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Research Article

Pharmacotherapy for Severe Malaria in Children Under Five Years Old in the Pediatric Department Gabriel TOURE Teaching Hospital Bamako

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Abstract

Introduction: Despite efforts to reduce the malaria burden, the disease remains a public health problem in Mali. The aim of this study was to analyse compliance with drug management for severe malaria in children under 5 years old.

Methodology: A retrospective cross-sectional descriptive study was carried out using data from June to December 2021 from the in the pediatric department Gabriel TOURE teaching hospital Bamako.

Results: During the six months period of the study, 238 patients were included. More than half of the children (55.5%) with severe malaria were male, with a sex ratio of 1.24. The main reasons for referral were anaemia (65.13%), followed by seizures (33.61%) and fever (26.47%). All patients with severe malaria were confirmed by paraclinical investigations. In accordance with NMCP guidelines, all patients with severe malaria were treated with artesunate. A total of 58.82% of patients received the combination of artemether and lumefantrine tablets. Regarding non-antimalarial drugs, paracetamol IV and ceftriaxone IV were the most widely administered drugs. Noncompliance concerns the lack of relay treatment with an oral artemisinin-based combination and antibiotic therapy based on the results of the blood count.

Conclusion: The nonconformities identified show the urgent need to focus on discharge prescribing oral artemisinin-based combination at discharge and the appropriate use of antibiotics.

Keywords: severe malaria, children, artesunate, compliance, Mali.

INTRODUCTION

The number of malaria cases worldwide was estimated at 247 million, and the number of malaria-related deaths was 619,000 in 2021. In Africa, 95% of malaria cases and 96% of deaths due to the disease were recorded. Of these deaths, 80% were 5-year-old children [1]. WHO recommendations on the use of insecticide-treated nets (ITNs) and seasonal malaria chemoprophylaxis for children are the main means of preventing malaria in Mali [2,3]. Despite these prevention methods, many cases of malaria are confirmed every year [4]. Rapid and effective antimalarial treatment for uncomplicated malaria is essential for preventing progression to severe malaria and death [5–7].

Severe malaria, defined as damage to vital organs, is characterized by biological confirmation (positive RDT or thick drop (TD) and thin smear (TS)), with the presence *of P. falciparum* associated with one or more clinical and/or biological manifestations such as shock, pulmonary oedema, seizuress, consciousness disorders, acidosis, anaemia or elevated parasitaemia [2,8,9]. Although efforts have been made to reduce the burden of malaria, it remains a public health problem in tropical and subtropical regions in many of the world's most resource-limited regions [10]. In Mali, malaria remains a major public health problem. In 2020, it was the main cause of morbidity (34%) and mortality (22%) according to data from the health information system. In Mali, the National Malaria Control Program (NMCP) guidelines recommend the following for the management of severe malaria: injectable artesunate is the first-line treatment, followed by IM artemether, followed by quinine via IV perfusion. Complications are treated according to clinical manifestations. A three-day treatment regimen with artemisinin-based combination therapy (ACT) should be used for follow-up [2]. The aim of this study was to analyse the pharmacotherapy management of severe malaria in children aged 0 to 5 years in the pediatric department Gabriel TOURE teaching hospital Bamako.

MATERIALS AND METHODS

Our study took place in the pediatric department Gabriel TOURE teaching hospital Bamako, a 3rd-level reference hospital in Mali's health pyramid. It is located in the Centre of Bamako, in commune III of the district of Bamako. The pediatric department is a reference point for the treatment of children's illnesses, and patients are referred to it from all over Mali. A descriptive cross-sectional study was carried out with retrospective data collected from June to December 2021. This study focused on children aged 0 to 5 years who were hospitalized for severe malaria in the pediatric department. The study included the records of 0-5 years old who were treated and followed up in the pediatric department for severe malaria according to the malaria severity criteria of the national program for malaria control in Mali (Table 1). Patients with incomplete records or missing information were not included. The number of children (n) included in the study sample was calculated to be 237. This size was determined using the Schwartz formula with an α error of 5%, a precision of 5% and a prevalence of malaria (uncomplicated and severe) in children under five of 19% [11]. A total of 237 patients were chosen for this severe malaria investigation. The variables studied were clinical signs on admission, treatment received during hospitalization, the nature of the antimalarial agent and other drugs, dosage, dose, duration of treatment, and type of antimalarial combination prescribed for relay treatment.

Table 1: Characteristics of severe malaria according to Mali's NMCP.

	Details of the NMCP text
Clinical manifestations	
Multiple seizuress	Two or more within 24 hours
Cardiovascular collapse	Systolic BP < 50 mm Hg in children
Respiratory distress	Acidosis
Prostration	Unable to walk or sit unaided
Haemoglobinuria	Coca Cola or dark-coloured urine
Jaundice	Yellow colouration of the skin and mucous membranes
Pulmonary oedema	Radiological definition
Abnormal bleeding	Coagulation disorder
Impaired consciousness or coma	-
Biological manifestations	
Hypoglycaemia	Blood glucose < 2.2 mmol/l or 0.4 g/l
Metabolic acidosis	Plasma bicarbonate < 15 mmol/l
Severe anaemia or extreme pallor	Hb < 5 g/dl or haematocrit < 15
Hyperparasitemia	Lactate > 100,000 µmol/l
Hyperlactatemia	Lactate > 5 µmol/l
Renal failure	Creatinine > 265 µmol/l
Microscopy (TD/BS)	All suspected cases of malaria must be systematically confirmed by RDT or GE/FM before treatment
Rapid diagnostic test (RDT)	

The presence of *P. falciparum* is associated with one or more of the clinical and/or biological manifestations.

Ethics and Consent to Participate declarations

The ethics committee of the Faculty of Pharmacy at the University of Science, Technics and Technologies in Bamako approved all the research protocols before the study began. The study was authorized by the hospital director and the head of the pediatric department. Data collected was for exclusive use by the investigators, and the confidentiality of the information obtained was respected.

Data collection and analysis

The data were collected electronically using a tablet and the Kobo toolbox platform. Descriptive and statistical analyses were carried out using the software Epi Info 6.04.

RESULTS

Sociodemographic data and reasons for referral

During the six months of the study, 238 patients were included. More than half of the children (55.5%) with severe malaria were male, with a sex ratio of 1.24. The main reasons for referral were anaemia (65.13%), followed by seizures (33.61%) and fever (26.47%) (Table 2).

Table 2: Reasons for referring children with malaria

Reference reasons	Frequency (n=238)	Percentage
Anaemia	155	65.13
Fever	63	26.47
Seizures	80	33.61
Coma	2	0.84
Respiratory difficulties	8	3.36
Anorexia	7	2.94
Diarrhea	2	0.84
Vomiting	6	2.52

Over 65% of patients were referred for anaemia, and over 33% were referred for seizures. Coma and diarrhea were less frequent.

Diagnosis and pharmacotherapy of severe malaria

All patients with severe malaria were confirmed on admission to the pediatric department. The most frequently prescribed complementary analyses were thick blood drop, blood smear, blood group and rhesus, haemoglobin and haematocrit levels. These analyses were performed for 94.1% of the patients. In addition to these analyses, brain CT, blood ionogram, C-reactive protein, transaminase, urea, bilirubin, chest X-ray and retroviral serology were performed for two patients (0.84%) (Table 3).

Table 3: Breakdown of children according to laboratory tests and X-rays prescribed

Laboratory tests	Frequency (n=238)	Percentage
TD et TS, BGR, HGL et HCT	224	94.12
TD et TS, BGR	3	1.26
TD et TS	2	0.84
HGB et haematocrit	5	2.10
TD et TS, BGR, HGL, HCT, CR, BGL*	2	0.84
RDT	2	0.84
Total	238	100

TD: thick drop; TS: thin smear; BGR: blood group and rhesus; HGL: haemoglobin level; HCT: haematocrit; CR: creatinine level; BGL: blood glucose level; * Cerebral tomodensitometry, C-reactive protein, transaminase, urea, ionogram, bilirubin, chest X-ray, retroviral serology.

All patients with severe malaria were treated with injectable artesunate. A total of 58.82% of patients received relay treatment in combination with an artemisinin-lumefantrine tablet. Emergency treatment for complications consisted of preventing hypoglycaemia (19.33%), dehydration (4.20%), severe anaemia (3.36%), fever (100%) and seizuress (33.61%). Among the drugs used, injectable paracetamol and injectable ceftriaxone were the most widely administered, with 100% and 61.76%, respectively. Injectable diazepam (18.91%) and injectable clonazepam (14.71%) were the anticonvulsants administered (Table 4).

Table 4: Drugs used to treat severe malaria and its complications

Prescribed molecules for specific antimalarial treatment		Frequency (n= 238)	Percentage
Artesunate injection		238	100
Artemether - lumefantrine tablet		140	58.82
Prescribed Molecules for emergency treatment of complications			
Fever	Paracetamol infusion solution	238	100.00
Seizuress	Diazepam injection	45	18.91
	Clonazepam injection	35	14.71
Hypoglycaemia	Glucose 10% solution for infusion	29	12.18
	Glucose 5% solution for infusion	17	7.14
Dehydration	Ringer lactate solution for infusion	9	3.78
	Saline solution for infusion	1	0.42
Severe anaemia	Blood bag	8	3.36
Vomiting	Metopimazine Injection	5	2.10
Antibiotics	Ceftriaxone injection	147	61.76
	Amoxicillin injection	32	13.45
Antiparasitic drugs	Albendazole tablet	6	2.52

The average duration of treatment with artesunate was 5 ± 1 days. However, this duration varied according to the reason for referral. Patients with anaemia and seizuress had an average treatment duration of 5 days. The duration of treatment was 6 days for patients with respiratory difficulties and 4 days for patients with fever. In all patients with severe malaria, the choice of molecules, dosage and duration of treatment complied with the guidelines of the National Malaria Control Program. Noncompliance concerned the absence of relay treatment with the artemisinin-based combination in 98 patients (41.18%), the use of injectable clonazepam in 35 patients (14.71%), the use of 5% glucose to correct hypoglycaemia in 17 patients (7.14%) and the use of probabilistic antibiotic therapy in 179 patients (75.21%) (Tables 5).

Table 5: Distribution of prescriptions according to compliance with the NMCP guidelines

Designations	Compliance with NMCP guidelines	
	Yes	No
Confirmation of severe malaria	238 (100%)	0
Molecules used for specific antimalarial treatment	238 (100%)	0
Dose, posology and duration of treatment	238 (100%)	0
Relay treatment with artemisinin-based combination	140 (58.82%)	98 (41.18%)
Molecules used to treat fever	238 (100%)	0
Molecules used to treat seizures	45 (56.25%)	35 (43.75%)
Molecules used to treat hypoglycaemia	29 (63.04%)	17 (36.96%)
Molecules used to treat dehydration	10 (100%)	0
Molecules used to treat severe anaemia	8 (100%)	0
Molecules used for probabilistic antibiotic therapy	59 (24.79%)	179 (75.21%)

DISCUSSION

The study involved 238 children with severe malaria in the pediatric department. The mean age was 3 years. This highlights the need for parents to pay particular attention to children to ensure that preventive interventions against malaria are effective. The M/F sex ratio was 1.24. This trend has been noted by several authors [12,13]. The main reasons for referring patients to the pediatric department Gabriel TOURE teaching hospital were anaemia and seizures, followed by fever. This result differs from that of Mutombo et al., who reported that 100% of patients had fever [13]. This difference can be explained by the fact that in this study, patients received treatment in health centres before being referred to the pediatric department. *P. falciparum* was identified in all patients. Anaemia (65.13%) and seizuress (33.61%) were the most common complications. These factors characterize severe malaria [2]. These results confirm those of other researchers, who found that anaemia and seizures were the most common clinical manifestations of severe malaria in children [14,15]. In fact, all patients with severe malaria were treated with injectable artesunate. It was the only antimalarial drug administered as an emergency treatment. This result differs from that found by Sy in Sikasso, who reported that injectable artemether was most commonly prescribed for severe malaria. However, the guidelines of the NMCP specify that injectable artesunate is the first-line drug for the treatment of severe malaria [2,16]. The following drugs were used to treat complications in descending order: paracetamol > ceftriaxone > diazepam > clonazepam > amoxicillin. This result is similar to that of Serengbe et *al*., who reported that antipyretics were used in 96.7% of patients, followed by anticonvulsants in 72.9%. The anticonvulsants used were phenobarbital and diazepam [17]. Indeed, the NMCP recommends administering injectable diazepam, and if seizuress persist, parenteral phenobarbital is recommended [2]. The use of clonazepam in this study may be based on the results of other studies. Indeed, studies have reported the persistence of seizuress despite the administration of diazepam and phenobarbital. Clonazepam was therefore administered until the seizuress had completely stopped [18–20]. The use of injectable clonazepam and 5% serum glucose were intentionally divergent and was justified and validated by the research team. Probabilistic antibiotic therapy, based on the results of the blood count, was an intentional deviation that was not justified and not validated by the research team. On the other hand, the nonprescription or non-administration of an artemisinin-based combination therapy (ACT) in tablet form as a relay treatment in 41.18% of patients was an unintentional divergence. However, the authors noted that a treatment duration of 5±1 consecutive days of injectable artesunate could justify not prescribing a relay treatment [21,22].

CONCLUSION

The results of this study have several positive implications. First, compliance of drug prescriptions with NMCP recommendations helps to prevent malaria-related morbidity and mortality. Furthermore, it saves health resources, ensures equitable access to care, prevents drug resistance and has a positive impact on public health. Finally, it is vital to draw the attention of prescribers to the importance of rational prescribing, particularly in regard to antibiotics.

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Conflicts of interest: We would like to make it clear that there are no conflicts of interest with regard to this article.

Abbreviations

NMCP: National Malaria Control Program;

ITNs: insecticide-treated nets;

ACT: artemisinin-based combination therapy;

TD: thick drop;

TS: thin smear;

BGR: blood group and rhesus;

HGL: haemoglobin level;

HCT: haematocrit;

CR: creatinine level;

BGL: blood glucose level;

RDT: rapid diagnostic test.

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