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Epidemiological, Clinical and Evolutionary Profile of Severe Malaria Cases in the Intensive Care Unit of the Tambohobe-Fianarantsoa Teaching Hospital

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Abstract

Objective: To determine the epidemiological, clinical and evolutionary profile of severe malaria cases.

Patients and Methods: Retrospective descriptive study carried out over a period of 36 months, bearing the cases of severe malaria in adults, treated at the Multipurpose Resuscitation Unit of the Tambohobe-Fianarantsoa Teaching Hospital.

Results: We selected 123 patients. The average age was 33.3 years old. The sex ratio was 2.3. The majority of patients resided in the central uplands (n = 113, 91.9%). The notion of stay in an endemic zone was noted in 68 patients (55.3%). Patients were referred by the basic and district health center in 68 cases (55.3%). The majority of patients (71.5%) came to the resuscitation department after the 24th hour of the onset of signs of severity. The antimalarial used was intravenous quinine in 64 cases (52%). Coma was the main clinical sign of severity (n = 96, 78%) followed by prostration (n = 27, 22%), seizure (n = 23, 18.7%) and renal failure (n = 16, 13%). The return of consciousness (Glasgow 15) was faster for patients receiving intravenous artesunate (p = 0.041). Mortality was not related to the antimalarial used (p = 0.362). The mortality rate during the study period was 38.2%.

Conclusion: In the presence of febrile disorders of young subjects, especially males, the rapid malaria diagnostic test should be carried out routinely. Severe malaria is marked by high mortality, especially among pregnant women.

Keywords: *Malaria; Intensive Care Unit; Tambohobe-Fianarantsoa*

Introduction

Severe malaria is defined by the presence of parasitaemia in the majority of asexual forms of Plasmodium falciparum and at least one clinical or biological criterion of severity defined by WHO in 2000 and modified in 2010 [1,2]. The clinical and biological criteria of severity are as follows: prostration, disturbance of consciousness: Modified Glasgow score < 10, repeated generalized seizures (more than 2 in 24 hours), respiratory distress, pulmonary edema: radiological definition, shock (PAS < 80 mmHg and peripheral signs of circulatory insufficiency), abnormal bleeding, hemoglobinuria (dark red urine, hemoglobinuria at the strip), renal failure (creatinine > 265 µmol/l and/or oliguria < 400 ml/d), hyper parasitaemia > 2% in endemic areas where transmission is low and > 5% in endemic areas where transmission is stable and high intensity, jaundice associated with an attack of another vital organ [2]. In France, about two hundred serious forms are recorded per year resulting in about twenty deaths [3]. In Guinea, one study recorded 54 cases of severe malaria during a 12-month

period [4]. To our knowledge, no study on severe malaria has been conducted in the intensive care unit of Tambohobe-Fianarantsoa University Hospital. The objective of this study is to determine the epidemiological, clinical and evolutionary profile of severe malaria cases.

Patients and Methods

This was a retrospective descriptive study carried out over a 36-month period, from January 2015 to December 2017, in cases of severe adult malaria treated in the Multipurpose Resuscitation Unit of Tambohobe-Fianarantsoa University Hospital. We used the Carestart™ Malaria HRP2/pLDH Malaria Rapid Compression Test (RDT) to confirm the diagnosis of malaria. The severity criteria used for diagnosis are those defined by WHO in 2000 and modified in 2010 [1,2].

The criteria for non-inclusion were: Plasmodium infection without severity criteria defined by WHO in 2000 and modified in 2010, infectious syndrome with signs of clinical and laboratory severity with a negative malaria RDT.

CHU Tambohobe-Fianarantsoa receives patients from the highlands and east coast of Madagascar. In other words, epidemiologically, the endemic area is in the equatorial facies on the east coast, where malaria is most prevalent, characterized by high perennial transmission and the non-endemic area in the highlands. For this purpose, we have studied the following parameters: age, sex, the time taken to take charge of the intensive care unit (the time between the onset of signs of seriousness and the arrival at the intensive care unit), the activity, the origin (highlands or East Coast), the notion of stay in the zone where the transmission is strong and perennial, the duration of the coma for the living patients (the period between the beginning of the specific treatment and the return of the consciousness), clinical signs of severity, biological signs of severity, the antimalarial drug used (quinine or artesunate), and mortality.

The data were collected on a pre-established farm return from the records and medical records of inpatients for severe malaria. Data entry was done from the Excel software. Data was analyzed using SPSS 20.0 software. The Chi-square test was used to investigate the existence of association between two qualitative variables. A difference was considered significant for a value of p less than 0.05.

Results

During the 36-month study period, 123 patients were hospitalized for severe malaria in the multipurpose intensive care unit of the Tambohobe-Fianarantsoa Teaching Hospital. The average age was 33.3 years with extremes of 15 to 84 years. Severe malaria was predominantly male (69.9%, sex ratio = 2.3). The majority of patients resided in the central uplands (n = 113, 91.9%). The notion of stay in an endemic zone was noted in 68 patients (55.3%). The patient sector was the primary sector in 70 cases (56.9%). Patients were referred by the basic and district health center in 68 cases (55.3%). The majority of patients (71.5%) came to the resuscitation department after the 24th hour of the onset of signs of severity. The antimalarial used was intravenous quinine in 64 cases (52%). The characteristics of the patients are summarized in table 1. The clinical signs of severity observed are summarized in table 2. Coma was the main clinical sign of severity (n = 96, 78%) followed by prostration (n = 27, 22%), seizure (n = 23, 18.7%) and renal failure (n = 16, 13%). After the initiation of antimalarial treatment (quinine or artesunate), comatose patients were awakened in less than 24 hours in 33 cases (34.4%), 24 to 48 hours in 34 cases (35.4%). The return of consciousness (Glasgow 15) was faster for intravenous artesunate patients (p = 0.041) (Table 3). The mortality was not related to the antimalarial used (p = 0.362) (Table 4). We recorded 2 cases of severe malaria among pregnant women with a 100% mortality rate. The mortality rate during the study period was 33.9% in 2015, with a peak in 2016 (50%) and 34.4% in 2017.

Parameters		
Average age (year)	**33,3**	
	Number (n)	**Frequency (%)**
Sex		
Male	86	69.9
Female	37	30.1
Residence		
Central Highlands	113	91.9
East Coast	10	8.1
Activity area		
Students	12	9.8
Primary	70	56.9
Secondary	13	10.6
Tertiary	28	22.8
Reference n (%)		
True referred	68	55.3
Referred auto	55	44.7
Duration of care in resuscitation n (%)		
Less than 24 hours	25	20.3
24 to 48 hours	53	43.1
More than 48 hours	45	36.6
Antimalarial used n (%)		
Quinine	64	52.0
artesunate	59	48.0
Evolution n (%)		
Favorable	76	61.8
Death	47	38.2

Table 1: *Patient characteristics (n = 123) reduction diminution.*

Clinical signs of severity	Number (n)	Percentage (%)
Glasgow score modified < 10	96	78.0
Prostration	27	22.0
Repeated generalized seizures	23	18.7
Oligurie	16	13.0
State of shock	14	11.4
Anemia	13	10.6
Respiratory distress	8	6.5
abnormal bleeding	7	5.7
Hemoglobinuria	4	3.3
Icterus	3	2.4

Table 2: *Clinical signs of severity.*

Time (hour)	< 24	24 - 48	48 - 72	72 - 96	More than 96	Total	P-value
Artesunate n (%)	18 (40)	20 (44.4)	3 (6.7)	1 (2.2)	3 (6.7)	45 (100)	0.041
Quinine n (%)	15 (29.4)	14 (27.5)	10 (19.6)	7 (13.7)	5 (9.8)	51 (100)	

Table 3: *Comatose patient consciousness return according to the antimalarial used.*

Antipaludeen	Survivor	Death	Total	P value
Artesunate n (%)	34 (57.6)	25 (42.4)	59 (100)	0.362
Quinine n (%)	42 (65.6)	22 (34.4)	64 (100)	

Table 4: *Evolution according to the antimalarial used.*

Discussion

This study determined that severe malaria affects mainly young and predominantly male subjects. The majority of patients resided in the central highlands. Severity criteria mainly represented coma. The return of consciousness was faster in patients treated with artesunate than those treated with quinine. The mortality of severe malaria was very high.

Male dominance was found in African literature [5-7]. The average age of our 33.3 year old patients is comparable to those in African studies. In Burkina-Faso in 2003 and Madagascar in 2009, studies reported the average age of patients aged 29.2 and 35.3 respectively [7,8]. In Africa, severe adult malaria mainly affects young people. The young population is more dynamic and more exposed to travel [9]. In our study, severe malaria mainly affected residents of the central uplands (n = 113, 91.9%). In the central highlands of Madagascar, malaria is unstable [10]. Residents of the central highlands lack protective immunity. Antimalarial premunition is acquired gradually during repeated re-infestations. In other words, the subject living in an endemic area was likely to acquire some resistance to malaria. This protective immunity is called premunition [11].

In addition, the notion of living in a malaria-endemic area (east coast) in 68 patients is a factor in the occurrence of severe malaria. The non-immune status of patients promotes the onset of the severe and potentially fatal form [12]. For patients living in the central highlands who have not been in a malaria-endemic area, the occurrence of the severe form could be explained by delayed management and self-medication. Untreated, untreated malaria could progress to severe malaria within 36 to 48 hours of onset of symptoms [13].

In our study, coma was the main clinical sign of severity. Studies have reported the prevalence of neurological signs of severity in severe malaria [5,7,8]. Rakotoarivelo., *et al*. [7] recommended the search for malaria in the presence of any febrile neurological disorder. In our study, 59 patients (48%) were treated with artesunate. Artesunate was used for the first time in 2016 in the intensive care unit of Fianarantsoa University Hospital. In 2005, the first large randomized study comparing intravenous artesunate with intravenous quinine showed that artesunate was superior to quinine in the treatment of severe malaria [14]. It was in 2006 that the WHO recommended artesunate as the treatment of choice for severe adult malaria [15]. In our study, the delay in the introduction of artesunate in the treatment of severe malaria is explained by the lack of supply of this drug. In our study, the return of consciousness was faster for patients treated with artesunate compared to those treated with quinine.

An AQUAMAT study [16] reported that development of coma after admission and deterioration of the coma scale was significantly lower in the artesunate group than in the quinine group. In our study, mortality reduction in patients treated with artesunate was not significant. This could be explained by the late arrival and in poor condition of patients in the hospital. A larger prospective study would re-evaluate these results. However, in 2012, an updated review of the Cochrane Collaboration collecting 1664 adult patients (age > 15-16 years) in five trials confirmed the superiority in terms of mortality of artesunate on quinine [17].

The mortality rate of 38.2% found in our study is very high compared to the literature. In Madagascar, in a university hospital in 2009 and in Burkina-Faso in 2003, authors reported mortality rates of 11.5% and 8%, respectively [7,8]. In our study, the 2 cases of severe malaria among pregnant women were all dead. Malaria is responsible for significant mortality in pregnant women [18].

Conclusion

The rapid malaria diagnostic test should be systematic in the presence of febrile disorders of young subjects, especially males. Severe malaria is marked by high mortality, especially among pregnant women. A similar study is needed to determine the predictive factors for severe malaria mortality in our intensive care unit.

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