



# Febrile Coma in the Pediatric Unit of the National University Teaching Hospital (CNHU) of Cotonou: Etiologic and Therapeutic Features and Outcome

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### Abstract

**Objective:** Describe the epidemiological, clinical and therapeutic features and the outcome of comas among febrile children in the CNHU- Cotonou.

**Material and methods:** This research work was a case-control and descriptive study focused on 97 children aged one (01) month to 15 years admitted to the said unit, from January 1 to December 31, 2014 for fever induced coma. Coma was assessed using Blantyre and Glasgow scores. The study involved all children with coma during more than 24 hours after admission and with temperature higher or equal to  $\geq 38^{\circ}\text{C}$ .

**Findings:** Mean age was 56 months and sex ratio 1.1. In addition to coma, respiratory distress, anemia and convulsions were identified respectively in 24, 16 and 31 cases. 61.9% of isolated pathogens were *Plasmodium Falciparum* but only case of *N meningitidis* and one case of *Klebsiella P* were registered. Bacterial meningitis with unidentified pathogen was found in 10 cases and no etiology was identified in 25 cases. Antimalarial drug was used in 61.9% of cases and probabilistic antibiotic therapy in 36% of cases. After-effects such as aphasia and blindness were observed on discharge of the patient in 14.4% of the cases. Death rate was 6.2%. Coma duration higher than 7 days was associated with occurrence of after-effects ( $P=0.04$ ).

**Conclusion:** Viral culture should be put in place in Benin in order to extend etiological research. The fight against malaria must be pursued.

### Keywords

Coma; Fever; Malaria; Children; Benin

## Introduction

Coma is a diagnostic and therapeutic emergency which may lead to life-threatening complications or worsen functional outcome. Waiting time for care must therefore be as short as possible. Different

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types of score enable its clinical assessment in children, especially Blantyre score and Glasgow score [1,2]. Association with fever leads to suspect first an infection of the central nervous system (CNS), and sometimes post-infectious encephalitis as in acute demyelinating encephalomyelitis [3]. However, in some cases no etiology was found out [4]. Whether the predominance of infectious agents is viral, bacterial, parasitic or fungal it varies according to their geographical location around the world [5]. If in Asia viral infections are the most common, in Africa malaria and bacterial infections seem to be predominant. But the prevalence of viral causes is probably underestimated because of diagnostic difficulties [5]. This research work aims to carry out an assessment fever induced coma in a pediatric unit in Sub-Saharan Africa through its epidemiological, clinical and therapeutic features as well as its outcome in order to improve its management.

## Material and Methods

The research work was carried out in the Pediatric Unit of the National University Teaching Hospital (CNHU) of Cotonou located in Benin. It was a case-control and descriptive study covering the period from January 1 to December 31, 2014. It was focused on children aged one month to 15 years admitted to the unit for altered consciousness in a context of fever. Blantyre score was used to assess coma in children up to 5 years old, and Glasgow score beyond that age. The study involved all children with Blantyre score  $\leq 3$  or Glasgow score  $\leq 10$  during at least 24 hours after admission, associated with temperature higher or equal to  $38^{\circ}\text{C}$ . Children with history of brain injury or encephalopathy were excluded. Malaria diagnosis was retained on the basis of thick blood smear test positive for *Plasmodium Falciparum*. Bacterial meningitis was diagnosed based on the analysis of cerebrospinal fluid (CSF), thus showing a number of white cells  $> 10/\text{mm}^3$  which defines high level of cells in the CSF, cerebrospinal fluid proteins  $> 0.40 \text{ g/l}$  for high level of cerebrospinal fluid proteins, glycorrachia  $<$  half of plasma glucose or simultaneous capillary glucose for hypoglycorrachia. Blood electrolytogram was systematically prescribed to eliminate the effect accompanied by possible ion channel disorders. The data were collected using a questionnaire completed with data retrieved from medical records. The variables collected were age, sex, time elapsed between the onset of symptoms and admission, treatment before admission, clinical condition on admission, paraclinical tests performed, treatment, length of stay in hospital, outcome, time of coma regression, existence or not of after-effects. Excel software was used for data processing. Ratios were compared using Chi-square test, and  $P$  value  $< 0.05$  was considered as significant.

## Results

### Sociodemographic characteristics

During the study period, only 97 children out of 4338 admissions met the inclusion criteria, i.e. a hospital-based prevalence of 2%. The respondents were 46 girls and 51 boys, with a sex ratio of 1.1. Patients' mean age was 56 months (extremes 1 and 168 months, standard deviation = 31.6 months). The predominant age group was the one from 12 to 59 months (46.4%).

### Time elapsed and treatment before admission

The time elapsed between the onset of symptoms and admission

varied between 4 and 7 days in 57.7% of cases, with an average of 4.9 days (extremes 0 and 30 days, standard deviation=3.9 days). Treatment before admission was performed in 55.6% of cases. In addition to antipyretics (100% of cases), treatment consisted of antibiotic drug in 14 cases (14.4%), antimalarial drug in 19 cases (19.6%) and combination of both drugs in 21 cases (21.6%).

### Clinical condition on admission

Blantyre score oscillated between 3/5 and 2/5 in 51 cases and Glasgow score was  $\leq 10$  in 46 cases. In addition to fever and coma, the main signs existing on admission are summarized in Table 1.

### Results of paraclinical tests

Thick blood smear test was performed in all children. It was positive for *Plasmodium falciparum* in 60 cases i.e. 61.9%. Bacterial meningitis was diagnosed in 11 cases, with isolation of a pathogen in only one case: *Neisseria meningitidis*. One blood culture out of the 32 performed had isolated a *Klebsiella Pneumoniae*. The blood electrolytograms performed in 36 cases (37.11%) were normal.

### Treatment

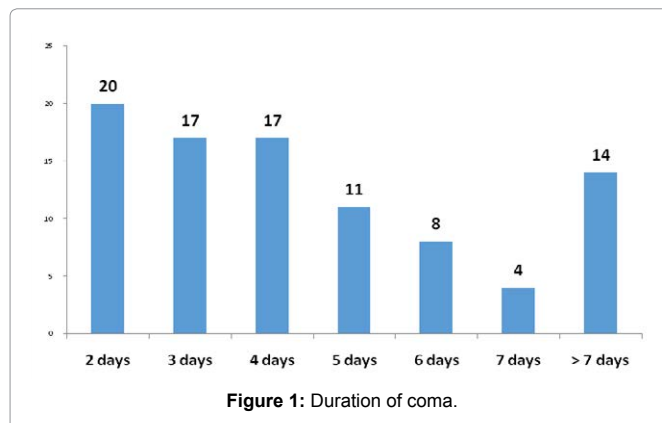
An antimalarial treatment was administered in 61.9% of cases; it was based on artesunate IV. The dosage used was 2.4 mg/kg every eight hours and then 2.4 mg/kg per day until oral administration is possible with artemisinin-based combination therapy. Except cases of malaria, nearly all children were provided probabilistic antibiotic therapy based on amoxicillin 200 mg/Kg/day or 3rd generation cephalosporin 100 mg/kg/day. In infants under 12 months of age, gentamicin was combined at 5 mg/kg/day during 48 hours. A readjustment was made according to antimicrobial susceptibility testing in both cases of positive culture. The adjuvant treatments consisted of antipyretics (intravenous paracetamol at 10 mg/kg/4h, intravenous acetyl lysine at 10 mg/kg/4h), anticonvulsants (intrarectal diazepam at 0.5mg/kg, intravenous phenobarbital at 10mg/kg), transfusion of packed red blood cells (PRBC) (10 cc/kg) and maintenance of fluid and electrolyte balance. Three children benefitted from mechanical ventilation.

### Outcome

The average duration of coma was 6.6 days (standard deviation=4.4 days). Figure 1 indicates duration of coma in children involved in the study. The average length of stay (ALOS) in hospital was 10.9 days (extremes 2 and 60 days, standard deviation =9.7 days). At the end of hospitalization, 77 children were cured, with full recovery; and 14 with after-effects. The types of after-effects identified were psychomotor agitation (n=4), paraparesis with difficulties to walk (n=4), aphasia (n=3), blindness (n=2). Duration of coma higher than seven days was significantly associated with onset of after-effects (P=0.004; OR= 10.5 [2.30; 50.06]). Death rate was 6.2%. Most of the children dead were under 12 months of age [5/6].

Table 1: Other physical signs on admission.

Signs	Size (n=)	Percentage (%)
Anemia	16	16.5
Respiratory distress	24	24.8
Generalized seizure	22	22.7
Partial seizures	9	9.2
Convulsive status epilepticus	3	3
Agitation	7	7.2
Popular rash	1	1



### Discussion

This case control study has allowed us to describe the clinical and therapeutic features as well as the outcome of fever induced coma in the pediatric unit of CNHU- Cotonou. During the study period, fever induced coma accounted for 2% of admissions in the unit. That rate is clearly lower than 16.3% reported by Asse et al. in Abidjan in a study focused on 404 non-traumatic comas induced by fever or not [6]. In our study, the age group mostly affected and sex ratio were comparable to those reported by other studies, thus confirming the vulnerability of children under five years of age [6,7]. The average time of 4.9 days between onset of symptoms and admission is long enough; it gives evidence of late medical consultation. Asse et al. and Moyen et al. have also made that observation [6,7]. The two main signs associated with coma were identical to those found out in 2012 by Bagnan et al. [8] in a study on cerebral malaria. As far as etiology is concerned this study confirms the data from literature indicating that severe *Plasmodium falciparum* malaria is the leading cause of fever induced coma in children in subtropical Africa, followed by forms of bacterial meningitis [6-9]. However, it is difficult to formally exclude the association of another cause for the existence of asymptomatic parasitemia in malaria-endemic areas was demonstrated. Moreover, a post-mortem study carried out in Malawi among children in whom cerebral malaria was diagnosed, had showed that 23% of the latter had another associated cause such as Reye's syndrome, rupture of arteriovenous malformation, inter alia [5]. It is also important to rule out comorbidity association represented by ion channel disorders such as dysnatremia and hypocalcemia. In this research work, prescribed blood electrolytogram had been performed in only one third of cases. The problem of accessibility to paraclinical tests already mentioned by other authors is still unsolved, and represents a limitation of this case-control study [5]. No cause was found out in 25 cases in this study. In England, in a study focused on 203 cases of encephalitis recruited on a prospective basis from 2005 to 2008, 37% had unknown cause [10]. We think that large-scale use of self-medication observed in this study (55.6% of cases) may have impact. Moreover, the responsibility of viral agents, which caused cases of encephalitis difficult to prove in our working conditions, cannot be excluded. Therefore, the unit should consider establishing a regional or international partnership that can help continue research on the cases that are apparently of unknown cause or origin (necessity of having a serum bank). In children, etiological research may be extended to other pathogens such as *Herpes Simplex virus (HSV)*, *Epstein-Barr virus (EBV)*, *Mycoplasma Pneumoniae* and *Mycobacterium Tuberculosis* [11]. In this research work, the average length of stay in hospital was 6.6 days;

this is higher than the one of four days on average reported by Asse et al. [6] and Moyen et al. [7]. The extreme length of stay of 60 days observed included convalescence phase for some patients coming from remote rural areas, and without possibility of access to physical therapy in their area. In this study, short term after-effects were found out in 14.7% of cases; this rate is higher than 7.9% identified by Moyen et al. [7] in their research work focused on 710 cases of coma all causes considered. The clinical features of those after-effects were identical to those found out by other authors [7,9]. Moyen et al. [7] also found a relationship between duration of coma and onset of after-effects. There were 6 dead children registered in the study i.e. 6.3%. This rate is clearly lower than 31.2%, 35.9%, and 27.6% reported by other authors [6,7,9]. It may be due to the fact that the treatment of severe malaria, the main etiology also identified by those authors, was implemented using artesunate IV in this study in compliance with the WHO recommendations [12]. Actually, compared to quinine and artemether used in the other studies, artesunate IV has a better impact on mortality [13,14]. Nearly all children dead in this study were under two years of age; this seems to confirm that age below two years is a mortality risk factor as found out by Asse wt al. [6] in Abidjan and Balaka et al. [9] in Lomé.

## Conclusion

Severe malaria remains the predominant factor in the etiology of fever induced coma in the pediatric unit of CNHU/Cotonou; however, it can be prevented and cured. Therefore, the fight against malaria remains a priority but the search for other causes, especially in case of prolonged coma, should not be ignored.

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