

## **Clinical Prediction Models for Pediatric In-Hospital Death Risk in Congolese Severe malaria Children Using Machine Learning Based-Algorithms**

### **I. FOCUS OF THE MANUSCRIPT**

Severe malaria (SM) is associated with a high risk of in-hospital death in resource-constrained countries. Improved risk-stratification methods can assist in referral decision-making and resource allocation. Investigators aim to 1) develop a prediction model for in-hospital death risk among children with severe malaria, compare its predictive performance to the current models, 2) validate previous models in our severe malaria population, and 3) assess the plasmodium-induced changes in clinical and biological parameters.

### **II. STUDY DESIGN**

- Type of study: Retrospective study of data collected prospectively during a period from January 30, 2017 to August 01, 2025.
- Study population: Children with severe malaria, admitted to the paediatric intensive care unit (PICU) of the Monkole Hospital Center (MHC) and the Kimbondo Pediatric Center (KPC), all in Kinshasa, DR.
- Inclusion criteria: Severe malaria children aged 2-9 years

### **III. STATISTICAL ANALYSIS PLAN**

#### **III.1. Descriptive statistics of the study population (Overall, Survivor and deceased children):**

##### Socio-demographic and anthropometric Data:

- Age
- Sex
- Geographical origin (district)

Data from Clinical Examination:

- Febrile episode
- Temperature
- Coma
- Blantyre coma scale
- Convulsions
- Pallor
- Jaundice
- Heart rate
- Respiratory rate
- Ketoacidosis respiration
- Hepatomegaly
- Splenomegaly
- Length of stay at PICU

Final Diagnoses and Antimalarial treatment

- Cerebral malaria
- Severe malaria Anaemia
- Severe respiratory malaria
- Antimalarial treatment using Artesunate
- Antimalarial treatment using Quinine

Laboratory Assessments

- PaCO<sub>2</sub>
- PaO<sub>2</sub>
- pH
- SBE
- Bicarbonate
- L-Lactate
- Glucose
- Potassium
- Sodium
- Calcium
- Magnesium
- Chlore
- Phosphore
- Blood urea nitrogen

- Creatinine
- Albumin
- Phosphate
- Hematocrit
- Total Bilirubin
- Parasitemia

### III.2. Approaches by objectives

**Objective 1.** To develop a prediction model for in-hospital death risk among children with severe malaria

- Study population and inclusion criteria: Severe malaria children aged 2-9 years
- Outcome (dichotomous): Death during hospitalization (Survivors = 0, Deceased = 1). The end of hospitalization is defined as death (patients who died) or recovery (patients who survived), assessed up to 1-week post-admission.
- Predictors: Data from socio-demographic, anthropometric, clinical examination and laboratory Assessments.

**Objective 2.** To validate previous models in our severe malaria population

- Study population and inclusion criteria: Severe malaria children aged 2-9 years
- Primary Outcome: Death during hospitalization (Survivors = 0, Deceased = 1)
- Secondary Outcome: Time-to-risk event (risk event = death = 1 and censored event = Survival = 0). The end of hospitalization is defined as death (patients who died) or recovery (patients who survived), assessed up to 1-week post-admission.
- Predictors: Data from socio-demographic, anthropometric, clinical examination and laboratory Assessments.

**Objective 3.** To assess the plasmodium-induced changes in clinical and biological parameters.

- Study population and inclusion criteria: Severe malaria children aged 2-9 years
- Primary Outcome: Death during hospitalization (Survivors = 0, Deceased = 1)
- Secondary Outcome: Multiple organ dysfunction (MOD  $\geq$  2 organ systems fail)
- Predictor: Parasitemia