)	0.00004
Dehydration	4	2	28.6	26.6	(3.9 - 180.3)	0.00000
Anemia	247	6	85.7	0.3	(0.06 - 1.4)	0.111
Coma	4	2	28.6	26.6	(3.9 - 180.3)	0.00000
Jaundice	14	2	28.6	7.3	(1.3 - 41.1)	0.0088
Hypoglycaemia	9	2	28.6	11.6	(1.9 - 68.1)	0.0007
Thrombopenia						
<100,000	6	2	28.6	17.6	(2.8 - 109.5)	0.0017
>100,000	10	3	42.9	4.3	(0.4 - 39.5)	0.155
Delay of consultation	272	7	100	5.0	(23.4 - 1.08)	0.023

4.2. Epidemiological Aspects

The hospital frequency of severe malaria was 34.4%, higher than those reported in the urban area of Brazzaville: 26.6% in 2010 [17] and 11.2% in 2016 [14]. The small size of the sample of this study on the other hand and the low rate of use of LLINs: 10.83% on the other hand explains these differences. Frequencies similar or higher than ours are reported in Africa. This is the case in Niger: 35% [11], in Benin: 52.6% [18] and in Mali: 55.8% [10] making serious malaria a public health problem. It is more observed in children under 60 months [3] [12] [14] [17] [19] [20] [21], a predominance explained by the absence of immunity. Indeed, according to Neige and Marsh [22], in areas where Plasmodium Falciparum malaria is endemic, severe malaria is mainly an infantile disease from the first months of life up to five years due to the acquisition of partial immunity. Children are relatively protected after birth due to the specific immunity acquired from their mother and the persistence of fetal hemoglobin [23]. But severe malaria is also observed in children over 60 months in areas of high endemicity [12] [14] [24]. This should encourage the ministries in charge of health to direct prevention programs to all age groups [25]. In the context of prevention, the distribution of LLINs to all populations at risk is the strategy of choice for health programs. The most effective and least expensive way to achieve this is, among other things, to provide them free of charge associated with communication strategies [3]. Severe malaria affects both sexes [10] [19] [20] [26] although a higher number of boys was reported in this study.

The well-known warning signs, which vary from one study to another, are dominated by fever, hypodynamia, pallor and convulsions and the examination signs, by splenomegaly and hepatomegaly [11] [19] [20] [27] [28].

Delay in consultation, a common occurrence in Africa [14] [19]-[28], is correlated with the occurrence of serious forms and death [10] [26] [29] [30]. In this study, the low socioeconomic and cultural level found respectively in 86.3% and 79.4% explains, among other things, the delay.

Signs of severity, which vary from one study to another, are dominated by anemia and convulsions as in Burkina Faso, Benin [31], Gabon and Togo [31] [32] [33]. In addition to anemia and neurological signs, respiratory distress is a predominant symptom in the DRC [20] and India [19]. The hypoglycaemia found in a low proportion is for Moyen and Okoko a factor of poor prognosis [14] [17] [18] [28] [30].

This study confirms the predominance of anemic and neurological forms [18] [20] [34] [35]. Anemia during malaria in Africa can be of multifactorial origin according to Imbert [35]. The essential mechanism is mechanical hemolysis due to the parasite itself making severe malaria the first cause of blood transfusion [36] [37].

Certain associated pathologies make malaria serious. Among which: malnutrition, dehydration and pneumonia [10] and meningitis in this study. Therapeutically, artesunate first, quinine and arthemeter are the molecules used [38] [39] as

recommended by WHO [3].

Severe malaria is still responsible for a significant number of deaths: 11.1% in Senegal [30], 10% in Mali [10], and 8.4% to 11.6% in the DRC [12] and 6.5% in Brazzaville [14]. We noted 2.5% of deaths whose main cause was anemic shock as already reported [10] [28]. The predictive factors of death are: coma, hypoglycemia, jaundice, hepatomegaly, thrombocytopenia and malnutrition [10] [30] [35] [40] and dehydration in this study.

The high frequency of severe malaria and its severity, as evidenced by a still high death rate, requires that prevention measures be strengthened, extend free treatment beyond five years [25], information, communication for behavior change parents faced with bad practices such as: self-medication and delays in consultation. However, primary prevention lies in improving the socioeconomic and cultural level of populations so that the strategy proposed by Margaret Chan [1] 2016-2030 of the WHO, namely: guaranteeing universal access to prevention, diagnosis and processing; accelerating efforts towards elimination and achieving malaria-free status and making malaria surveillance a core intervention a success.

5. Conclusion

In summary, severe malaria is an important cause of morbidity and mortality in rural areas of Congo (cuvette). It is observed more in children under five years of age, but does not spare the oldest. The main clinical forms are anemic and neurological. The factors associated with death are hypoglycemia, coma, jaundice, hepatomegaly, thrombocytopenia, dehydration and malnutrition. The large number of cases of severe malaria in the department of the basin requires that the national program to fight against malaria be strengthened by insisting on a wide distribution of long-lasting impregnated mosquito nets and strengthening the measure of free treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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