

Severe Adult Malaria at Brazzaville University Hospital: Prevalence and Associated Factors

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ABSTRACT

Objective: To determine the prevalence of severe malaria in young adults and find out associated factors.

Patients and Methods: This is a cross-sectional descriptive and analytical study of severe malaria cases recorded in the Infectious Diseases Department between April 2018 and April 2019.

Results: This study covers 60 cases (15.62% of admissions) of patients aged 37.68 +/- 15.50 (16-78), female (n = 39, 65%), students (n = 18) 30%, single (n = 40, 66.7%), low-income (n = 32, 53.3%), and immunocompromised to HIV type 1 (n = 15, 25%) living in Brazzaville (100%). The insecticide-treated mosquito net had not been used in the majority of cases (n = 55, 90%). Fever and headache were the most common reasons for consultation in 80% and 76.7%, respectively. Neurological failure was found in 35 patients (58.3%). There was one coma among 31.6% of cases. Other signs of severity were respiratory failure (n = 3, 5%), jaundice (n = 7, 11.7%), anemia (n = 17, 28.3%), and hyperparasitaemia (n = 7; 11.7%). Thickness was positive in 56 cases (93.3%) and parasitaemia was greater than 4% in all patients (100%). Artesunate was the most administered molecule in 41 patients (68.3%) and the average duration of its use was 3.0 days ± 1.2 (1-5 days). The mean duration of hospitalization was 5.52 days ± 2.53 (2-14 days). In 59 patients (98.3%) there was a favorable evolution. Lethality was 1.7% due to anemic shock.

Conclusion: It comes out after discussion that the severe malaria of adults remains a current situation at the Brazzaville CHU. The neurological form is the most common and the management is easy. It is therefore important to strengthen the preventive measures of this parasitic endemic.

Keywords

Malaria, Immunity, Female anopheles, Brazzaville University Hospital.

Introduction

Severe malaria remains a true diagnostic and therapeutic emergency and constitutes a real public health problem in sub-Saharan Africa where children under 5, pregnant women and non-immune expatriates continue to pay the highest proportion [1].

If yesterday, cases of severe malaria were less frequent among adult-youth residing in endemic areas because of the premunition, the current epidemiological data provide the frequency of cases of severe malaria in adults who lost the premunition after being more exposed to infective bites of female anopheles [2]. In the Congo, few studies provide information on the situation of this parasitic endemic in the adult population, hence this study aims to determine the frequency of severe malaria and associated factors in adult hospitalized patients.

Patients and Methods

We conducted a descriptive and analytical cross-sectional study of severe malaria cases recorded in the Infectious Diseases Department of the University Hospital of Brazzaville covering the period stepping from April 1, 2018 to April 30, 2019.

This survey concerns patients aged at least 18 years old, regardless of gender and HIV status, living in Congo, who had not lived in a non-endemic area for at least two years, in which no pathology that can interfere with malaria has been diagnosed. The following characteristics were defined in accordance with the patients notably: epidemiological (sex, age, place of residence, notion of chemo anti-malaria prophylaxis, notion of use of anti-malaria preventive measures, HIV status), clinical (consultation reason, consultation time, signs of gravity), diagnosis (results of the thick drop and the parasite density), therapeutics (the time taken in charge, the molecule used and the duration of its use), evolutionary (duration of hospitalization, cure, death and cause of death).

Severe malaria has been defined by the detection of *Plasmodium falciparum* at the thick-film associated with at least one severity criterion defined by the WHO [1]. *Plasmodium falciparum* parasitaemia expressed as the number of parasitized red blood cells per microliter of blood (GRP / μl) was calculated from the reading of 200 thin smear microscopic fields and based on 4 million red blood cells per microliter of blood performed in the Parasitology-Mycology laboratory of the University Hospital of Brazzaville.

The data were collected using an Excel spreadsheet and analyzed using the software EPI-Info 3.3.2. Qualitative variables were presented in terms of numbers, percentage and quantitative variables on average plus or minus standard deviation. The comparison of qualitative variables used the Chi-square test and the quantitative variables in the Student's test. For all these variables, the required level of significance was set at less than 0.05.

Results

We have collected sixty out of a total of 384 patients admitted to the Infectious Diseases department during the study period (15.62% of admissions). Patients with mean age of 37.68 ± 15.50 (16-78 years), females (n = 39, 65%), students (n = 18, 30%), single (n = 40, 66.7%), low socioeconomic status (n = 32, 53.3%) and immunocompromised to HIV (n = 15, 25%). All patients resided in Brazzaville for at least two years (100%). For the mechanical preventive measures, the long-lasting insecticide-treated mosquito net was not used in the majority of cases (n = 55, 90%). Only one patient was on chemo prophylaxis against malaria (1.7%). Fever and headache were the most common reasons for consultation in 80% and 76.7% respectively (Table 1). Neurological failure was found in 35 patients (58.3%). There was one coma in 31.6% of cases. Other signs of severity were respiratory failure (n = 3, 5%), jaundice (n = 7, 11.7%), anemia (n = 17, 28.3%), and hyperparasitaemia (n = 7, 11.7%) (Table 2). At parasitological level, the thick drop was positive in 56 cases (93.3%) and *plasmodium falciparum* was the only species found in all cases. The parasite density was below 10,000 parasitized red

blood cells/ μl in almost all patients. Parasitaemia was greater than 4% in all patients (100%). Artesunate was the most prescribed molecule in 41 patients (68.3%) followed by quinine infusion (n = 14, 23.3%). The mean duration of artesunate use was 3.0 days \pm 1.2 (1-5 days). The mean duration of hospitalization was 5.52 days \pm 2.53 (2-14 days). In 59 patients (98.3%), there was a favorable evolution concluded by the healing. Lethality was 1.7% due to anemic shock. There was no statistically significant association between the occurrence of malaria and the factors studied in all patients (Table 3).

Consultation reasons	n	%
Headache Fever	46	76,7
Vomiting	27	45,0
Diarrhea	7	11,7
Dehydration	2	3,3
Denutrition	2	3,3
OMI	0	0

Table 1: Basic reasons for patient consultation.

Sign of gravity		n	%
Neurological failure	Onibulation	14	23,3
	Confusion	10	16,7
	Drowsiness	0	0
	Convulsion	10	16,7
	Prostration	1	1,7
	Coma	5	8,3
Respiratory failure	Interstitial image	3	5
Other sign	Clinical bleeding	9	15
	Icterus	7	11,7
	Macroscopic Hemoglobinuria	5	8,3
	Deep anemia	17	28,3
	Hyperparasitaemia	7	11,7
	Renal failure	3	5

Table 2: Different signs of malaria severity discovered in patients.

Variables	GE				OR	IC95%	P
	Positive		Negative				
	n	%	n	%			
Age Scale	<20 years	7	12,5	0	0		0,45
	20-29 years	14	25	1	25	1	0,09-10,4
	30-39 years	12	21,4	2	50	0,27	0,035-2,1
	40-49 years	9	16,1	0	0		0,38
	50-59 years	8	14,3	1	25	0,5	0,04-5,4
	≥ 60 years	6	10,7	0	0		0,49
Sex	M	18	32,1	3	75	0,15	0,015-1,62
	F	38	67,9	1	25	6,3	0,61-65
Profession	Official workers	12	21,4	2	50	0,27	0,035-2,1
	Ouvrier	4	7,1	1	25	0,23	0,019-2,7
	Students/Pupils	17	30,4	1	25	1,3	0,12-13,4

Socio-economic status	Low	30	57,7	2	50	1,3	0,17-10,4	0,76
	Mean	25	44,6	2	50	0,8	0,1-6,1	0,83
HIV Status	Positive	14	25	1	25	1	0,8-1,1	0,6
	Negative	42	75	3	75	1	0,1-8,9	0,6

Table 3: Associate factors.

Discussion

Few studies in Congo have addressed severe malaria in adults living in the city for more than two years and we think that this is the first study conducted in the Infectious Diseases Department of the Brazzaville University Hospital which is a reference service for the management of severe cases of this endemic parasite. In Congo, for five years, free malaria treatment for children and pregnant women has been instituted because of the morbidity and mortality related to this endemic disease among the populations mentioned, while this work lays emphasis on the epidemiological reality of this parasitosis in the adult population as reported elsewhere [2,3].

The prevalence of severe malaria in young adults is high in Congo, where climatic, entomological and environmental conditions favor the emergence of female Anopheles. It is lower in Côte d'Ivoire and Senegal [3,4]. In Madagascar, the country where malaria is the second largest public health problem, the prevalence of endemic disease is 7.6% [5]. Methodological and especially climatic differences largely justify these recorded differences in prevalence. Adults-female youth are the most affected in this study as reported in Madagascar and Abidjan [3,5]. It is a category of population no longer exposed to infesting mosquito bites and easily loses premunity as reported in the literature [1,2,3,5]. In one-third of the cases, we find learners/students, single and low socioeconomic who are affected by malaria endemic without significant difference as reported elsewhere [5,6]. HIV infection was the predominant site in one-quarter of patients with no causal link to malaria. However, co-infected patients sometimes had two signs of malaria severity, namely coma-like neurological failure and anemia, probably related to a decrease in transient immunosuppression-induced cell-mediated immunity in plasmodium neuropaludism falciparum. The same observation had already been made in Burkina-FASSO [7,8]. All patients affected by malaria had been living in the city for at least two years. It was therefore likely indigenous-Congolese cases as reported in the subregion [3,5].

Urbanization, self-medication or even incomplete treatments for cases of simple malaria encountered in the target population, climatic variations, entomological changes and resistance problems specific to the species concerned would largely justify case of severe malaria in this adult population residing in the city [3,4,5,9]. Only one patient was on anti-malaria chemoprophylaxis and none of the adults were sleeping under a long-lasting insecticide-treated bednet. These data are similar to Eholié's in Côte d'Ivoire where the unique reason for this preventive measure was the change in their place of residence [3]. Tropical fever should always be malaria-like first since it was found in almost all patients on admission. In Burkina Faso, the mean admission temperature for adults with

severe malaria was $39^{\circ}\text{C} \pm 1$ and fever was the main reason for consultation in Abidjan [3,6]. Among the criteria for severity of malaria found in patients, a neurological failure was predominant with prevalence of coma. In fact, Plasmodium falciparum, the plasmodial species concerned is the only one to realize its erythrocytic schizogony in the visceral capillaries, cerebral ones in particular, resulting in these serious forms of tissue lesions. These data are consistent with that described in the literature [3,10]. At the parasitological level, the thick drop was positive in 93.3% of cases and plasmodium falciparum was the unique species found in all cases. In rather small proportions, a thick negative drop was found in the patients. These were cases that received either uncompleted treatment for cases of uncomplicated malaria in the health facilities of the place, or even patients who benefited from a thick drop at very low parasitaemia as described in the literature [3]. In Parasitologically confirmed patients, in almost all cases, parasitaemia at more than 4% defined a severity criterion as reported by WHO [1]. Injectable artesunate was the most prescribed molecule in the majority of patients.

It is a recommended first-line molecule in all cases of severe malaria because of its effectiveness, its delay in action and the reduction of parasitaemia. The advantages of this molecule are not new facts as described in the literature [11]. Indeed, this artemisinin derivative is characterized by a rapid and strong parasiticidal on circulating plasmodial strains; in addition, artesunate IV has shown greater efficiency than quinine in severe falciparum malaria. The short average duration of use of artesunate is related to the therapeutic benefit obtained from the first 24h at the correct dose; the relay being made by an ACT. A similar study conducted in Cote d'Ivoire in 2004 used intravenous quinine in 172 among 336 patients admitted for severe malaria with a mean duration of antimalarial treatment of 4.2 days, with extremes ranging from 3 to 7 days [3]. The average duration of hospitalization of patients in our series seems short in relation to the molecules used. It is 3.7 days in Burkina Faso [6]. The evolution of malaria cases was considered favorable in the vast majority of cases and this in relation to the short time of diagnosis and management. The mortality rate in our series remains lower than that of many African authors, particularly in Côte d'Ivoire (15%), Burkina Faso (8%), Senegal (21%), and Burundi (22%). These studies used intravenous quinine and IM artemether in addition to delays in diagnosis and case management. Our study, like that carried out in Côte d'Ivoire, does not find out a link between malaria and HIV as a factor of poor prognosis [3].

Conclusion

This contribution shows that severe adult malaria is still prevalent at Brazzaville University Hospital with a fairly high frequency. These are the native cases that have probably lost the guard. The neurological location of this endemic parasite is the most common. If early and effective management partly justifies the low mortality rate, the prevention of this disease in this category of population is possible.

References

1. Kaper JB, Nataro JP, Mobley HLT. Pathogenic Escherichia

- coli. *Nat Rev Microbiol*. 2004; 2: 123-140.
2. Levine MM. Escherichia coli that cause diarrhea: enterotoxigenic, enteropathogenic, enteroinvasive, enterohemorrhagic, and enteroadherent. *J Infect Dis*. 1987; 155: 377-389.
 3. Nataro JP, Kaper JB. Diarrheagenic Escherichia coli. *Clin Microbiol Rev*. 1998; 11: 142-201.
 4. Johnson JR, Russo TA. Uropathogenic Escherichia coli as Agents of Diverse Non-Urinary Tract Extra intestinal Infections. *J Infect Dis*. 2002; 186: 859-864.
 5. Nielubowicz GR, Mobley HL. Host-pathogen interactions in urinary tract infection. *Nat Rev Urol*. 2010; 7: 430-441.
 6. Zalmanovici TA, Green H, Paul M, et al. Antimicrobial agents for treating uncomplicated urinary tract infection in women. *Cochrane Database Syst Rev*. 2010; 10: CD007182.
 7. François JEHL. Comité de l'Antibiogramme de la Société Française de Microbiologie, Recommendations. 2016; 1.
 8. Caroline Dallenne, Anaëlle Da Costa, Dominique Decre, et al. Development of a set of multiplex PCR assays for the detection of genes encoding important β -lactamases in Enterobacteriaceae. *J Antimicrob Chemother*. 2010; 65: 490-495.
 9. George A Jacoby, Nancy Gacharna, Todd A Black, et al. Temporal Appearance of Plasmid-Mediated Quinolone Resistance Genes. *Antimicrob Agents Chemother*. 2009; 53: 1665-1666.
 10. Tabbouche S, Khudary R, Beyrouthy R, et al. Detection of genes TEM, OXA, SHV and CTX-M in 73 clinical isolates of Escherichia coli producers of extended spectrum β -lactamases and determination of their susceptibility to antibiotics. *The International Arabic Journal of Antimicrobial Agents*. 2011; 1: 15.
 11. Letters to the Editor, Dissemination in Portugal of CTX-M-15-, OXA-1-, and TEM-1-Producing Enterobacteriaceae Strains Containing the aac(6)-Ib-crGene, Which Encodes an Aminoglycoside- and Fluoroquinolone-Modifying Enzyme. *American society for Microbiology*. 2006; 3220-3221.
 12. Elifburcubali, LeylaAcik, Nedim Sultan. Phenotypic and molecular characterization of SHV, TEM, CTXM and extended – spectrum betalactamase produced by Escherichia coli, Acinetobacter baumannii and Klebsiella isolates in a Turkish hospital. *African journal of Microbiology research*. 2010; 4: 650-654.
 13. Ruppé E. Épidémiologie des β -lactamases à spectre élargi: l'avènement des CTX-M. *Antibiotiques*. 2010; 12: 3-16.
 14. Ozgumus OB, Tosun I, Aydin F, et al. Horizontal dissemination of TEM and SHV type β -lactamase genes carrying resistance plasmids amongst clinical isolates of Enterobacteriaceae. *Brazil J Microbiol*. 2008; 39: 636-643.
 15. Kiratisin P, Apisarntharak A, Laesripa C, et al. Molecular characterization and epidemiology of extended-spectrum β -lactamase producing Escherichia coli and Klebsiella pneumonia isolates causing health care-associated infection in Thailand, where the CTX-M family is endemic. *Antimicrob Agents Chemother*. 2008; 52: 2818-2824.
 16. Carattoli A, Garcia FA, Varesi P, et al. Molecular epidemiology of Escherichia coli producing extended-spectrum β -lactamases isolated in Rome, Italy. *J Clin Microbiol*. 2008; 46: 103-108.
 17. Turpti B, Pendey M, Varma M, et al. Prevalence of TEM, SHV and CTX-M β -lactamase genes in the urinary isolates of a tertiary care hospital. *Avicenna journal of Medicine*. 2017; 7: 12-16.
 18. Eftekhari F, Mastegar M, Gololipoor A, et al. Detection of extended spectrum β -lactamases in urinary isolates of Klebsiella pneumoniae in relation to Bla SHV, Bla TEM, Bla CTX-M gene carriage. *Iran J Public Health*. 2012; 41: 127-132.
 19. Ibrahim Al –Subol, Nihadyoussef. Prevalence of CTX-M, TEM and SHV β -lactamases in clinical Isolates of Escherichia coli and Klebsiella pneumoniae isolated from Aleppo University Hospitals, Aleppo, Syria. *Clinical Infectious Diseases*. 2015; 10: e 22540.
 20. Ingrid Cécile Djuikoue, Omer Njajou, Hortense Gonsu Kamga, et al. Prevalence of CTX-M β -lactamases in Escherichia coli from community-acquired urinary tract infections and associated risk factors among women in Cameroon. *Journal of Epidemiological Research*. 2017; 3: 51-56.
 21. Kargar M, MoeinJahromi F, Doosti A, et al. Résistance à différentes générations de quinolones dans des souches de Streptococcus pneumoniae isolées dans des hôpitaux de Shiraz. *Comp Clin Pathol*. 2015; 24: 533-536.
 22. Martínez-Martínez L, Pascual A, Jacoby GA. Quinolone resistance from a transferable plasmid. *Lancet*. 1998; 351: 797-799.
 23. Mokhtari-Farsani A, Doosti A, Mohammadalipour Z. Présence de gènes Qnr liés à la résistance aux quinolones, première, deuxième et troisième génération chez Escherichia coli diarrhéogène. *J Patient Saf Infect Control*. 2016; 4: 5-9.
 24. Farzaneh Firoozeh, Mohammad Zibaei, YounesSoleimani-Asl. Detection of plasmid-mediated qnr genes among the quinolone-resistant Escherichia coli isolates in Iran. *J Infect Dev Ctries*. 2014; 8: 818-822.
 25. Boni-Cissé, Méité S, Coulibaly ND, et al. Prévalence des gènes QNR chez Klebsiella pneumoniae isolés dans le service de pédiatrie du CHU de Yopougon à Abidjan Côte d'Ivoire. *Rev Int Méd*. 2012; 1: 131-135.
 26. Bouchakour M, Zerouali K, Gros Claude JD, et al. Plasmid-mediated quinolone resistance in expanded spectrum β -lactamase producing Enterobacteriaceae in Morocco. *J Infect Dev Ctries*. 2010; 4: 779-803.