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Febrile Seizures in Children at the Departmental Teaching Hospital of Ouémé Plateau: Etiologies and Risk Factors for Death

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Abstract

Background: Febrile seizures are the most frequent neurological disorder in pediatrics. They have multiple etiologies and require urgent management. The aim of this survey was to study febrile seizures in children at the Departmental Teaching Hospital of Ouémé Plateau (DTH/OP). **Method:** This was a cross-sectional survey, conducted from January 1, 2020, to December 31, 2020, in the pediatric department of the DTH/OP. Children aged 1 month to 18 years, hospitalized for febrile seizures recognized at the anamnesis and/or during the physical examination were included in this study. **Results:** The frequency of seizures was 17.08% (510/2986). The male to female ratio was equal to 1.4. The mean age was 44.27 ± 40.75 months. The seizure was generalized tonic-clonic in 77.9% of cases and localized in 11.6% of cases. The main etiologies were severe malaria (75.5%), sepsis (21.6%), enteric infections (14.9%) and pneumonia (10.2%). Diazepam was the anticonvulsant treatment used in the first intention (79.7%). Most of the children were hospitalized for 3 to 7 days. The recovery rate was 82.3% and the fatality rate was equal to 17.7%. Eight children presented sequelae. There was a statistically significant link between the children's clinical outcome and age ($p < 0.001$); severe malaria ($p < 0.001$); sepsis ($p < 0.001$) and enteric infections ($p = 0.003$). **Conclusion:** Febrile seizures were frequent in the pediatric emergency department of the DTH/OP. There is a need to intensify sensitization on malaria prevention measures in the community and improve case management at the hospital.

Keywords

Febrile Seizures, Severe Malaria, Sepsis, Child

1. Introduction

Seizures are the most frequent neurological reason for consultation in pediatric emergency departments. They account for approximately 2% of emergency department visits in children's hospitals in the United States [1]. In sub-Saharan Africa, seizures account for up to 18.3% of pediatric emergency department visits and are associated with fever in 80% of the cases [2]. When they occur in the context of hyperthermia, they are referred to as febrile seizures, and their definition and etiologies vary according to the authors. For the majority of western authors, febrile seizures are the consequence of a cerebral dysfunction induced by the fever, without central nervous system infection. In this survey, seizures in relation to a simple rise in temperature were referred to as febrile crises or hyperthermic seizures, whereas the term febrile seizures were used to refer to seizures related to either a simple rise in temperature or a central nervous system infection as well. While in the West the etiologies of febrile seizures are dominated by viral infections [3], in sub-Saharan Africa malaria and meningitis are leading causes of seizures in infants and young children [2].

Seizures febrile or not are associated with a high risk of cerebral palsy, epilepsy, and even death. The prognosis seems to be more related to the etiology and the extent of brain damage than to the seizures themselves [4].

Febrile convulsions are frequent in pediatric emergencies at the CHU OP, the etiologies are multiple and there is a case management protocol. However, there are cases of death of children admitted for febrile convulsion or sometimes children who recover with sequelae. Hence, the objective of this study was to investigate febrile seizures in children aged 1 month to 18 years hospitalized in the pediatric department of the DTH/OP in order to improve management.

2. Method

This was a prospective descriptive and analytical study conducted in the pediatric department of the DTH/OP from January 1st to December 31st, 2020. Children aged 1 month to 18 years admitted to the department for febrile seizures recognized at the anamnesis and/or during the physical examination were all included in the study. Children with recurrent seizures and those with non-febrile seizures were not included.

A simple seizure was defined as a generalized, bilateral, symmetrical seizure lasting < 15 minutes, unique within 24 hours in a child aged ≥ 12 months, with good psychomotor development [3].

The presence of only one of the following criteria was sufficient to define a complex seizure: partial or hemi-body seizure, duration > 15 minutes, repetition of the seizure within 24 hours, age of the child < 12 months, post-critical deficit or even transient focal signs following the crisis [3].

Data were collected using a survey form and included sociodemographic data (age, sex), clinical data (history of febrile seizures, neonatal resuscitation, or low birth weight, psychomotor development, immunization, temperature, features of

seizures, associated extra-neurological signs), biological data (thick blood drop, cytobacteriological and biochemical examination of the cerebrospinal fluid, blood culture, full blood count test, cytobacteriological examination of the urine), diagnosis, treatment, and outcome. The data were analyzed using SPSS 20 software. Comparisons were made with the chi-square (χ^2) statistical test and Fisher's exact test. The threshold for significance was $p < 0.05$.

3. Results

3.1. Socio-Demographic and Clinical Characteristics

During the study period, 510 cases of febrile seizures were recorded out of 2986 hospitalizations, *i.e.* a frequency of 17.08%. The age group 12 - 59 months was the most affected (60.6%), the mean age was 44.27 ± 40.75 months with extremes of 1 month and 192 months. The sex ratio of male to female was equal to 1.4. In this survey, there were two peaks in the frequency of seizures during July (81 cases), August (62 cases), and then, November (52 cases), December (42 cases), and January (56 cases). Socio-demographic and clinical characteristics are summarized in Table 1 & Table 2. Most of the children were admitted to the pediatric emergency department of the DTH/OP more than 48 hours (81.7%) after the onset of the disease symptoms. Immunization status was up to date according to the Expanded Program of Immunization (EPI) in 88.5% of cases. There was a history of febrile seizures in 14 children. Six children had a history of resuscitation at birth and ten had growth retardation. One child had a history of paternal epilepsy. On admission, the temperature was very high, greater than or equal to 39˚C in 48.4% of cases (247). The mean temperature was 38.9˚C ± 0.7. The extremes

Table 1. Demographic and clinical characteristics of patients with seizures.

Age (months)	01 - 12	75 (14.7%)
	≥12	435 (85.3%)
Sex	Male	295 (57.8%)
	Female	215 (42.2%)
Personal history	Ressucitation	06/464 (1.3%)
	Febrile seizure	14 /453(3.1%)
	Vaccination status up to date	391/442 (88.5)
	Growth retardation	10/461 (2.2%)
Délai d'admission (504)	<48 hours	92 (18.3%)
	≥48 hours	412 (81.7%)
Temperature	38˚C - 39˚C	263 (51.6%)
	≥39˚C	247 (48.4%)
Type of seizure	Focal	88/369 (23.8%)
	Generalized	281/369 (76.2%)

Table 2. Factors associated with death in children with seizures.

Factors		Deceased	p
Age group	01 - 11 months (62)	22 (35.5%)	<0.001
	12 - 59 months (271)	44 (16.2%)	
	05 - 09 years (79)	06 (08.2%)	
	10 - 15 years (30)	07 (23.3%)	
	>15 years old (04)	00 (00%)	
Enteric infections (n = 68)		20 (29.4%)	0.003
Sepsis (93)		27 (29.0%)	<0.001
Severe malaria (n = 346)		49 (14.2%)	<0.001

were 38˚C and 41˚C. Regarding the characteristics of the seizures, children aged one year and above were affected in a majority (n = 435; 85.3%). The seizures were recurrent within 24 hours in 51.84% of cases (n = 264) and their duration was specified in 288 cases. It was less than 5 min, between 5 and 10 min, and more than 15 min respectively in 64.6%, 22.6%, and 12.8% of cases. The location of the seizures was known in 369 cases. The majority were generalized (n = 281; 72.2%). They were complex in 64% (236) of cases and simple in 36% (133). Clinical signs associated with the seizures were coma (62.7%), pallor (84.3%), and respiratory distress (32%).

3.2. Paraclinical Aspects

The thick blood drop performed in all children gave a positive result in 385 (75.5%) cases. The cytobacteriological and biochemical examination of cerebrospinal fluid (CSF) obtained by lumbar puncture was performed in 153 children (30%) and the white cells count was elevated in 18 children. No germ was identified.

3.3. Etiological Aspect

There were various etiologies of seizures. Severe malaria was the leading cause of seizures (75.5%) followed by sepsis (21.6%), enteric infections (14.9%), and pneumonia (10.2%). Viral infections were last among the etiologies of seizures after méningitis (3.9%), ENT infection (3.7%), and urinary tract infection (2.7%).

3.4. Therapeutic Aspect

One hundred and thirty-seven children (26.9%) were given a traditional treatment before admission. The etiological treatments used were antimalarials (75.5%) and antibiotics (55.5%). Considering the anticonvulsant treatment, diazepam was used in 79.7% of cases, phenobarbital in 13% of cases, and clonazepam in 7.3% of cases. Diazepam-phenobarbital, diazepam-clonazepam and phenobarbital-clonazepam combinations were used in 6.1%, 3.9% and 0.6% of cases respectively. Six child-

ren (1.2%) had received all three anticonvulsants.

3.5. Evolution

The majority of children had a hospital stay of 3 to 7 days. The average length of stay was 6.37 ± 4.7 days. Sixty-four children were lost to follow-up. The outcome was favorable in 82.3% of cases (367/446) and the fatality rate was 17.7% (79/446). The fatality rate was significantly higher in the under-12 months' age group ($p < 0.001$). The most fatal diseases were enteric infection ($p = 0.003$), sepsis ($p < 0.001$) and malaria ($p < 0.001$). There was no relationship between the clinical outcome and the type of crisis. We recorded sequelae in 8 children (1.8%), who all presented with complex seizures. These sequelae were motor deficits (2 cases), pelvic floor and locomotor disorders (1 case), stiffness (1 case), limb hypertonia (2 cases), axial hypotonia (1 case), and language disorder (1 case).

4. Discussion

The frequency of febrile seizures in the study was 17.08% (510/2986). Several sub-Saharan authors have reported frequencies ranging from 8.4% (308/3747) to 14.3% (266/1854) [5] [6] [7]. Differences in selection criteria between the studies could explain these variations in the frequency of febrile seizures.

The male sex was predominant with a sex ratio of 1.4. In the literature, the same predominance of males has been generally observed [3] [4] [5] [6] [7]. However, in an Ivorian study, a sex ratio equal to 1 was reported [8]. The majority of children (60.6%) were 1 to 5 years old. Nzame *et al.* in Gabon and Miwipopo *et al.* in China found a predominance of the age groups 1 month to 5 years (67.6%) and 1 year to 5 years (96.5%) respectively [5] [9].

In the study, we recorded two peaks in the frequency of febrile seizures. The first peak in frequency corresponds to the end of the main rainy season in Benin, which represents a period of high malaria transmission. This seasonal variation had been observed in the literature with different frequency peaks in the year according to the period of recrudescence of malaria in the area [5] [10]. The second peak of seizures in this study corresponds to the long dry season with the harmattan period which constitutes a period of pneumonia recrudescence.

Complex seizures were more frequent in the study (64%) compared to 36% of simple seizures. Djoman Apie in Abidjan had made a similar observation with 67.9% of complex seizures [8]. In the West, seizures associated with fever are generally febrile crises or hyperthermic seizures and are dominated by simple crises [3]. In this study, the majority of crises were generalized (76.2%). Several authors had reported this predominance of generalized seizures [5] [6] [9]. Nonetheless, Alao in Benin found a predominance of localized crises (50.30%) [11].

Severe malaria was the leading cause of seizures (75.5%) followed by sepsis (21.6%) enteric infections (14.9%), pneumonia, and meningitis. Several studies conducted in sub-Saharan Africa found that malaria was generally the leading cause of seizures, particularly when it comes to seizures associated with fever [5]

[6] [7] [8]. The explanation is that malaria is endemic in the region and is the first cause of morbidity in children under five years, who are the most affected by seizures associated with fever. Apart from malaria, the other frequently reported etiologies were meningitis and sepsis [8]. In a study in Gabon, febrile crises or hyperpyretic seizures were reported as the second most common etiology for seizures associated with fever (41.2%) in children aged 1 month to 15 years. On the other hand, febrile crises were the leading cause of seizures associated with fever in the age group of 1 to 4 years, preceding malaria (22.1%) [5]. The main causes of those febrile crises were ENT infections (46.4%), bronchopneumonia (21.4%), and gastroenteritis (21.4%). These results are consistent with those of Western studies which report more frequent febrile crises, especially before the age of five years, but of viral causes essentially [3] [12]. The differences in methods between the studies, particularly with regard to the definition of hyperpyretic seizures, certainly explain the difference between the other African studies and that of Nzamé.

The fatality rate of seizures associated with fever was equal to 17.7%. This was three times higher than that reported in a Gabonese study (5.9%) involving a much smaller series (n = 68) [5]. However, Dembélé in Mali found a case fatality rate almost two and a half times higher 41.6% (n = 255) [7]. These large variabilities in case fatality rate could be related to the study population. Dembélé's study concerned under 5 years children affected by infectious diseases causing the most important fatality rate and morbidity. There was a statistically significant link between age and outcome in children with seizures associated with fever. The fatality rate was significantly higher in under 12 months children ($p < 0.001$). This is explained by the fragility of children in this period of life in relation to an immune immaturity that makes them susceptible to infectious diseases responsible for seizures associated with fever in the sub-Saharan region. The most fatal diseases were enteric infections, sepsis, and meningitis with fatality rates equal to 29.4%, 29%, and 16.7% respectively. In Mali, cerebral malaria was the most fatal disease causing seizures (48%) followed by meningitis (25.6%) [7]. Treatment for severe malaria is free in Benin for children under 5 years old. This would explain the lower malaria lethality observed during the study. The high fatality rate of enteric infections could be related to some associated metabolic disorders which are not always detected because the parents don't pay sometimes for the serum electrolyte panel due to difficult financial situations. Regarding sepsis, its management requires resuscitation measures, some of which are not easily accessible (vasoactive drugs, mechanical ventilation) in our work context.

The study was cross-sectional, which exposes the risk of lack of data in relation to the poor keeping of medical records (several missing information such as history, duration of seizures, complete description of seizures).

5. Conclusion

Febrile seizures were frequent and severe with significant lethality. The etiologies

were dominated by severe malaria, sepsis, enteric infections, and pneumonia. It is necessary to improve the management of digestive infections, sepsis, and malaria, especially in children under one year.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

Variables	Modalities	Choice
General informations		
Age (month):		
Gender	1. Male 2. Female	/___/
Religion	1. Animist 2. Jéhovah's witness 3. Catholic 4. Evangelical 5. Islamic 6. Other (specify)	/___/
Résidences	1. Porto-Novo 2. Adjohoun 3. Adjarra 4. Avrankou 5. Misserete 6. Sakete 7. Pobe 8. Dangbo 9. Azowlisse 10. Aguegues 11. Other (specify)	/___/
Father's profession	1. Civil servant / employee 2. Trader 3. Worker /craftsman 4. Pupil/ student / apprentice 5. Unemployed	/___/
Mother's occupation	6. Other (specify)	/___/
Clinical informations		
Date and time of admission		
Admission mode	1. Referred 2. Not referred	/___/
If referred, specify the referral center		
Mode of transport	1. Motorcycle 2. Car 3. Ambulance	/___/
Reason fo radmission	1. Pallor 2. Seizure 3. Coma 4. Agitation 5. Fever 6. Respiratory distress 7. Digestive disorders 8. Icterus 9. Edema	/___/

Continued

		10. Anxiety 11. Headache 12. Delirium 13. Inability to drink 14. Ostéo-articular pain 15. Others (specify)	
Onset of symptoms before admission			
Assessment before admission		1. Hémoglobin level……. 2. Hématocrit……. 3. VGM …… 4. MCHC ……. 5. NB …… 6. TDR ……. 7. GE/DP …….	
Personal history	Low birth weight	1. Yes 2. No	/___/
	Febrile seizure	1. Yes 2. No If yes, specify the age of the 1st attack /___/	/___/
	Epilepsy	1. Yes 2. No	/___/
	Vaccination status not up to date	1. Yes 2. No	/___/
	Growth retardation	1. Yes 2. No	/___/
Family history	Father	1. Epilepsy 2. Febrile seizure 3. Other (specify)	/___/
	Mother		/___/
	Siblings		/___/
Physical examination			
Weight (Kg)			
Size (cm)			
Pallor		1. Not 2. Moderate 3. Severe	/___/
Respiratory distress		1. Yes 2. No	/___/
Coma		1. Yes 2. No	/___/
If coma, specify		Blantyre score = /5 or Glasgow score = /15	
Kernig sign		1. Yes 2. No	/___/

Continued

Brudzinski sign		1. Yes 2. No	/___/
Tachycardia		1. Yes 2. No	/___/
Dehydration		1. Yes 2. No	/___/
Jaundice		1. Yes 2. No	/___/
Edeme		1. Yes 2. No	/___/
Other			
Description of the seizure	Duration	1. Less than 15 min 2. More than 15 min	/___/
	Number	1. One during 24 h 2. Recurrent in 24 h	/___/
	Type	1. Partial 2. Généralized 3. Rolling eyes 4. Clonic 5. Tonic 6. Tonic-clonic	/___/
	Post-critical anomaly	1. Coma (score) 2. Hemiplegia 3. Strabismus 4. None	/___/
	Other		
Extra-neurological signs	ENT infection	1. Yes 2. No	/___/
	Digestive infection	1. Yes 2. No	/___/
	Pneumonia	1. Yes 2. No	/___/
	Other		
Paraclinical parameters			
GE/DP		1. Yes 2. No If, yes DP =	/___/
Lumbar punction		1. Clear 2. Trouble 3. Hématic 4. PL not done 5. If, PL done, specify CSF ECB results:	/___/

Continued

		• GR = • GB = • Germes = • Glycorrachie Proteinorrachie	
NFS		• Hb = • Hte = • VGM = • TCMH = • CCMH = • NB = • PNN = • Lympho =	
CRP			
EEG			
Hemoglobin electrophoresis			
Fond d'œil			
Others			
Cause of fever			
Treatment			
Treatment before admission		1. Yes 2. No	/___/
Traditional treatment		1. Yes 2. No If yes, specify:	/___/
Modern treatment		1. Yes 2. No If yes, specify: • Nature: • Dose: • Duration: • Place:	/___/
Treatment during hospitalization	Antipyretics	1. Yes 2. No	/___/
	Valium	1. 1 times 2. 2 times 3. 3 times 4. No	/___/
	Gardenal	1. Yes 2. No	/___/
	Rivotril drops	1. Yes 2. No	/___/
Etiological treatment of fever			

Continued

Immediate recurrence	1. Yes 2. No If yes, the number:	
EVOLUTION		
Duration of hospitalization		
Healing without sequelae	1. Yes 2. No	/___/
Recovery with sequelae	1. Yes 2. No If yes, specifyr:	/___/
Exit against medical advice	1. Yes 2. No	/___/
Evasion	1. Yes 2. No	/___/
Transfer	1. Yes 2. No	/___/
Death	1. Yes 2. No	/___/
If death, specify	1. Before treatment 2. Despite the well-conducted treatment 3. During the first hour of hospitalization 4. During the 2nd hour of hospitalization 5. During the 3rd hour of hospitalization 6. During the 24 hours of hospitalization 7. During the 48 hours of hospitalization 8. After 48 hours of hospitalization /___/	/___/