

# Neurological Complications Associated with Severe Malaria at the Albert Royer National Children's Hospital, Dakar, Senegal

Aminata Mbaye<sup>1\*</sup>, Rokhaya Diagne<sup>2</sup>, Ndeye Fatou Sow<sup>3</sup>, Awa Kane<sup>1</sup>, Mouhamadou Taib Babou<sup>1</sup>, Pascale Ndongo Njock<sup>1</sup>, Papa Moctar Faye<sup>1</sup>, Moustapha Ndiaye<sup>2</sup>, Ousmane Ndiaye<sup>1</sup>

<sup>1</sup>Albert Royer Children's Hospital (CHNEAR), Dakar, Senegal

<sup>2</sup>Neurology Department, Fann National University Hospital, Dakar, Senegal

<sup>3</sup>Dalal Jam Hospital, Dakar, Senegal

Email: \*drmbayeaminata@gmail.com

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## Abstract

**Introduction:** Neurological complications associated with severe malaria constitute a medical emergency with high morbidity and mortality. The objective of our study was to determine their epidemiological, clinical, paraclinical, and therapeutic aspects. **Methodology:** This was a retrospective, descriptive, and analytical study conducted at Albert Royer National Children's Hospital in Dakar from January 1, 2021 to December 31, 2022. **Results:** We included 53 patients, of whom 32 were male. The mean age was 5.64 years, ranging from 7 months to 15 years. Thirty-nine patients (73.6%) were from Dakar and 26.4% from other regions. Only 9 patients used long-lasting mosquito bed nets, and all resided in the region of Dakar. The mean consultation time was 3.8 days. Prostration was the most common neurological sign (41.5%), followed by seizures (35.8%). We observed anemia in 47 patients (90%), hyperleukocytosis in 32 patients (60.4%) and thrombocytopenia in 29 patients (54.7%). Eight patients (31.4%) had renal failure with a mean glomerular filtration rate of 94.31 ml/min/1.73m<sup>2</sup>. For the parasitological diagnosis of malaria, the rapid diagnostic test was positive in 50 patients (94.33%) and the thick blood smear was positive in all patients, with a mean parasite density of 15,288 p/ml. All children were hospitalized for a mean duration of 7 days and injectable artesunate was the most used molecule (94.3%). The outcome was favorable in 43 patients (81%), with complete recovery, and 10 children (19%) died. We did not find a statistically significant p-value explaining risk of death. **Conclusion:** Neurological complications of severe malaria require early and appropriate management to reduce morbidity and mortality.

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## Keywords

Severe Malaria, Neurological Form, Children, CHNEAR

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### 1. Introduction

Severe malaria is defined by the presence of *Plasmodium falciparum*, *knowlesi*, or *vivax* trophozoites in the blood, associated with clinical and laboratory manifestations, all grouped into WHO severity criteria. Malaria is a public health concern with a case fatality rate between 9% and 14% [1]. With the emergence of the COVID-19 pandemic in 2019, malaria prevention campaigns declined, limiting access to essential prevention tools and preventing early diagnosis and treatment. The overall objective of our study was therefore to determine the current hospital prevalence of neurological complications associated with severe malaria.

### 2. Materials and Methods

This is a retrospective, descriptive, and analytical single-center study conducted from January 1, 2021 to December 31, 2022, at the Albert Royer National Children's Hospital (CHNEAR) in Dakar. The study included any patient under 15 years of age with a positive rapid malaria diagnostic test and/or a thick blood smear and neurological signs according to the 2015 WHO criteria [2]. Patients with incomplete or unusable medical records were not included.

### 3. Results

During the study period, we identified 107 patients with severe malaria, 49.53% of whom had neurological complications. The mean age was 5.6 years (7 months to 15 years). Thirty-two patients were male (60.4%), with a sex ratio of 1.52. The most common age range was 7 months to 5 years (47.16%), followed by 5 to 10 years (35.8%) and 10 years (17%).

Thirty-nine patients (73.6%) resided in Dakar, 9 patients (17%) in the Dakar suburbs, 3 (5.7%) in Guinea Conakry, and 2 (4%) outside of Dakar region. Forty-five children (84.9%) were up-to-date on their immunization status according to the Expanded Program of Immunization (EPI), and eight children (15.1%) had incomplete immunization status. Regarding the patient's comorbidities, one patient had sickle cell trait AS, another had severe acute malnutrition, and another had cerebral palsy. Only nine patients from Dakar region used long-lasting mosquito bed nets.

#### 3.1. Clinical Characteristics

The mean time between the onset of clinical signs and consultation was 3.8 days (1 to 10 days). Prostration was the most common neurological sign in 22 children (41.5%), followed by seizures (35.8%), obtundation (15%), coma (9.4%), and neck

stiffness (5.7%). Fever was observed in all our patients and respiratory distress in 23 patients (43.4%) (Table 1).

**Table 1.** Clinical signs of severe malaria in our patients.

| Clinical signs of severe malaria | Effective | Percentage (%) |
|----------------------------------|-----------|----------------|
| Impaired consciousness           | 13        | 24             |
| Prostration                      | 22        | 41.5           |
| Convulsions                      | 19        | 35.8           |
| Respiratory distress             | 23        | 43.4           |
| Jaundice                         | 10        | 19             |
| Macroscopique hemoglobinuria     | 7         | 13.3           |
| Circulatory collapse             | 2         | 4              |
| Hypoglycemia                     | 1         | 2              |

### 3.2. Paraclinical Characteristics

The rapid diagnostic test was positive in 50 patients (94.33%) and the thick and thin blood films were positive in all patients (*Plasmodium falciparum*). The mean parasite density was 15,288 p/ml [36 - 210,450 p/ml] (Table 2).

**Table 2.** Mean parasite density according to patient age.

| Age range            | Effective | Mean parasite density (p/ml) |
|----------------------|-----------|------------------------------|
| [7 months - 2 years] | 4         | 3866                         |
| [2 - 5 years]        | 21        | 25,599                       |
| [5 - 10 years]       | 19        | 8180                         |
| ≥10 years            | 9         | 11,312                       |

Forty-nine patients (92.5%) had positive CRP, 47 patients (88.7%) had anemia, of which 29 patients (54.7%) had a hemoglobin level of <8 g/dl. 29 patients had thrombocytopenia (Table 3).

**Table 3.** Biological abnormalities observed in patients.

| Biological abnormalities                  | Effective | Percentage (%) |
|---|-----------|----------------|
| Positive CRP (>6 mg/l)                    | 49        | 92.5           |
| Anemia                                    | 47        | 88.7           |
| Leukocytosis                              | 32        | 60.4           |
| Thrombocytopenia                          | 29        | 54.7           |
| Hyponatremia                              | 19        | 35.8           |
| Increase serum creatinine                 | 8         | 15             |
| Elevated transaminases (ASAT, ALAT)       | 3         | 5.6            |
| Hyperbilirubinemia (total and conjugated) | 2         | 3.7            |

### 3.3. Therapeutic and Clinical Outcome Characteristics

All children were admitted with a mean duration time of 7 days (range 1 to 15 days). Injectable artesunate was the most frequently used medication (94.3%), followed by artemether (5.7%). Eleven patients received anticonvulsants. Clinical outcome was favorable in 43 patients (81%). 10 children (19%) died. No death risk factors were identified (**Table 4**).

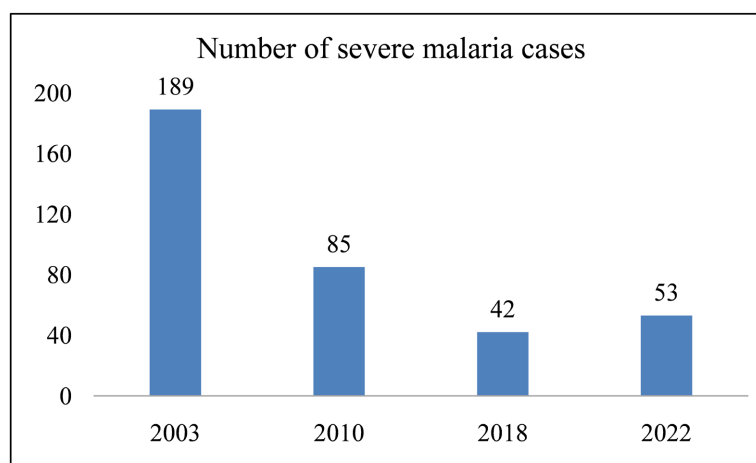
**Table 4.** Death risk factors.

|                                |                 | Death | Recovery | P     |
|--------------------------------|-----------------|-------|----------|-------|
| Age range                      |                 |       |          |       |
| -                              | [0 - 5 years]   | 6     | 19       | 0.291 |
| -                              | [5 - 10 years]  | 2     | 17       | 0.217 |
| -                              | [10 - 15 years] | 2     | 7        | 0.558 |
| Impaired consciousness         | No              | 5     | 17       | 0.345 |
|                                | Yes             | 5     | 16       |       |
| Respiratory distress           | No              | 7     | 39       | 0.114 |
|                                | Yes             | 3     | 4        |       |
|                                | Yes             | 2     | 3        |       |
| Anemia < 8 g/dl                | Non             | 5     | 19       | 0.505 |
|                                | Oui             | 5     | 24       |       |
| Parasite density < 5000        | Non             | 2     | 19       | 0.147 |
|                                | Oui             | 8     | 24       |       |
| Time to presentation < 5 jours | No              | 3     | 5        | 0.163 |
|                                | Yes             | 7     | 38       |       |

## 4. Discussion

According to studies conducted in Senegal, neurological complications of severe malaria are very common. In our study, neurological complications represent 49.53% of all severe forms of malaria. This frequency is lower than that found in the literature, with a frequency between 75% and 95% [3] [4]. This is a characteristic of countries with low malaria endemicity, whereas in Central Africa, areas of high endemicity, anemic forms dominate [5]. Between 2020 and 2021, 58% of the Senegalese population had access to long-lasting insecticide mosquito bed nets, of which 46% reported sleeping under a mosquito bed net [6]. However, in our study, their use was very low (0.17%), unlike that found in the literature and these patients were all coming from Dakar region.

In Senegal, from 2003 until 2018, there has been a drastic decrease in the number of severe malaria cases in its neurological form (**Figure 1**). However, between 2021 and 2022, there has been an increase in cases, with 53 patients collected. This increase could be explained by the occurrence of the COVID-19 pandemic, which coincides with a decrease in preventive measures against malaria in favor of COVID-19.



**Figure 1.** Number of severe malaria cases per year in Senegal.

Children under 5 years of age were the most concerned in our study, with a frequency of 47.2%. Our results are similar to those of Camara *et al.*, who found 114 cases (75%) in this age group, as well as Gueye, who reported 23 cases (52.25%) in his study carried out at CHNEAR between 2019-2020 [7]. This could be explained in particular by the late acquisition of antimalarial immunity (premunity), which is strongly linked to the level of transmission in the region. Indeed, Senegal is located in malaria endemic zone II. Our study was conducted in an urban area where the level of transmission is low. As a result, the acquisition of immunity was late in our patients. This could also explain the severe forms in this age group.

According to studies, the average time to consultation varies between 4.4 and 6 days, while in our study, we observed a shorter time of 3.8 days [8]. This long time to consultation constitutes a factor of poor prognosis [9]-[11].

There is no relationship between parasite density (high or low) and the occurrence of neurological signs, with a p-value of 0.147 for a density varying between 36 - 210,450 parasites per microliter, and in other data between 66 - 96,480 parasites per microliter [7].

In our study, as in the literature, other signs of severe malaria can be found at variable frequencies, such as jaundice (26.5%) and anemia (21.6%). The neurological and anemic complications have a case fatality rate of 6.1% [12]. Four patients with neurological complications died, but we did not identify any poor prognostic factors associated with death. The neurological complications, especially cerebral malaria, are serious due to their lethality (12.8% and 14.3%), and the risk of long-term sequelae [13].

However, over the years, malaria-related morbidity and mortality in Senegal appear to have decreased, and this overall decline is confirmed by the results of the latest national hospital-based malaria survey [14]. With prompt and adequate management, clinical course and outcome of neurological complications of severe malaria are usually good, as described in our study, where the outcome was favorable in 81.1% of our patients.

## 5. Conclusion

As the world's leading endemic parasitic disease, malaria remains a public health priority in developing countries like Senegal. Despite progress in prevention and treatment, severe malaria is responsible for significant morbidity and mortality in Sub-Saharan Africa.

## Conflicts of Interest

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

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