Chapter

Malaria Lethality in Children under 5 Years of Age and Study of Risk Factors in MbujiMayi Paediatric Environment, a Neglected Deadly Epidemic in the Democratic of Republic of Congo

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Abstract

The objective of this study was to determine the risk factors for malaria lethality in the MbujiMayi paediatric environment, a follow-up study of hospitalised cases over 5 years was conducted between January 2016 and December 2020 in the four hospitals. The case rate was 6.9% for the total (139 cases of death for 2017 cases of severe malaria for 5 years,) and varied from year to year (10.7% in 2016 to 4.6% in 2020). Cox Proportional Risk Model results including significant covariates in multivariate analysis [HR (IC95%)]. In multivariate analysis, two models were considered. The case-fatality rate was independently associated with late arrival after 48 hours [3.1 (1.9–5.1); $p < 0.001$], types of pre-hospital recourse such as recourse to the church [1.4 (1.1–2.1),; $p = 0.042$) and tradipractor [3.2 (1.8–6.1); $p < 0.001$] for severe malaria, children under 12 months of age [1.8 (1.2–2.8); $p < 0.001$], those with circulatory collapse [2.6 (1.1–6.1); $p < 0.001$] and those in deep coma [1.9 (1.1–3.4); $p = 0.016$]. The second model with the number of associated syndromes, showed that the risk was 1.7 plus for children with a complex clinical picture, made up of the combination of several signs [1.7 (1.1–2.6); $p < 0.001$]. These results highlight the need for more information campaigns to encourage people to seek institutional care for malaria. Our results also suggest that prophylactic treatment may be advisable for children under 5 years of age.

Keywords: Severe malaria, lethality, child, Risk factors, MbujiMayi, RDC

1. Introduction

Malaria is the first global endemic parasitic disease and its transmission has been reported in about a hundred countries worldwide [1]. Africa is, by far, the most affected continent, twenty-nine countries accounted for 95% of malaria cases globally. Nigeria (27%), the Democratic Republic of the Congo (12%), Uganda (5%),

Mozambique (4%) and Niger (3%) accounted for about 51% of all cases globally Millions of people around the world still do not have access to malaria prevention and treatment, while most cases and deaths are neither reported nor recorded [1, 2]. In the Democratic Republic of Congo, malaria remains the leading cause of consultations, hospitalisations, and deaths. The 2019 National Malaria Control Programme report shows more than twenty-one million cases of malaria, including nineteen million cases of simple malaria and two million cases of severe malaria, as well as thirteen thousand seventy-two malaria-related deaths, including nine thousand eight hundred and fifty-five children under the age of five, i.e., 75% [3]. However, some progress has been noted over the last decade. Proportional morbidity in children under five years of age has decreased from 41% in 2010 to 37% in 2014. Infant mortality fell from 92‰ in 2010 to 58‰ in 2014. Despite this progress, the disease remains endemic in all twenty-six provinces of the country [4].

Many provinces are affected Thus, the proportion of positive children is highest in the Kasai (29% in Kasai Oriental, 32% in Kasai Occidental), Katanga (32%), Maniema (34%) and especially in Province Orientale (38%) [5, 6].

Malaria constitutes a heavy socio-economic burden, especially in MbujiMayi (Kasai-Oriental), where a large part of the population has been destitute since the fall of the Bakwanga mining company (Miba). In this context, access to health care is a problem for the population, which is why many Congolese people in MbujiMayi have been resorting to self-medication and others to traditional medicine to date [6].

The DRC is still paying a heavy price due to malaria. Every hour, somewhere in DRC, "at least 3 families are bereaved because of malaria and more than two children lose their lives due to malaria" [6]. In addition to the coronavirus pandemic that the DRC has been facing since 10 March 2020, the burden of severe malaria in terms of death, especially in the under-five age group, remains considerable. The country is facing an increase in the epidemiological trend of malaria and malaria deaths despite efforts to step up interventions. The development of factors associated with high malaria lethality in children would help to better guide rapid and effective management.

2. Objectives

The objectives were fixed:

- Estimate the breakdown of survival time for children under 5 years of age with severe malaria over the past 5 years,
- determine the risk factors associated with lethality explained by severe malaria in hospitalised children over the past 5 years.

3. Methods

3.1 Context of the study

The town of MbujiMayi is the provincial capital of Kasai-Oriental, which is one of the 26 provinces that make up the Democratic Republic of Congo (DRC). After the new division, this town has 10 health zones considering their demographic density, each of which has a general referral hospital. It comprises 167 health areas (AS), 166 of which are covered by functional health centres. This city covers an area of 168,126 Km2. This city is in the North and is naturally bordered by the Bipemba River, from

its source to its confluence with the Muya River and from the latter downstream to its mouth in the Mbuji-Mayi River, thus forming the border with the Territory of Lupatapata. South bounded by the Kanshi River upstream to its point of intersection with the Bena Mbaya Road, a locality located in the Lupatapata Territory.

To the East by the Mbuji-Mayi River upstream to its confluence with the Kanshi River bordering the Katanda et Tshilenge Territory. To the West by the Bena Mbaya road up to the limit of the Makala village. From there to its easternmost point and from this point, straight ahead to the source of the Bipemba River bordering the Lupatapata Territory. Four hospitals were selected and are represented by black dots in **Figure 1**.

3.2 Study environment

The study was performed in four reference hospitals in MbujiMayi. we chose 3 referral hospitals and a provincial hospital: The general referral hospital Saint Jean Baptiste in the Bonzola health zone, Dipumba which is a provincial hospital, the general referral hospital Présbytérien in the Dibindi health zone and the general referral hospital Christ-Roi in the Bipemba health zone. The choice was guided by their high attendance of children aged 0–59 months suffering from severe malaria.

3.3 Target population

This study considered statistical units, all children aged 0–59 months having been admitted to the paediatric ward of three general referral hospitals and a provincial hospital for severe *Plasmodium falciparum* malaria confirmed in the period of our research. The diagnoses were confirmed by identification of the hematozoan parasite via thick smears or blood smears and diagnostic immunological tests with

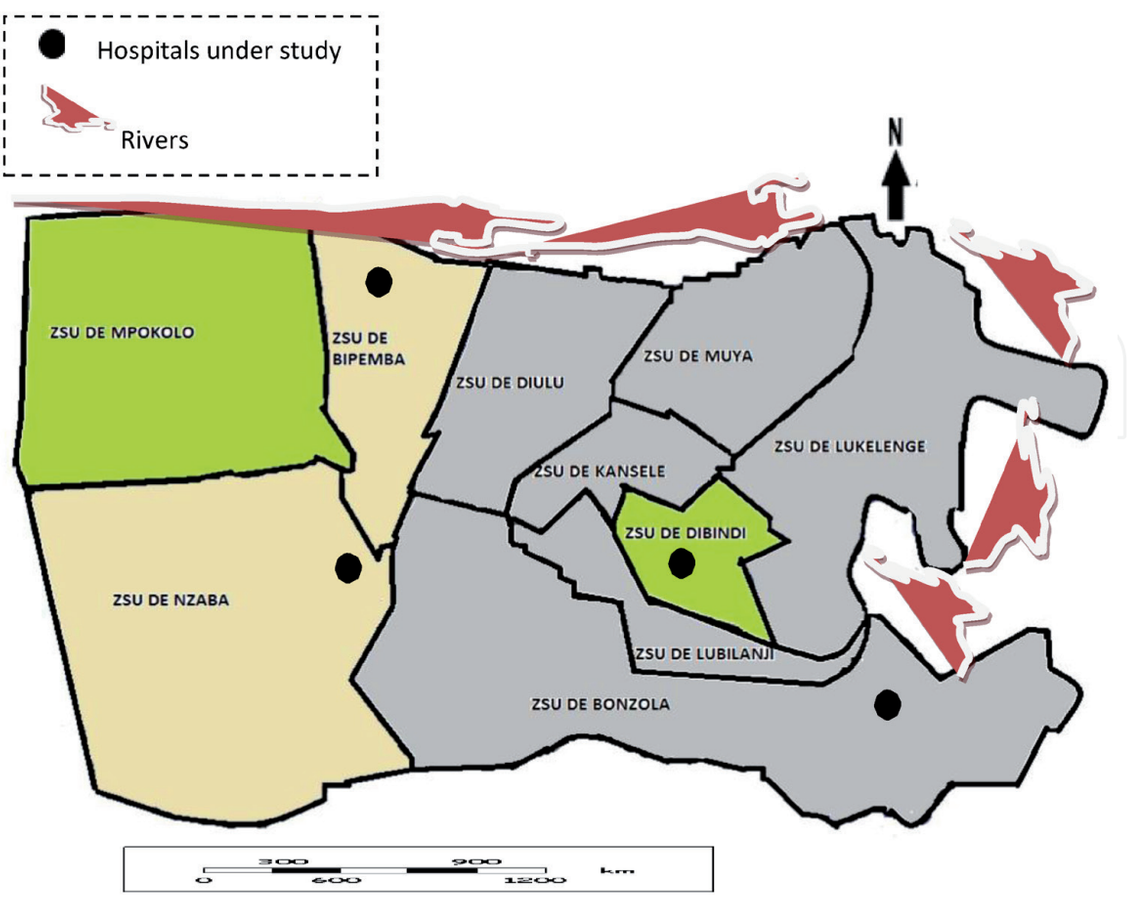

Figure 1.
Health mapping of MbujiMayi town (RDC) showing the location of the hospitals under study.

antigenic strips (i.e., immunochromatographic assay tests) that were performed on whole blood and the associated severities of clinical and biological signs (according to the WHO 2000) [7, 8].

3.4 Inclusion and exclusion criteria

This was an exhaustive sample: all children aged 0 to 59 months, 2017 children hospitalised in MbujiMayi's general reference hospitals for severe malaria from 2016 to 2020, i.e. from 1 January 2016 to 31 December 2020 were enlisted.

3.5 Statistical analyses

Quantitative data are presented as a mean ± standard deviation (SD) for monitoring data, and qualitative data as percentages. Lethality prognostic factors were analysed in uni-variate and multi-variate (Cox model). Survival analysis was carried out according to the Kaplan–Meier method. The logrank test was used to compare survival curves. The Cox model was used to express the instantaneous risk of death as a function of presumed risk factors, considering the time to death. The raw and adjusted risk ratios (HR) and their 95% confidence intervals were derived from the Cox model and the proportionality of the risks was checked by the parallelism of the curves. The statistical significance level used was 5% ($P < 0.05$). All calculations were performed with the STATATH 16 statistical software.

4. Results

The results in this study show that the average age of children with severe malaria was 31 months, statistically comparable by gender (31.3 ± 17.5 months for boys vs. 30.5 ± 17.4 months for girls, student test, $p = 0.334$). Of the 2017 children hospitalised for severe malaria, 1,150 were male or 54.8%. 59.3% lived in the peri-urban area. Nearly all had insecticide-treated mosquito net. And most of the parents were self-employed, without a permanent job, representing 18.9%, proxi of very low socio-economic level.

Evolution of case-fatality rates in children under 5 suffering from severe malaria from 2016 to 2020. The results of this **Figure 2** show that the case-fatality rate

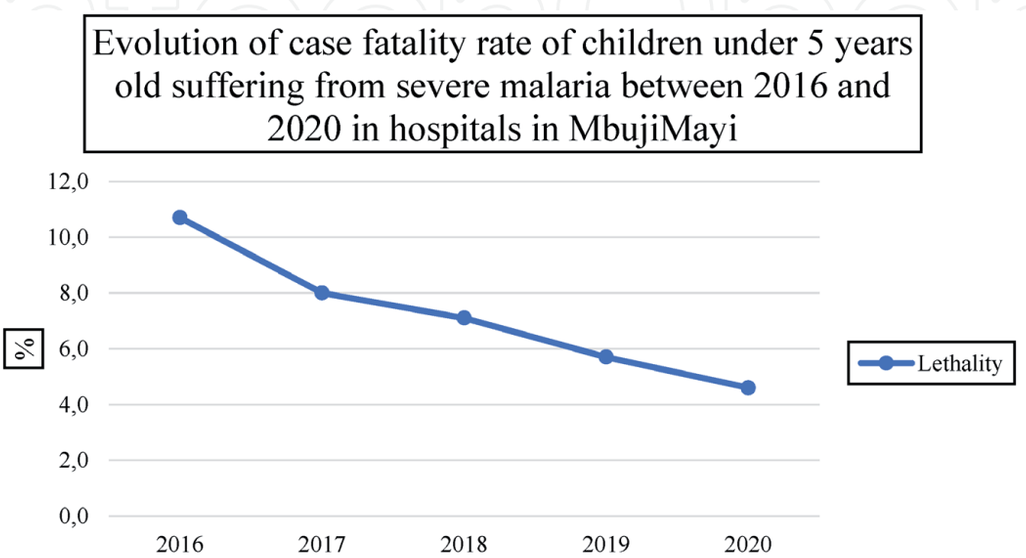

Figure 2.
Trends in case fatality rates among children under 5 years of age with severe malaria from 2016 to 2020).

was more than 6% overall (139 cases of death for 2017 cases of severe malaria for 5 years, or 6.9%) and varied from year to year. The rate decreased gradually from year to year, with a higher rate in 2016 (10.7%) and less than 6% in 2020 (4.6%).

Prognostic factors for lethality in children with severe malaria according to the Cox proportional risk model in uni-variate analysis. Severity factors associated with malaria lethality in uni-variate analysis were demonstrated: the risk of death was twice as high for children with generalised convulsions [2.6(1.8–3.8); $p < 0.001$], three times as high for those in deep coma [3.7(2.6–5.5); $p < 0.001$] and respiratory distress [3.8(2.1–7.1); $p < 0.001$]. All else being equal, the risk of death was more than 10 times higher for children with circulatory collapse (Shock) [10.8(5.1–23.3); $p < 0.001$]. late arrival after 48 hours [5.7(3.7–8.6); $p < 0.001$], and the age of the children, especially those under 12 months of age [27(18–3.9); $p < 0.001$], were also the risk factors highlighted in this study. On the other hand, possession of an insecticide-treated nets proved to be a protective factor [0.1(0.2–0.3); $p < 0.001$], so the risk of dying was less than 1. Statistically, the differences were significant. Cox Proportional Risk Model results including significant covariates in multivariate analysis.

In multivariate analysis, two models were considered. The first model with severity signs taken separately. After adjustment, the case-fatality rate was independently associated with late arrival after 48 hours, types of pre-hospital recourse such as recourse to the church and tradipractor for severe malaria, children under 12 months of age, those with circulatory collapse and those in deep coma. The second model with the number of associated syndromes, adjusted for age, sex, type of

parameters	**Hazard Adjusted Ratio (IC95%)**	**P**
Model 1		
Late arrival ≥48 h	3,1(1,9-5,1)	<0,001
Pre-hospital appeal		
Self-medication	1	
churches	1,4(1,1-2,1)	0,042
Tradipraticiens	3,2(1,8-6,1)	<0,001
Age (months)		
<12	1,8(1,2-2,8)	<0,001
≥12	1	
Circulatory Collapse		
Yes	2,6(1,1-6,1)	<0,001
Not	1	
Deep Coma		
Yes	1,9(1,1-3,4)	0,016
Not	1	
Model 2		
Number of associated syndromes		
<2	1	
≥2	1,7(1,1-2,6)	0,016

Table 1.
Cox proportional risk model results including significant covariates in multivariate analysis.

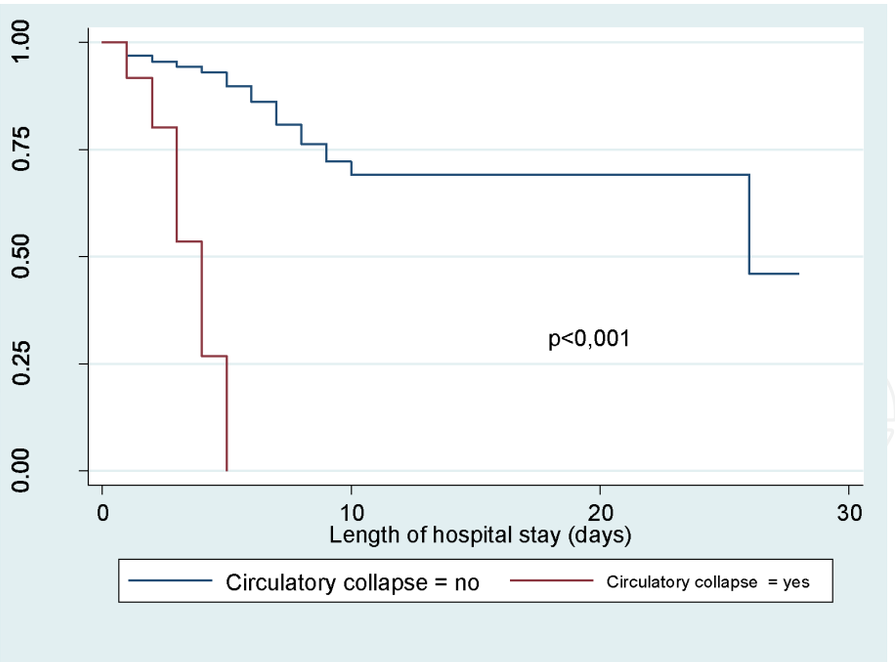

Figure 3.
Kaplan–Meier curve of the duration of follow-up without death observed in 2017 children between 2016 and 2020 depending on the presence or no circulatory collapse as a sign of severity).

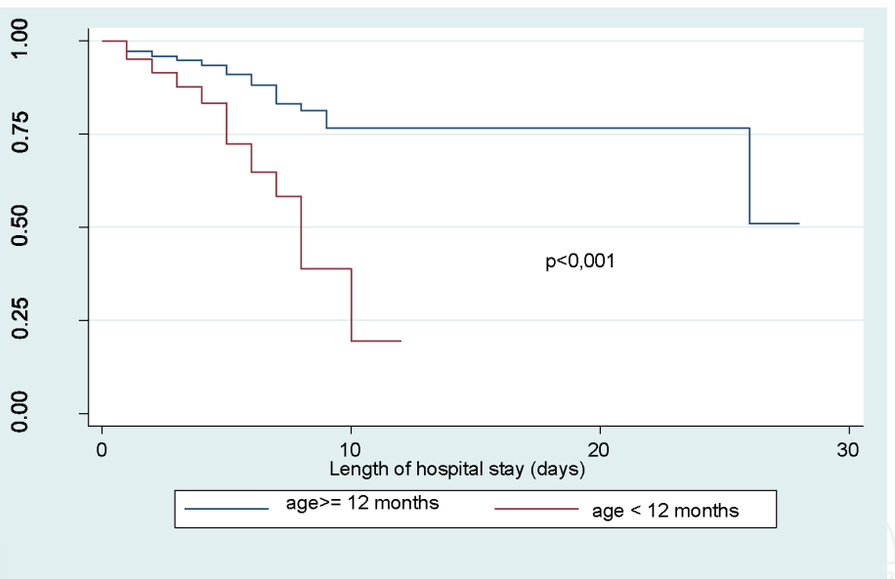

Figure 4.
Kaplan–Meier curve of follow-up without death observed in 2017 children under 12 months and 12 months and more between 2016 and 2020).

recourse and late management showed that the risk was 1.7 plus for children with a complex clinical picture, made up of the combination of several signs [1.7 (1.1–2.6); $p < 0.001$] (**Table 1**).

The different survival curves as a function of the gravity factors associated with malarial lethality in multi-variate analysis.

Figure 3 shows an early shift in the survival curve of children with circulatory collapse compared to children without circulatory collapse. Statistically, the difference was significant (log-rank test, $p < 0.001$).

Figure 4 shows an early shift in the survival curve for children under 12 months of age compared with that of children aged 12 months and over. Statistically, the difference was significant (log-rank test, $p < 0.001$).

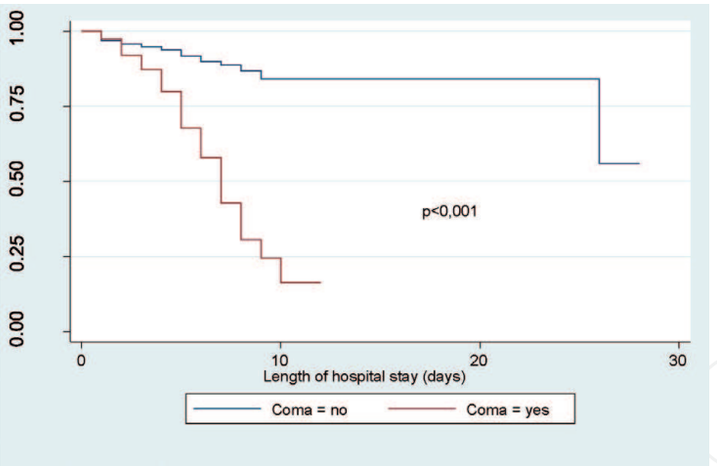

Figure 5.
Kaplan–Meier curve of the duration of follow-up without death observed in 2017 children between 2016 and 2020 with coma or not as a sign of severity.

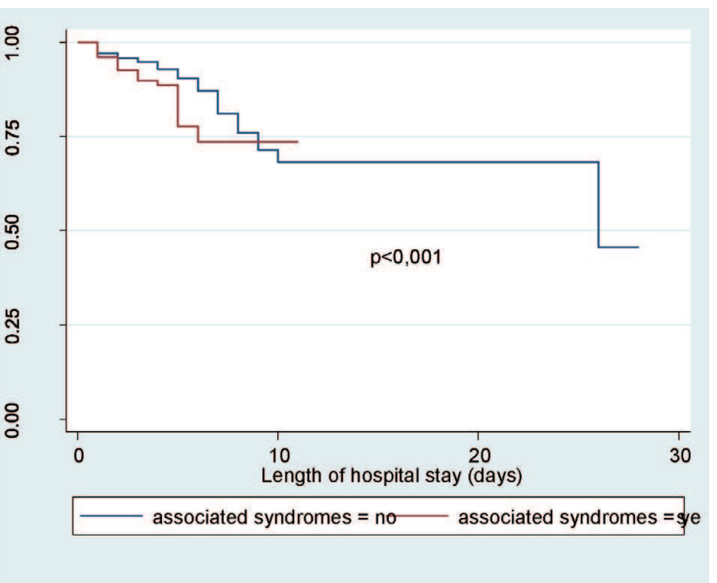

Figure 6.
Kaplan–Meier curve of follow-up duration without death observed in 2017 children between 2016 and 2020 with associated syndrome or without associated syndrome.

Figure 5 shows an early shift in the survival curve of children with coma compared to children without coma. Statistically, the difference was significant (log-rank test, $p < 0.001$).

Figure 6 shows an early shift in the survival curve of children with associated syndromes compared to children without associated syndromes. Statistically, the difference was significant (log-rank test, $p < 0.001$).

5. Discussion

In the present study, the case fatality rate was significantly related to the number of associated clinical syndromes and in many studies conducted elsewhere [9, 10], clinical polymorphism has been shown to be a poor prognostic factor. A complex clinical picture, consisting of a combination of two or more syndromes, has a poor prognosis, especially if management is delayed. The case fatality rate due to severe malaria in children aged 0–59 months in Mbujimayi and its evolution was observed

on a sample of 2017 cases hospitalised for severe malaria from 2016 to 2020. During this period, 139 cases of death, i.e. a case-fatality rate of 6.9%, were recorded. As for the evolution over the last 5 years, our results show that the case-fatality rate was more than 6% overall and varied according to the year. The rate decreased progressively from year to year, higher in 2016, less than 6% in 2020. However, this does not mean that the case-fatality rate has decreased over the years. Many cases die without the possibility to be consulted due to lack of financial means [9]. Families are forced to bleed themselves dry to meet the exorbitant cost of treatment, which is a factor in the lack of recourse to modern facilities.

Malaria case fatality remains variable across countries and circumstances. In their studies Ilunga and al [8] found a case-fatality rate of about 5.3% in the city-province of Kinshasa. Considering the importance of signs of severity and the syndrome associated with malaria lethality, our study reveals that the lethality rate was independently associated with late arrival after 48 hours and that the types of pre-hospital recourse such as recourse to church and traditional healers for severe malaria, children under 12 months of age, those with circulatory collapse and those in deep coma. In addition to this, the number of associated syndromes, adjusted for age, sex, type of referral and late management, showed that the risk was 1.7 more for children who presented with a complex clinical picture, consisting of a combination of several signs. All of these were also the risk factors identified in this study for children who were managed. The duration of hospitalisation (delay) is the time elapsed between the onset of the disease and the hospitalisation of the patient. Our results show that this time varies between 2 and 3 days, which confirms the hypothesis that the delay in the management of severe malaria is an important factor in the positive evolution of severe malaria cases in the DRC (malaria becomes very lethal). The results of studies in other African countries also note the same types of risks linked to the lethality of severe malaria. According to the results obtained in our study, the possession of insecticide-treated nets was found to be an effective protective factor in that the risk of dying was less than 1. Statistically, the differences were significant. However, the misuse of this important input by the population for such purposes as football post nets, fishing nets, curtains, poultry rearing, and many other uses should be noted with regret.

Lengeler and al [10] notes that the use of LLIN reduces overall mortality by about 6 lives of children aged 0–59 months that are saved annually. LLIN also reduces clinical episodes of uncomplicated malaria due to *Plasmodium falciparum* and *Plasmodium vivax* by 50%. The effectiveness of LLIN has been widely demonstrated through several other studies whose consistent results have led WHO to recommend it to the various countries affected by this malaria scourge [11].

This lethality observed in the reference hospitals of MbujiMayi is similar to that found in Kinshasa [8] and in other African countries, notably Uganda [12] and Benin [13], but remains lower than that found by several authors in the DRC and in other contexts [11, 14–17]. The study of severity factors associated with malaria lethality in multivariate analysis leads to results like those of univariate analyses. In our study, as in those of other authors [8, 14, 15], prognosis also depends on late hospital admission.

Late hospitalisation of patients contributed to a significant increase in case fatality in our study. Raobijaona et al. [18] showed that the mortality rate was 45% if the delay in care was more than 3 days compared to 8.5% if the child was hospitalised within 24 hours [8, 19]. Our results confirm the frequency and prognostic value of the neurological form. The relevance of this factor in children has been highlighted in other African countries with higher endemicity, such as the DRC [13, 20, 21].

6. Conclusion

The morbid and deadly burden of severe malaria is enormous. As for the evolution of case-fatality rates among children under 5 years old suffering from severe malaria from 2016 to 2020, our results show that the case-fatality rate was over 6% overall and varied from year to year. The rate decreased progressively from year to year, with a higher rate in 2016, less than 6% in 2020.

Compared to the prognostic factors of lethality in children with severe malaria according to the Cox proportional risk model in Uni-variate analysis, we found the results that the severity factors associated with malaria lethality show that the risk of death was 2 times higher for children with generalised convulsions, 3 times higher risk of death for those in deep coma and respiratory distress. All other things being equal, the risk of death was more than 10 times higher for children with circulatory collapse. Late care, the types of pre-hospital care, the age of the children, especially those under 12 months of age, were also the risk factors highlighted in this study.

Rapid and effective management seems necessary if the burden of severe malaria is to be drastically reduced. This epidemic is becoming increasingly neglected with the advent of Codiv 19 and the situation is likely to be out of control with the negative repercussions in the fight against malaria.

Acknowledgements

Our thanks to the first-degree students of Istm Kinshasa and to the authorities of the hospital institutions of the city of MbujiMayi for having facilitated the task of data collection.

Conflict of interest

"The authors declare no conflict of interest."

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