



**ORIGINAL RESEARCH PAPER**

**Medical Science**

**MORTALITY FACTORS FOR SEVERE MALARIA IN ADULTS IN THE INTENSIVE CARE UNIT OF TAMBOHOBE-FIARANTSOA TEACHING HOSPITAL.**

**KEY WORDS:** Predictive factor, mortality, malaria, fianarantsoa

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<b>ABSTRACT</b>	<b>Objective:</b> To determine predictive factors for severe adult malaria mortality in Teaching Hospital of Fianarantsoa.
	<b>Patients and methods:</b> This is a descriptive retrospective study carried out over a period of 36 months, dealing with cases of severe adult malaria, treated at the Medical-Surgical Intensive Care Unit of the Tambohobe-Fianarantsoa Teaching Hospital. The patients were divided into two groups: a group of survivors and a group of deceased persons. A comparative study was carried out by analyzing: the age of the patients, the gender, the time of care in intensive care, the sector of activity, the origin, the clinical signs of gravity, the biological signs of gravity, the reference, the antimalarial used.
	<b>Results :</b> We selected 123 patients. Age greater than 45 years was associated with mortality ( $p = 0.011$ ). The mortality of severe malaria was predominantly male ( $n = 34/47, 72.3\%$ ) ( $p = 0.645$ ). The delay in treatment beyond 24 hours was significantly related to mortality ( $p < 0.0001$ ) and patient self-reference ( $p < 0.0001$ ). Respiratory failure was found in the 8 patients (6.5%) with a mortality rate of 87.5% ( $p = 0.003$ ).
	<b>Conclusion:</b> Predictors of severe malaria mortality were: age, delayed management, patient self-referral, and respiratory failure.

**Introduction**

In 2011, WHO experienced a significant decline in global malaria mortality rates over the last 10 years [1]. In France, mortality due to severe imported malaria remains in the order of 5 to 10% despite optimal means [2, 3]. In Burkina-Faso, in 2003, a study reported a malaria mortality rate of 8% [4]. In Madagascar, in 2009, authors reported a mortality rate of 11.5% [5]. No studies have addressed the mortality factors of severe malaria in adults in teaching hospital Tambohobe Fianarantsoa. This information is essential to improve care. Our objective is to identify predictive factors of mortality of severe adult malaria in hospital of Fianarantsoa.

**Patients and methods**

This was a retrospective descriptive study carried out over a period of 36 months, from January 2015 to December 2017 on cases of severe adult malaria, treated at the Medical-Surgical Intensive Care Unit of Tambohobe-Fianarantsoa Teaching Hospital, Madagascar. Severe malaria was defined by the presence of parasitaemia in the majority of cases of asexual forms of Plasmodium falciparum and at least one clinical or biological criterion of severity defined by the WHO in 2000 and modified in 2010. 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, state of shock (PAS  $< 80$  mmHg and peripheral signs of circulatory insufficiency), abnormal bleeding, hemoglobinuria (dark red urine, strip hemoglobinuria), renal failure (creatinine  $> 265\mu\text{mol/L}$  and / or oliguria  $< 400\text{ml/day}$ ), hyper parasitaemia  $> 2\%$  in endemic areas where transmission is of low intensity and  $> 5\%$  in endemic areas where transmission is stable and of high intensity, jaundice associated with involvement of another vital organ. We used the Carestart™ Malaria HRP2 / pLDH Combo Rapid Diagnostic Test (RDT) to confirm the diagnosis of malaria. 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 but a negative malaria RDT.

These patients were divided into two groups: a group of survivors and a group of deceased. A comparative study was carried out by analyzing: the age of patients, divided into two groups: patients under 45 and those over 45; gender ; the duration of care in intensive care (defined as the time elapsed between the beginning of the signs of gravity and the arrival at the resuscitation department); It has been divided into two parts: lower and higher than 24 hours; the primary economic activity sector (breeder, farmer); secondary (craftsman, industrial worker); tertiary (service sector), provenance (central highlands, east coast); clinical signs of severity; biological signs of severity; the reference mode was divided into two: true referred (patient transferred or evacuated by a basic or district health center or by a medical office to a referral center) and referred self (patient presenting directly to the Tambohobe Teaching Hospital) ; the antimalarial used (quinine or artesunate).

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 using 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 mortality rate during the study period was 38.2% ( $n = 47$ ). Table I presents the sociodemographic characteristics of surviving patients and deceased patients. The average age of surviving and deceased patients was 30.5 years and 37.8 years, respectively. The risk of death increased significantly with age. Age greater than 45 years was associated with mortality ( $p = 0.011$ ). The mortality of severe malaria was predominantly male ( $n = 34, 72.3\%$ ) ( $p = 0.645$ ). Time limit of treatment beyond 24 hours ( $p < 0.0001$ ) and patient self-

referral ( $p < 0.0001$ ) were significantly related to mortality. On the other hand, there was no significant link between malaria lethality and place of residence ( $p = 0.577$ ) and sectors of economic activity ( $p > 0.05$ ).

Mortality was not related to the antimalarial used ( $p = 0.362$ ). The clinico-biological characteristics of patients' severity are summarized in Table II. Coma with Glasgow less than 10 was the main clinical sign of severity with a mortality rate of 36.4%. It was not associated with mortality ( $p = 0.099$ ). Respiratory failure was found in the 8 patients (6.5%) with a mortality rate of 87.5%. Respiratory failure was significantly associated with mortality ( $p = 0.003$ ).

**Table I: Sociodemographic Characteristics of Surviving Patients and Deceased Patients**

Parameters	Deceased n (%)	Survivors n (%)	Value p
Age over 45 years	65 (67,7)	31 (32,3)	0,011
Origin	44 (38,9)	69 (61,1)	0,577
Central Highland	3 (38,2)	7 (61,8)	
East Coast			
Sector of economic activity			
Primary sector	29 (35,4)	53 (64,6)	0,399
Secondary sector	4 (30,8)	9 (69,2)	0,559
Tertiary sector	14 (50)	14 (50)	0,144
Support time	1 (4)	24 (96)	0,0001
Less than 24 hours	46 (46,9)	52 (53,1)	
More than 24 hours			
Reference	14 (21,2)	52 (78,8)	0,0001
True referred	33 (57,9)	24 (42,1)	
Self-referred			

**Table II: Clinico-biological characteristics of surviving and deceased patients**

Signs of gravity	Deceased n (%)	Survivors n (%)	Value p
Glasgow score <10	33 (36,4)	63 (63,6)	0,099
Prostration	12 (48)	13 (52)	0,259
Seizures	7 (30,4)	16 (69,6)	0,395
Oliguria	5 (31,2)	11 (68,8)	0,539
State of shock	8 (57,1)	6 (42,9)	0,121
Anemia	7 (53,8)	6 (46,2)	0,220
Respiratory failure	7 (87,5)	1 (12,5)	0,003
Abnormal bleeding	2 (28,6)	5 (71,4)	0,599
Hemoglobinuria	2 (50)	2 (50)	0,622
Icterus	2 (66,7)	1 (33,3)	0,304

**Discussion**

This study made it possible to determine the predictive factors of mortality of severe malaria. Predictors of mortality observed were age > 45 years, delayed management, patient self-referral, and respiratory failure.

The mortality rate (38.2%) of severe malaria in our study was higher compared to the literature. In Burkina-Faso in 2003, in Madagascar, in a hospital of the capital in 2009, in Senegal in 2010, authors reported mortality rates of 8%, 11.5% and 17% respectively [4, 5, 6].

The very high mortality rate in our study was significantly related to delayed treatment. Several factors could be the cause of delayed care, including self-medication and self-referrals. In the rural area, self-medication is the behavior of first resort. Patients buy the drugs from untrained local vendors. In Madagascar in 2009 and in Côte d'Ivoire in 2004, studies reported that 23% of patients with severe malaria practiced self-medication [5, 7]. In our study, almost half of the patients (46.3%) presented themselves directly to the Tambohobe Teaching Hospital. This patient self-referral practice was significantly related to mortality. Patients decide to stay in control of their lives and are unaware of the severity of their illness.

This attitude results in late resorting to modern health structures. The diagnosis and early treatment of malaria access remain the only guarantors of a favorable evolution [8]. In our study, the persistence of coma beyond 24 hours motivated peripheral health facilities to refer patients. Referred patients received the recommended dose of antimalarial prior to transfer. As a result, the prognosis of referred patients was better compared to self-referred patients.

In our study, age over 45 years was a factor of poor prognosis. Studies have found that age is a factor of poor prognosis [3, 6]. The high mortality of the subjects over 45 years could be explained by a neglected morbid association. Indeed, it is important to find and manage comorbidities in all cases of malaria especially in the elderly [9]. In our study, the higher mortality rate of patients with respiratory failure of 87.5% versus 45.2% reported by Breenel F et al [3] could be explained by the lack of respiratory support equipment necessary for the management of Acute Respiratory Distress Syndrome (ARDS). As a result, staffing this equipment could improve the prognosis of our patients. As in our study, respiratory distress was significantly related to mortality [3, 6, 10]. During severe malaria, the lung is particularly fragile and many factors participate to hypoxemia: parasite-induced lesional edema, excessive filling in case of shock, excessive hydrosodea intake in case of anuria, pneumopathie bacterial or inhalation, edema associated with bacteremia [11, 12, 13].

Unlike Brueenel et al [3], the classical notion of the association between coma depth and mortality has not been verified in our study. In our study, malaria was confirmed only by a malaria RDT. The introduction of malaria RDTs in all health facilities in Madagascar allows the rapid diagnosis and treatment of patients with malaria. The absence of accurate diagnosis in peripheral health facilities may lead to a prescription that does not comply with the recommendation [5]. This means of diagnosis is developing and becoming more and more efficient [14]. One study reported a 3.6% to 86% increase in the diagnostic confirmation of RDT [15]. However, it does not currently allow evaluation of parasitaemia [16]. Parasitological diagnosis should be carried out primarily by thin smear and thick smear [17]. This study was limited by the absence of parasitaemia and complete biological assessments.

**Conclusion**

This study identified predictors of severe malaria mortality such as age, delayed management, patient self-referral and respiratory failure.

A similar prospective study is needed to look for other mortality factors of severe malaria.

**REFERENCES**

- World Health Organization. World malaria report 2011. Geneva: WHO, 2011 [http://www.who.int/malaria/world\\_malaria\\_report\\_2011/en/](http://www.who.int/malaria/world_malaria_report_2011/en/)
- Société de pathologie infectieuse de langue française, Collège des universitaires de maladies infectieuses et tropicales, Société de réanimation de langue française. Recommendations for clinical practice. Management and prevention of imported Plasmodium falciparum malaria. (Revision 2007 of the 1999 Consensus conference). Med Mal Infect 2008;38:39-117.
- Bruneel F, Tubach F, Corne P et al. Severe imported falciparum malaria: a cohort study in 400 critically ill adults. PLoS One 2010;5:e13236.
- Diallo AH, Guiguemde TR, Ki-Zerbo G. Aspects cliniques et parasitologiques du paludisme grave de l'adulte en milieu urbain de Bobo-Dioulasso (Burkina-Faso). Bull Soc Pathol Exot. 2003;96(2):99-100.
- Rakotoarivelo RA, Raveloson HFR, Andrianasolo R et al. Aspects cliniques et thérapeutiques du paludisme grave de l'adulte en milieu hospitalier à Antananarivo, Madagascar. Bull Soc Pathol Exot. 2009;102(4):215-216.
- Diop SA, Ndour CT, Dia NM et al. Aspects actuels du paludisme grave de l'adulte à la clinique des maladies infectieuses du CHNU de Fann de Dakar (Sénégal). Médecine d'Afrique Noire. 2010;57(4):193-197.
- Eholie SP, Ehui E, Adou-Bryn K, Kouame KE et al. – Paludisme grave de l'adulte autochtone à Abidjan (Côte d'Ivoire). Bull Soc Pathol Exot, 2004, 97, 340-344. <http://www.pathexo.fr/pages/articles/2004/2004-T97-5/2551.html>
- Godet C, Le Moal G, Rodier MH et al. Paludisme d'importation : il faut renforcer le message de prévention. Med Mal infect. 2004;34(11):546-54.
- Savado M, Ouédraogo A, Sondo KA. Aspects épidémiologique, cliniques et thérapeutiques du paludisme au Centre Hospitalier Yalgado Ouédraogo de Ouagadougou, Burkina Faso. Méd Afr Noire. 2014;61(7):373-378.
- Kouamé K, Brouh Y, Soro L et al. Paludisme grave chez les expatriés en réanimation à Abidjan. Ann Fr Anesth Réanim. 2002;21:359-364.
- Société de pathologie infectieuse de langue française, Collège des universitaires de maladies infectieuses et tropicales, Société de réanimation de langue française. Recommendations for clinical practice. Management and prevention of imported

- Plasmodium falciparum malaria. (Revision 2007 of the 1999 Consensus conference). *Med Mal Infect* 2008;38:39-117.
- 12- World Health Organization. Guidelines for the treatment of malaria (second edition). Geneva: WHO, 2010 [http:// www.who.int/ malaria/publications/ atoz/ 9789241547925/ en/index.html](http://www.who.int/malaria/publications/atoz/9789241547925/en/index.html)
  - 13- Taylor WR, Hanson J, Turner GD, White NJ, Dondorp AM. Respiratory manifestations of malaria. *Chest* 2012;142:492-505.
  - 14- Stauffer WM, Cartwright CP, Olson DA et al. Diagnostic performance of rapid diagnostic tests versus blood smears for malaria in US clinical practice. *Clin Infect Dis* 2009;49:908-13.
  - 15- Thiam S, Thior M, Faye B et al. Major reduction in anti-malarial drug consumption in Senegal after nation-wide introduction of malaria rapid diagnostic tests. 2011; volume 6. [www.plosone.org](http://www.plosone.org).
  - 16- World Health Organization. Malaria Rapid Diagnostic Test Performance. Results of WHO product testing of malaria RDTs: Round 3 (2010-2011). Geneva : WHO, 2011 [http:// www.who.int/malaria/publications/atoz/9789241502566/ en/index.html](http://www.who.int/malaria/publications/atoz/9789241502566/en/index.html)
  - 17- Société de pathologie infectieuse de langue française, Collège des universitaires de maladies infectieuses et tropicales, Société de réanimation de langue française. Recommendations for clinical practice. Management and prevention of imported Plasmodium falciparum malaria. (Revision 2007 of the 1999 Consensus conference). *Med Mal Infect* 2008;38:39-117.