

## RESEARCH ARTICLE

## Acute renal failure as severe malaria complication in Lubumbashi: Management and follow-up in an under-equipped setting

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**Abstract: Purpose** Acute renal failure (ARF) or acute kidney injury (AKI) is one of the major criteria for the severity of malaria according to WHO. The objective was to determine the frequency as well as to evaluate the management and follow-up of ARF during malaria in children in Lubumbashi. **Material and methods** This is a descriptive cross-sectional study over 48 months (January 1st, 2016 to December 30th, 2019) carried out at the pediatric service of the University Clinics of Lubumbashi. All children with an ARF with a positive thick blood smear were included in the study. Data were analyzed with SPSS 19 software. **Results** During this period, 910 patients (49.1%) were admitted for malaria. Among them, 14 patients, *i.e.* an intra-hospital prevalence of 0.78%, of which 6 boys (42.9%) and 8 girls (57.1%) had ARF. The mean age is  $7.9 \pm 3.5$  years. The serum creatinine level was between 0.54 and 15.2 mg/dL with a mean of 5.7 mg/dL. Kidney dialysis was only effective in 3 patients (21.4%) and diuretics were given 100% in all children. The mean length of stay was  $13.4 \pm 8.7$  days (range: 1 day and 18 days). Mortality was 21.4%. **Conclusion** The present study shows that ARF in childhood malaria in Lubumbashi is infrequent but of high mortality in our environment with limited resources where care is lacking and monitoring difficult.

**Keywords:** renal failure, Malaria, children, Lubumbashi

### 1 Introduction

Acute kidney injury (AKI) or acute renal failure (ARF) is one of the major criteria for the severity of malaria according to the World Health Organization (WHO) definition. *Plasmodium falciparum* is an important cause of ARF in highly endemic areas. Its occurrence is rapidly life-threatening<sup>[1,2]</sup>. The mechanism of this ARF in

malaria appears to be acute tubular necrosis related to hemoglobinuria<sup>[3]</sup>. In children, this complication is rare, but formidable in children, who have a very high mortality rate and are readily associated with cerebral malaria<sup>[4,5]</sup>. Several studies have shown that the association between ARF and severe malaria in children is responsible for high morbidity and mortality, especially in areas where there is a shortage of resources including renal replacement therapy, and appropriate dialysis equipment. However, in developing countries this association is a serious health problem, access to dialysis remains difficult and expensive<sup>[6-13]</sup>. Data on ARF in childhood malaria in the Democratic Republic of Congo (DRC) are sparse. With the aim of documenting the profile of ARI during malaria in pediatric hospitals in Kinshasa, a study showed that it represented 23.6%, dialysis was performed in 24.0%, and the mortality rate was 12.6%<sup>[14]</sup>. In Lubumbashi, a pediatric case of ARF during malaria was treated in a logistically under-equipped setting. For lack of dialysis, the combination of furosemide and dopamine was given while the latter resolved<sup>[15]</sup>.

In view of the above, management and follow-up are still difficult, although ARF in malaria is a rare complication. Access to dialysis remains difficult and expensive,

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thus contributing to high morbidity and mortality in our communities. Thus, by carrying out this study, our objective is to determine the prevalence as well as to evaluate the management and follow-up of ARF in childhood malaria in Lubumbashi.

## 2 Materials and methods

This is a descriptive cross-sectional study carried out over 48 months, *i.e.* a period from January 1<sup>st</sup>, 2016 to December 30<sup>th</sup>, 2019 at the pediatric service of the University Clinics of Lubumbashi in the DRC. Children aged 1 to 17 years admitted to this service constituted the study population. The inclusion criteria were as follows: to have a positive thick blood smear associated with signs of severe malaria and to have severe renal failure according to Acute Kidney Injury Network (AKIN) criteria<sup>[16]</sup>. Malaria has been defined as any situation including fever persisting within 48 hours, positive (thick blood film test and thin blood test) to plasmodium falciparum. ARF was defined by disruption of renal function with urinary excretion of less than 12 ml/kg/24 hours and serum creatinine  $> 265 \mu\text{mol/L}$ , *i.e.* 3 mg/100 mL<sup>[17]</sup>. Oliguria has been defined as a low production of urine documented as inferior to 12 ml/kg per 24 hours. The AKIN score was calculated. Renal ultrasound was requested in the presence of severe renal impairment.

Data were collected from the Excel file. The statistical analysis was carried out using SPSS 19 software.

## 3 Results

During the study period, 1,789 patients were hospitalized, of which 892 (49.8%) children were admitted for malaria. Among these 892 children, 14 presented with an ARF due to malaria, *i.e.* an intra-hospital prevalence of 0.78%. These were 6 boys (42.9%) and 8 girls (57.1%) and the sex ratio of 1.33 in favor of girls. The mean age was  $7.9 \pm 3.5$  years (range: 2 and 17 years). The main reasons for consultation were highly dark colored urine (28.6%), vomiting and/or diarrhea (21.4%), febrile seizures (14.3%), coma (14.3%), pallor of extremities (14.3%) and edema of the eyelids and lower limbs (7.1%). Six (42.9%) patients had been treated with a combination therapy based on artemisinin; 3 (21.4%) patients had received quinine and 3 others (21.4%) had been treated with indigenous products during the days preceding their hospitalization. On admission, oliguria was observed in 11 patients (78.6%) (Table 1).

Serum creatinine level was between 0.54 and 15.2 mg/dL with a mean of  $5.7 \pm 1.4$  mg/dL. The mean hemoglobin level was  $6.2 \pm 2.9$  mg/dL (range: 3.9 and 8.7 mg/dL) and the mean urea is  $64.1 \pm 12.3$  mg/dL (range:

24 and 111 mg/dL).

In addition to the antimalarial treatment which consisted of the administration of an injectable artemisinin derivative, dialysis was recommended in all patients. In our series, 12 (85.7%) patients were treated with injectable artemisinin derivatives and only 3 patients (21.4%) had received dialysis sessions; 64.2% of patients received transfusion and a loop diuretic (furosemide) was used in all patients during hospitalization. The course was marked by the occurrence of polyuria in 8 patients (57.1%). The mean length of stay in hospital was  $13.4 \pm 8.7$  days (range: 1 and 18 days). Death was noted in 3 patients (21.4%) (Table 1).

## 4 Discussion

Our study reports an intra-hospital prevalence of ARF during malaria in children of 0.78%. In the literature, prevalences ranging from 0.3% to 30.4% have been reported<sup>[7,9,12,14]</sup>. The frequency of ARF in malaria varies depending on the location of patient recruitment. This could be explained by a high prevalence of the hemoglobinuria form, self-medication with antimalarial drugs at risk of developing an ARF and the small size of our sample. Different prevalences of ARF can also be explained according to the circulating species; some species with an accentuated tropism for the kidney than others.

The present study reports a sex ratio was 1.33 in favor of female and the mean age of  $7.9 \pm 3.5$  years. These results agree with those found in Cotonou (Benin) where the sex ratio was 1.4 and a mean age of 7 years<sup>[9]</sup>. On the other hand, they differ from those noted in Libreville (Gabon) who showed a mean age of  $102.2 \pm 66.7$  months with a sex ratio of 1<sup>[7]</sup>. We don't have a clear explanation for a female predominance. From an age perspective, ARF in malaria occurs more frequently in children over 5 years of age, as confirmed by our study and other studies<sup>[4,14,18]</sup>. ARF in malaria can be functional, linked to dehydration through digestive loss or due to hyperthermia. It can also be organic, related to acute tubular necrosis resulting from obstruction of capillaries and postcapillary venules by parasitized red blood cells. Two main phenomena explain this vascular obstruction: cytoadhesion which would only be observed in the event of infection by *Plasmodium falciparum* and rosetting.

Clinically, blackwater fever was retained on the combination of fever, highly dark colored urine, anemia, oligo-anuric ARF and hyperkalaemia as observed both in our series and in the literature. This complication is thought to be due to the combination of a double sensitization of red blood cells to *Plasmodium falciparum* on the one

**Table 1.** Description of 14 children with acute renal failure during malaria in Lubumbashi

Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Age (years)	17	6	7	6	9	10	12	15	2	8	10	5	13	11
Sex	F	M	M	F	M	F	M	M	F	F	M	F	F	F
Combination therapy based on artemisinin at home	-	+	-	-	+	-	+	+	-	-	+	-	-	+
Quinine at home	+	-	-	-	-	+	-	-	+	-	-	-	-	-
Indigenous products at home	-	-	+	-	-	-	-	-	+	-	-	-	+	-
Febrile seizures	-	-	-	-	+	-	-	-	-	-	-	+	-	-
Pallor mucocutaneous / jaundice	-	+	-	-	-	-	-	-	-	-	-	+	-	-
Vomiting and/or diarrhea	-	-	+	+	-	-	-	-	+	-	-	-	-	-
Edema of the eyelids and lower limbs	-	-	-	-	-	+	-	-	-	-	-	-	-	-
Coma	+	-	-	-	-	-	-	-	-	-	-	-	-	+
Hepatosplenomegaly	+	-	+	-	+	-	-	+	-	+	+	-	+	+
Highly dark colored urine	-	+	-	-	-	+	+	-	-	-	-	-	+	-
Anuria	-	-	+	+	-	-	-	-	-	-	-	-	-	-
Oliguria	-	+	-	-	+	+	+	+	+	+	+	+	+	+
Hemoglobin (mg/dL)	8.7	5	7	6.7	5.3	4.8	7.2	3.9	7.4	8	7	5.2	6	5
Serum urea (mg/dL)	24	34	55	111	87	74	52	39	68	47	62	91	61	92
Serum creatinine (mg/dL)	0.54	1.6	6.82	15.2	12.2	2.7	3.1	5.8	2.1	7.2	10.2	1.6	8.6	1.9
Kaliemia (mmol/l)	7.3	4.9	9.7	9.1	10.1	3.5	4.5	6.9	6.4	4.3	3.6	1.6	4.1	5.2
Quinine	-	-	-	+	+	-	-	-	-	-	-	-	-	-
Injectable artesunate	+	+	+	-	-	+	+	+	+	+	+	+	+	+
Antipyretics	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Anti-convulsants	-	+	-	-	-	-	-	+	-	-	-	-	-	-
Antibiotics	-	-	+	+	+	-	-	+	-	-	-	-	-	-
Transfusion	-	+	+	+	+	+	-	+	-	-	-	+	+	+
Diuretics	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Extrarenal purification (dialysis)	-	-	-	-	-	-	+	+	-	-	-	-	+	-
Diuresis (polyuria)	+	-	+	+	+	+	+	+	-	-	-	-	-	+
Death	-	+	-	-	-	-	-	-	+	-	-	+	-	-

Note: M: male; F: female; +: Yes/Present; -: No/Absent

hand; and on the other hand, to the amino alcohols responsible for hemolysis<sup>[7,15,19]</sup>. This could be explained by self-medication and the prescription of antimalarials in the face of fever in our environment, the occurrence of blackwater fever following antimalarials received before admission and yet another hospital administration which would be responsible for hemolysis more marked which may explain the occurrence of hemolytic uremic syndrome. Blackwater fever can be explained by other conditions not wanted in our study as G6PD deficiency.

The present study reports a mean serum creatinine level of 5.7 mg/dL; corroborating result with that reported in Cotonou (Benin) where the mean serum creatinine at the time of diagnosis was 5.6 mg/dL (range: 1.6 and 13 mg/dL)<sup>[9]</sup>. Identification of an ARF was based primarily on serum hypercreatinine, which is not an ideal marker, but gives an indication of kidney function, which is routine and inexpensive. It should be noted that other blood and urine markers have not been studied and present as possible early markers of ARF, such as cystatin<sup>[16]</sup>. Based on the hemoglobin level, the mean was 6.2 mg/dL. This mean is almost the same with that reported by de Keita (6.1±1.7 g/dL)<sup>[20]</sup>. This is explained by anemia as one of the complications of severe malaria following massive hemolysis and poor bone marrow regeneration.

In all of our patients, a loop diuretic (furosemide) was used to induce and restore urine output with a view to improving the prognosis. Although too controversial by other studies<sup>[21,22]</sup>, this use of furosemide has been re-

ported in several studies conducted in poorly equipped settings such as ours<sup>[7,14]</sup>. The low use of dialysis in our study (3 cases only) is explained by the complexity of the technique and the lack of equipment suitable for pediatric age (<10 years) as well as the very high cost in our environment with limited resources. Lalya *et al.*<sup>[9]</sup> confirm that dialysis helps fight complications and should be started as soon as possible to improve the prognosis of ARF regardless of the etiology. Regarding the outcome, it was marked by the occurrence of polyuria in 8 patients (57.1%), the mean length of stay was 13.4±8.7 days and death was observed in 3 patients (21.4%). These results almost corroborate those of Essola *et al.*<sup>[7]</sup> who reported a mean length of stay of 10.8±4.3 days. Mortality in children with ARF during malaria is often associated with the neurological form of malaria as demonstrated in African literature<sup>[7,9,14]</sup>. The high death rates reported in African studies could be explained by the fact that the dialysis necessary for management of this ARF is not always available. In addition, there is late transfer (at advanced stages of the disease), ignorance and lack of information thus constituting factors of poor outcome.

## 5 Conclusion

The present study shows that ARF in childhood malaria in Lubumbashi is infrequent but of high mortality in our environment with limited resources where care is lacking and monitoring difficult. Thus, prevention, early diag-

nosis and correct management of malaria, the creation of a pediatric nephrology unit, the training of healthcare professionals, the provision of suitable dialysis equipment and the subsidy of its cost, are therefore assets for improving child health.

### Conflicts of interest

The authors declare that they have no conflict of interest

### Authors' contributions

All authors participated in the development and conduct of this study, and all have read and approved the final version of the manuscript.

### References

- [1] OMS. Rapport sur le paludisme en Afrique. 2003: 46-51.
- [2] Mutombo AM, Mukuku O, Tshibanda KN, *et al.* Severe malaria and death risk factors among children under 5 years at Jason Sendwe Hospital in Democratic Republic of Congo. *Pan African Medical Journal*, 2018, **29**: 184. <https://doi.org/10.11604/pamj.2018.29.184.15235>
- [3] Da Silva Junior GB, Pinto JR, Barros EJJ, *et al.* Kidney involvement in malaria: An update. *Revista Do Instituto De Medicina Tropical De So Paulo*, 2017, **59**(53): 1-6. <https://doi.org/10.1590/s1678-9946201759053>
- [4] Kapoor K and Gupta S. Malarial acute kidney injury in a paediatric intensive care unit. *Tropical Doctor*, 2012, **42**(4): 203-205. <https://doi.org/10.1258/td.2012.120196>
- [5] Kissou SA, Essouma RC, Barro M, *et al.* Acute renal failure and Plasmodium falciparum malaria: A case report. *Archives De Pédiatrie Organe Officiel De La Société Française De Pédiatrie*, 2012, **19**(1): 34-37. <https://doi.org/10.1016/j.arcped.2011.10.007>
- [6] Mabilia-Babela JR, Kaly-Ibala R, Ganga-Zandzou PS, *et al.* Severe malaria complicated by acute renal insufficiency. About one observation. *Bulletin de la Société de pathologie exotique*, 2002, **95**(2): 74-75.
- [7] Essola L, Mowangue PS, Minko J, *et al.* Management of acute renal failure in severe malaria in children at the University Teaching Hospital of Libreville: A study of 12 cases. *Health Science and Disease*, 2019, **20**(4): 57-61.
- [8] Muhamedhussein MS, Ghosh S, Khanbhai K, *et al.* Prevalence and Factors Associated with Acute Kidney Injury among Malaria Patients in Dar es Salaam: A Cross-Sectional Study. *Malaria Research & Treatment*, 2019, **2019**: 1-7. <https://doi.org/10.1155/2019/4396108>
- [9] Lalya F, Sagbo G, Bagnan L, *et al.* Malaria-associated acute renal failure in children at the university hospital CNHU-Hubert K. Maga of Cotonou, Benin. *Rev Afr Anesth Med Urgence*, 2014, **19**(1): 39-42.
- [10] Olowu WA, Niang A, Osafo C, *et al.* Outcomes of acute kidney injury in children and adults in sub-Saharan Africa: A systematic review. *Lancet Glob Heat*, 2016, **4**(4): e242-e250. [https://doi.org/10.1016/S2214-109X\(15\)00322-8](https://doi.org/10.1016/S2214-109X(15)00322-8)
- [11] Esezobor CI, Ladapo TA, Osinaike B, *et al.* Paediatric Acute Kidney Injury in a Tertiary Hospital in Nigeria: Prevalence, Causes and Mortality Rate. *PLoS One*, 2012, **7**(12): 1-6. <https://doi.org/10.1371/journal.pone.0051229>
- [12] Kochar DK, Tanwar GS, Khatri PC, *et al.* Clinical features of children hospitalized with malaria - A study from Bikaner, Northwest India. *American Journal of Tropical Medicine & Hygiene*, 2010, **83**(5): 981-989. <https://doi.org/10.4269/ajtmh.2010.09-0633>
- [13] Romão Jr JE. The outcome of Acute Kidney Injury in patients with severe Malaria. *Journal of Clinical Nephrology*, 2017, **1**(1): 48-54. <https://doi.org/10.29328/journal.jcn.1001007>
- [14] Kunuanunua TS, Nsibu CN, Gini-Ehungu JL, *et al.* Acute renal failure and severe malaria in Congolese children living in Kinshasa, Democratic Republic of Congo. *Nephrologie & Thérapeutique*, 2013, **9**(3): 160-165. <https://doi.org/10.1016/j.nephro.2013.01.001>
- [15] Tshisuz NC, Kamona KL, Mukelengue MK, *et al.* Insuffisance rénale aigue compliquant un paludisme grave a plasmodium falciparum: prise en charge dans un milieu peu equipe. *Revue Medicale Des Grands Lacs*, 2012, **1**(3): 182.
- [16] Ponte B and Saudan P. L'insuffisance rénale aiguë en 2008. *Revue medicale suisse*, 2008, **4**: 568-575. <https://doi.org/10.1016/j.nephro.2008.03.010>
- [17] Mutombo AM, Kamona YM, Tshibanda CN, *et al.* Paludisme grave chez les enfants de moins de 5 ans à l'hôpital Panda à Likasi, République Démocratique du Congo. *Revue de l'Infirmier Congolais*, 2018, **2**(2): 4-10.
- [18] Naqvi R, Ahmad E, Akhtar F, *et al.* Outcome in severe acute renal failure associated with malaria. *Nephrol Dial Transplant*, 2003, **18**(9): 1820-1823. <https://doi.org/10.1093/ndt/gfg260>
- [19] Savadogo H, Coulibaly G, Bandaogo V, *et al.* Hemoglobinuria in children hospitalized in ouagadougou: Short term inpatient care and prognosis. *The Pan African medical journal*, 2019, **34**: 1-10. <https://doi.org/10.11604/pamj.2019.34.165.14729>
- [20] Lemrabort AT, Tondi Z, Cisse M, *et al.* Acute Renal Failure in Severe Malaria in West Africa: A Retrospective Study Conducted between 2011 and 2014 at Aristide Le Dantec Hospital in Dakar, Senegal. *Journal of Kidney*, 2017, **3**(1): 1-4.
- [21] Bagshaw SM, Delaney A, Haase M, *et al.* Loop diuretics in the management of acute renal failure: a systematic review and meta-analysis. *Critical Care & Resuscitation*, 2007, **9**(1): 60-68.
- [22] Liangos O, Rao M, Balakrishnan VS, *et al.* Relationship of urine output to dialysis initiation and mortality in acute renal failure. *Nephron Clinical Practice*, 2005, **99**(2): 56-60. <https://doi.org/10.1159/000083134>