Demographic and aetiological factors of paediatric status epilepticus: A South African retrospective observational study

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Background. Status epilepticus (SE) is a common medical neurological emergency in childhood, and it is often serious and life-threatening. There is a paucity of data on the aetiology and demographics of affected children in resource-limited countries.
Objective. To understand the demographics and describe common causes of convulsive SE (CSE) in our local paediatric population.
Methods. We conducted a retrospective review of the demographics, clinical features, and characterisation of CSE of children who presented to the emergency department at Red Cross War Memorial Children's Hospital, in Cape Town, South Africa, between 2016 and 2018.
Results. More than half (*n*=63; 53%) of the 119 children were male. The median (interquartile range) age was 29.6 (14.8 - 76.1) months: 22 (18%) were <12 months; 63 (53%) were 1 - 5 years; and 34 (29%) were >5 years. Thirty-one (26%) were moderately to severely underweight-for-age and 5 (4%) were HIV-infected. In seizure semiology, 82 (71%) had generalised convulsive seizures and 34 (29%) had focal seizures. Based on International League Against Epilepsy-classified aetiology, 74 (62%) were secondary to acute infective cause, 12 (10%) were classified as electroclinical syndrome, 9 (8%) were remote and 25 (22%) had unknown aetiology. A recorded tympanic membrane temperature of ≥38 °C was found in 49 (44%) of 112 children and 36 were below the age of 5 years, supporting the diagnosis of febrile SE in these children. Fifty children (42%) were known with epilepsy-related breakthrough seizures. Imaging was abnormal in 24 (42%) of 57 children. Cerebrospinal fluid findings were abnormal in 7 (12%) of 57 children. Most children (*n*=87; 75%) were stabilised adequately for admission to the short-stay ward, however, eight required admission to the intensive care unit. No deaths were recorded in the cohort.
Conclusion. Concordant with other studies, acute infections were the most common cause of SE in our setting.

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Convulsive status epilepticus (CSE) is defined as continuous seizure activity, without an arresting phase, or recurrent seizures, without regaining consciousness in between, for more than 5 minutes.[1] The estimated prevalence and mortality of paediatric CSE varies, with higher rates noted during the first few years of life.[2-7] Furthermore, a high prevalence rate of paediatric CSE in the first year of life has been observed in studies conducted in high-income countries where mortality is lower than it is in resource-constrained countries.[8] Paediatric CSE is considered to be a serious medical emergency worldwide and is associated with morbidity and death.[9,12]

According to a 2018 review, about 3 to 42 per 100 000 children are affected by CSE per year globally, with ~3% mortality.[9] However, in sub-Saharan Africa, the incidence of SE appears to be higher. This may be attributed to the high burden of infectious and non-infectious (chronic) diseases in addition to late presentation to the hospital. According to a Kilifi hospital-based cohort study[12] conducted in a rural Kenyan population, the lower limit of the incidence of CSE was 35 per 100 000/year in children aged 0 to 13 years. This was considered an underestimation, as many children demised before reaching the hospital. The incidence was eight times higher than a London-based cohort once probable cases were also included.[10-12]
Age is a fundamental element when considering the epidemiology of CSE. Furthermore, substantial differences also exist within the paediatric population, specifically when comparing younger and older children in terms of incidence, aetiology, prior history of seizures or neurological deficits.[13] Children who present to hospitals in sub-Saharan Africa commonly have fever-related seizures, mostly secondary to malaria.[10] This may have a regional bias, but other infective causes documented in similar resource-poor settings include respiratory tract infections, gastroenteritis, and neonatal seizures.[1,10-12,14,15]

The aims of interventions for CSE are to stop the seizure, provide adequate symptomatic support and treat the underlying cause. These interventions reduce adverse outcomes. An early and robust (aggressive) medical intervention, as well as identification of modifiable predisposing factors for prolonged seizures, is required to achieve effective treatment. In addition, resource-limited settings cannot follow the same treatment protocols prescribed by centres in resource-equipped countries owing to lack of access to medications and intensive care unit (ICU) services. This has necessitated a more bespoke approach to the management of these patients. This includes the use of phenobarbital which, despite it not being promoted in resource-equipped countries, has been found to be safe and effective as a second-line agent for the management of paediatric CSE.[16]

Unfavourable outcomes after an episode of paediatric CSE include subsequent epilepsy, permanent neurological deficits, cognitive impairment and death.[17] Aetiology is an important determinant of the outcome as evidenced by some epidemiological studies and clinical series – rapid identification of aetiology prevents subsequent neurological morbidity and mortality. [7,18-20]

According to the International League Against Epilepsy (ILAE), epilepsy is defined as unprovoked seizures more than 24 hours apart. However, in the present study, our patients presented with provoked seizures. Furthermore, the ILAE has expanded the aetiology axis, hence SE can be provoked by a known disorder which may be genetic, metabolic, structural, infectious or toxic.[1]

There is a paucity of data on the aetiological and demographic factors that play a role in paediatric CSE in sub-Saharan Africa, specifically in South Africa (SA). Most of the currently available research on CSE is based on studies conducted in high-income countries and it is not known if the same trends are applicable in resource-limited sub-Saharan African countries. Therefore, the aim of this study was to explore these factors and to compare the findings with those reported in other regions.

Methods

Study design and participants

We conducted a retrospective descriptive study over a 24-month period (May 2016 - May 2018) at Red Cross War Memorial Children's Hospital (RCWMCH), in Cape Town, SA. All children presenting in CSE were included in the study.

Study setting

RCWMCH is a tertiary healthcare facility providing comprehensive and dedicated paediatric services with a full range of subspecialities at quaternary, tertiary, and secondary levels of care to children. RCWMCH is the largest children's hospital in sub-Saharan Africa and provides healthcare to a wide sector of the population from rural, peri-urban and urban areas. All children received the standard of care stipulated in the SE protocol at RCWMCH. This includes monitoring of heart rate, respiratory rate, blood glucose level, blood pressure and peripheral temperature, with varying interventions such as lumbar puncture and empirical antimicrobial cover for children with a suspected infective cause, anti-seizure medication (ASM) levels (where indicated) and neuroimaging for children who have focal seizures.

Data collection

The outcomes of interest included the demography of African children with CSE, as well as aetiology and semiology of CSE in accordance with the ILAE classification.[1] All children meeting the inclusion criteria were included. We collected demographic data, clinical data and special investigation findings on all children who presented with CSE to the medical emergency room. The initial recruitment process involved identifying all children from the emergency room admission register who were documented as having seizures at admission to the medical emergency room. Children who were not in CSE were excluded. A total of 119 children met the inclusion criteria (Fig. 1).

To assess if other comorbidities, such as growth and nutrition, previous illness, and compliance with medication, were major determinants of patient outcomes, patient data were extracted from medical records. Variables included demographics, date of admission, mode of transportation, weight-for-age *z*-scores, past medical history, drug history, seizure information, adherence to anti-epileptic drugs, admission ward and special investigation findings, as well as final diagnosis at discharge.

Definitions

CSE was defined according to the ILAE criteria,[1] i.e., prolonged or recurrent seizures without regaining consciousness between seizures for >5 minutes. CSE was classified according to the ILAE Task Force on classification of SE using the following four-axis framework: semiology; aetiology; age; and EEG correlates,[1] however, our study did not include EEG correlates. A previous study conducted in our setting by Burman *et al.*[16] detailed treatment regimens and management of these children, therefore this aspect was not included in our study. Thereafter, the diagnostic axes provided a framework for describing our study population.

Statistical analysis

Demographic characteristics were summarised as frequencies and percentages and tabulated (Table 1). Continuous data were tested for normality and the appropriate conventional descriptive methods, mean values with standard deviation (SD) or median values with interquartile ranges (IQRs), were used to describe the dataset. Data were entered anonymously into a secure REDCap database and analysed using STATA version 16 (StataCorp., USA).

Ethics

Confidentiality and anonymity were maintained and data were only accessed by the investigators via a password-protected computer. Ethics approval for the study was obtained from the University of Cape Town's Faculty of Health Sciences Human Research and Ethics Committee (HREC ref no. 622/2017).

Results

The demographics and past medical history at admission are shown in Table 1, the median (IQR) age was 29.6 (14.8 - 76.1) months. All HIV-infected patients (*n*=5; 4.2%) were on antiretroviral treatment. In terms of nutrition, thirty-one (26%) children were moderately to severely underweight-for-age and no other nutritional indicators were documented.

Nearly half of the children (*n*=54; 48.7%) were self-referred and came directly from home, 31 (26%) were referred from community health centres and 55 (51%) children were transported to the hospital by ambulance. In our cohort, 50 (42%) children were known with epilepsy and 44 (88%) of them were on ASMs, of whom

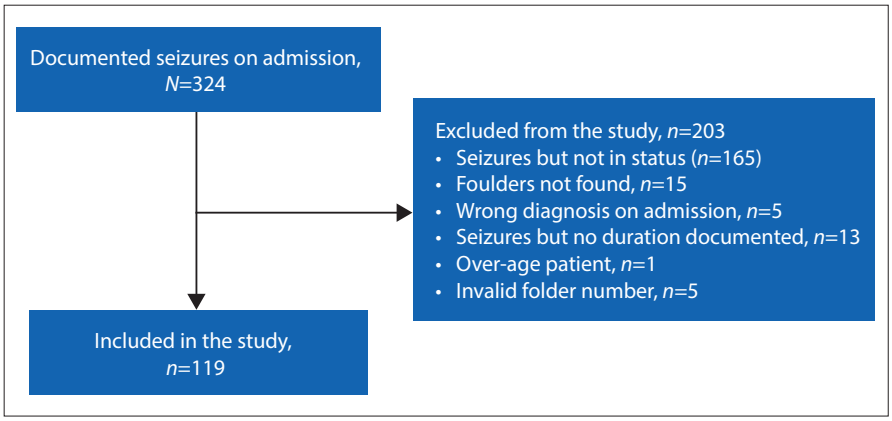

Fig. 1. Flow diagram of the study recruitment process.

10 (23%) reported a history of non-compliance. Twenty-one (42%) of the children known to have epilepsy had drug levels done, 5 20%) of whom recorded sub-therapeutic levels. The remaining children (*n*=16; 80%) had levels within the therapeutic range. The total number of children receiving benzodiazepine prehospital was 33 (28%) and 72 (62%) required ASM in the emergency department. Time to seizure cessation was not well documented.

Regarding investigations, 57 children had a lumbar puncture and 7 (12%) of those were abnormal – one had moderate pleocytosis (32 polymorphs and 55 lymphocytes), raised protein content (11.68g/L) and cultured *Mycobacterium tuberculosis* in the cerebrospinal fluid, while the remaining 6 samples had nonspecific mild pleocytosis with negative cultures. Polymerase chain reaction assays for viruses were not routinely done at that time. Computerised tomography (CT) head imaging was conducted in nearly half of the children (*n*=57/119; 48%) children; 24 (42%) of the 57 CT scans were abnormal. Abnormal findings included cerebral oedema (*n*=4), tuberculous meningitis (TBM; *n*=1), bifrontal empyema (*n*=1), hydrocephalus (*n*=1), pan paranasal sinusitis (*n*=2), cerebral infarction (*n*=2), neurocysticercosis (*n*=1), bilateral peri-mesencephalic cysts (*n*=1), brain atrophy (*n*=4), cerebellar encephalomalacia (*n*=1), frontal white-matter hypodensities (*n*=2) and mild basal meningeal enhancement (*n*=1). Three patients were noted to have functional ventriculoperitoneal shunts *in situ*.

The seizures were further classified according to semiology and aetiology (Table 2). The most common seizure semiology was generalised CSE (*n*=82; 71%) owing to an acute aetiology (*n*=74; 62%).

A recorded tympanic membrane temperature of ≥38 °C was recorded for 49 (44%) of 112 children; 38 of them were below the age of 5 years, with 2 of them showing pleocytosis on cerebral spinal fluid and they were subsequently excluded from the febrile seizures category. The final diagnosis at discharge in 74 children in CSE with an acute infectious aetiology is as illustrated in (Table 3). Forty-seven of those with an infectious aetiology had an upper respiratory tract infection. Thirteen children had a lower respiratory tract infection, 7 had a CNS infection, 5 had acute gastroenteritis and other infections included otitis media (*n*=4), urinary tract infection (*n*=1), neurocysticercosis (*n*=1) and congenital cytomegalovirus (CMV) infection (*n*=1).

Eight children were admitted to the ICU, while most children (*n*=87; 75%), were stable enough for admission to the short-stay ward. Reasons for admission to ICU included: required airway protection related to recurrent seizures (*n*=1); episodes of apnoea post ASM administration (*n*=2); depressed level of consciousness (*n*=3); and 2 were postoperative patients – incision and drainage of an abscess (*n*=1) and insertion of an extra-ventricular drain (*n*=1), respectively. No mortalities were reported in our study.

Discussion

In this study we have been able to describe the demographics and aetiologies of CSE in 119 children who accessed care at a

Table 1. Demographics of children presenting with convulsive status epilepticus

Variable	*n* (%)
Sex, male	56 (47)
Age (months), median (IQR)	29.6 (14.8 - 76.1)
Age (years)	
<1	22 (18)
1 - 5	63 (53)
5 - 12	33 (28)
>12	1 (1)
Nutritional status (weight-for-age z-score)	
Normal	88 (74)
Moderately UWFA	15 (13)
Severely UWFA	16 (13)
HIV status	
Infected*	5 (4)
Uninfected	113 (95)
Unknown	1 (1)
Premorbid conditions	
Cerebral palsy	20 (17)
Epilepsy	50 (42)
Developmental delay	40 (34)
HIV encephalopathy†	4 (3)
Congenital heart disease	1 (1)
Underlying syndrome	8 (7)
Previous TBM	1 (1)
Previous TBI	3 (3)
Preterm (GA <37 weeks)	20 (17)
HIE at birth	2 (2)

IQR = interquartile range; UWFA = underweight-for-age; TBM = tuberculous meningitis; TBI = traumatic brain injury; HIE = hypoxic ischaemic encephalopathy; GA = gestational age.
*Some children presented with more than one premorbid condition.
†Of the 5 who were HIV-infected, 4 had HIV encephalopathy.

Table 2. Semiology and aetiology of seizures according to the ILAE

Variable	*n* (%)
Semiology	
Generalised	82 (71)
Focal evolving into bilateral CSE	34 (29)
Axis aetiology	
Acute (infectious/stroke)	74 (62)
Electroclinical syndrome	12 (10)
Remote	9 (8)
Progressive	0
Unknown	24 (20)

ILAE = International League Against Epilepsy; CSE = convulsive status epilepticus.

Table 3. Final diagnosis at discharge in children in CSE with an acute infectious aetiology (*N*=74)

Diagnosis associated with CSE	*n* (%)
URTI (pharyngitis, tonsilitis, sinusitis)	47
LRTI (pneumonia)	13
CNS infections (meningitis, encephalitis)	7
Acute gastroenteritis	5
Otitis media	4
Sepsis	2
Congenital CMV infection	1
Urinary tract infection	1
Neurocysticercosis	1
Total*	81

CSE = convulsive status epilepticus; URTI = upper respiratory tract infection; LRTI = lower respiratory tract infection; CNS = central nervous system; CMV = cytomegalovirus.
*There is an overlap in patients who presented with more than one diagnosis at discharge.

public children's tertiary hospital in an African setting. There were 22 (19%) infants in our cohort. This was similar to a cross-sectional study by Barzegar *et al*.[21] in Iran, where 20.9% of their 43 children (under the age of 15 years) were younger than 12 months of age. These results support that children less than 1 year are more affected by CSE. In a multi-centre population-based study, Gurcharran *et al*.[9] noted that the peak age incidence of CSE in children in Virginia, Minnesota and London was less than one year. Other studies from Iran,[21] Taiwan [22] and London [23] showed that 46.5%, 51.8% and 55% of children were aged 1 - 5 years, respectively, concordant with our finding of 53% (*n*=63) of the children in the same age category. This is also supported by the Consequences of Prolonged Febrile Seizures in Childhood (FEBSTAT) studies, although they specifically focused on the infantile age group.[24]

Nearly a third (26%) of our children were moderately to severely malnourished, which was comparable with a retrospective Kenyan study[12] (children aged 1 month to 13 years), which reported malnutrition in 32% of their 155 confirmed CSE cases. The Kenyan study was the only comparative study for nutritional data, which may be attributable to the fact that the other studies were conducted in high-income countries where malnutrition may not be a major health concern. According to the SA Child Gauge 2020, one in four SA children under the age of 5 years (27%) are stunted. Although we did not dwell on classification of the cerebral palsy, we speculate that children with cerebral palsy (and possibly those with other chronic medical conditions (*n*=56; 47%)) often have some form of feeding difficulty. These factors could also be confounding, as we had a significant number of children who were underweight-for-age.[25] In addition, a significant number of the patients seen at RCWMCH come from very poor and marginalised communities.

A recorded tympanic membrane temperature of ≥38 °C was noted in 44% of our patients. Similarly, a multicentre study[27] of 3 785 Chinese children (aged 29 days to 18 years) reported 36.8% (*n*=1 385) were pyrexial, and a Kenyan study reported 48% of their confirmed CSE cases presented with a fever.[12] Although we do not routinely test for human herpes virus 6 or 7, it has been identified as one of the common causes of fever in young children presenting with febrile status epilepticus (SE).[24]

Regarding transportation and referrals, 43% of our children utilised private transport whereas 48% of the patients were self-referred. This gives us an indication that children who self-present or use private transport are less likely to receive ASM prior to arriving at a health facility and this increases the likelihood of having a prolonged seizure. This was supported by the fact that only 27.7% (*n*=33/119) received a benzodiazepine prior to presentation at RCWMCH; Although we could not calculate the exact time to intervene, we can conclude that it was prolonged based on the mode of transportation, self-referrals from home and the small number receiving benzodiazepines prior to arrival at RCWMCH. This is further supported by a study done in SA[16] in which the time to intervene was 50 minutes. In some resource-limited countries, seizures last longer compared with high-income countries owing to limited access to hospitals, clinics and emergency medical transport.[12]

Despite the high prevalence of HIV disease, traumatic brain injuries, tuberculous meningitis (TBM), and hypoxic ischaemic encephalopathy in SA,[28,29] the documented past medical history in the present study identified relatively small numbers of these conditions. In an acute setting, the priority is to stabilise the patient hence the past medical history may not be adequately documented, and this may lead to an underestimation of these conditions. Children with traumatic brain injury are more prone to developing seizures which can later evolve into post-traumatic epilepsy. [30,31] In our study, a previous history of traumatic brain injury was noted in 2.5% of children. – one patient had a history of TBM, and another had TBM related to the acute presentation. Seizures are a common presentation in TBM and are more likely to be experienced in childhood owing to the immaturity of the immune system, the CNS and the blood brain barrier. If seizures are recurrent and uncontrolled, they can evolve into SE with resultant brain damage.[32]

Seizure semiology (Table 2) was varied, with generalised tonic-clonic seizures being the most common and accounting for 71% of our cases. This finding was in accordance with previous reports by Wang *et al*.[27] in China, who reported that 66% (*n*=2 317) of their cohort aged 1 month to 18 years had generalised tonic-clonic seizures. They also reported that acute symptomatic aetiology of SE accounted for 42.8% (*n*=1 819), with unknown aetiology accounting for more than half of their cases 58.8% (*n*=2 503), electroclinical syndrome for 1.6% (*n*=69), and progressive aetiology for 0.6% (*n*=27). In contrast, our study had a higher incidence of acute symptomatic aetiology (62%) and unknown aetiology only accounted for 21%. Our electroclinical syndromes and progressive aetiology cases were much higher at 10% and 8%, respectively. An 8-year retrospective analysis of 76 SA children (aged 1 month to 13 years) admitted to a tertiary paediatric intensive care unit (PICU) with CSE reported a much higher acute symptomatic aetiology at 80%.[14]

Most seizures in our study were due to an acute aetiology with the most common causes identified as respiratory tract infections, otitis media, acute gastroenteritis and CNS infections, concordant with findings from earlier studies.[12] In contrast, a prospective study of 70 Indian children (aged 6 months to 12 years) by Kumar *et al*.,[33] described the most common acute aetiology attributed to CNS infections, e.g. viral encephalitis, pyogenic meningitis, tuberculous meningitis and cerebral malaria.

Patients with pre-existing epilepsy are more vulnerable to breakthrough seizures with intercurrent infections.[34] In our cohort, 42% of the children had pre-existing epilepsy. This coupled with the high number of infections, the history of non-compliance to ASMs (23%), and the low levels of ASMs detected in 20% of those on medication could have contributed to the occurrence of seizures. Only 42% (*n*=21) of the children on ASM had documented drug levels, indicating that more than 50% of the children had unknown and unrecorded drug levels. In an acute setting, the priority may have been to stabilise the patient.

Most of our cohort with an acute infection (*n*=60/74) had a respiratory tract infection documented as their discharge diagnosis, including pharyngitis, tonsillitis, sinusitis and pneumonia. According to a review article by Bomwalhd *et al*.,[35] respiratory viral infections can be associated with neurological manifestations such as seizures and SE. Viral respiratory diseases are a critical health problem and account for the high rates of morbidity and mortality, especially in immunocompromised individuals, young children and the elderly. [36] Five of our patients had acute gastroenteritis. A review article by Kim[37] described children with mild acute gastroenteritis who presented with both febrile and afebrile seizures in Korea. Although we did not dwell on the specific aetiology of the acute gastroenteritis, Higuchi *et al*.,[38] from Japan described the clinical features of convulsions with rotavirus and norovirus gastroenteritis as similar, except for fever which was more frequently present in those with rotavirus gastroenteritis. In Iran, a case-control study of 165 children aged 6 months to 5 years, conducted by Mayhar *et al*.[39] showed that there was a significant link between urinary tract infections and febrile seizures. Our cohort reported one patient who presented in SE with a proven diagnosis of a urinary tract infection.

Higher rates of epilepsy are associated with the presence of intracranial calcifications in congenital infections such as toxoplasmosis, other infections, rubella, cytomegalovirus, and herpes simplex (TORCH) aetiologies.[40] The present study identified one case of congenital CMV infection. The risk of postnatal seizures is higher in patients with congenital CMV and in children with congenital infections associated with intracranial calcifications. Suzuki *et al.*,[41] reported that 37% of their 19-patient cohort with congenital CMV developed epilepsy. The proportion of children in our study presenting with CSE secondary to a CNS infection was 12%. This was lower than reported in the Chinese retrospective multi-centre study (n=4 255 children aged 1 month to 18 years) at 22% (n=932)[27] and 81% from a prospective Indian study[33] of 70 children (aged 6 months to 12 years). At our institution this may be attributed to the fact that we do not routinely test for all viruses on cerebrospinal fluid, owing to resource constraints. Additionally, requesting an extensive viral panel on cerebrospinal fluid may not have altered the management of SE significantly except in the cases where herpes or CMV are identified. Furthermore, there may be regional biases because the area in which the Indian study was conducted has an increased incidence of Japanese encephalitis.

Whereas the study identified an acute aetiology as the most common cause of CSE, we also noted the evidence of local influence in reported studies. In a cross-sectional study from India, Shriyan *et al.*, [42] reported that 52.8% of their 104 CSE cases (1 to 12 years of age) were attributed to an acute infection and 41% and 14% of those acute infections were due to neurocysticercosis and tuberculous meningitis, respectively. Similarly, our study had acute aetiology detected in 62% of children, but with only one case each of tuberculous meningitis and neurocysticercosis. In contrast, a Kenyan retrospective study[12] of 388 children aged between 1 month and 13 years, as well as a prospective Nigerian cross sectional-study[43] of 39 children (aged 4 months to 8 years), both noted many of their patients presented with malaria, i.e., 65% and 70%, respectively. As the Western Cape province is not a malaria-endemic zone it was not surprising that none of our patients presented with malaria.

The zero mortality rate in this study was comparable with that reported in high-income settings, as illustrated by an epidemiological study of 120 children (1 month to 15 years) from Japan[44] and a 5-year retrospective review of 137 children (aged 1 month to 15 years) admitted to a PICU in London.[23] This could be attributed to the fact that our patients are able to access treatment within 5 minutes of admission to the emergency ward[16] and the hospital staff are able to manage CSE appropriately. In contrast, studies from Nigeria,[43] Kenya,[12] Pakistan[45] and India[33] have reported high mortality rates, i.e., 23%, 22%, 11% and 31%, respectively. Deaths can be attributed to the underlying cause of CSE or as a result of the complications of the CSE itself,[33] as well as the fact that infective causes are associated with an increased risk of mortality.[3,6,7] The higher mortality rates in resource-poor countries can be attributed to unorthodox cultural practices where patients with CSE are taken to traditional healers prior to seeking medical attention.[28] Kumar *et al.*,[33] also highlighted poor literacy and a lack of transport, which delays access to treatment. This results in a prolonged time interval from onset of CSE to the commencement of treatment, as evidenced by an earlier SA study.[16] Furthermore, poor management of CSE in hospitals, lack of staff to manage CSE appropriately and the lack of equipment such as infusion pumps and ventilators, contribute to high mortality rates in sub-Saharan Africa.[10-12,43]

The long-term effects of CSE in our cohort remains unknown. This information was also not routinely documented in the patients' folders. In this regard, a neurodevelopmental follow-up plan should be clearly documented for every child presenting with CSE.

Based on our study findings and the above comparisons, we conclude that the aetiological spectrum of CSE in resource-limited countries is divergent when compared with resource-equipped countries. The aetiologies differ further within the sub-Saharan African setting owing to endemic influences as in the case of malaria, tuberculosis and neurocysticercosis.[3,12,40,43,45] Notably, whereas these comparisons were made within a similar population group, the definitions of CSE differed and therefore we may have deviations from the methodologies and the directness of the study question.

According to the 2020 UNAIDS Global HIV AIDS Statistics report,[46] most people living with HIV are in low- and middle-income countries. Inclusion of HIV data was relevant for our study as SA has high prevalence of HIV in its paediatric and adult populations. Surprisingly, despite the high HIV prevalence, we identified a low percentage (4.2%) of children who were HIV-positive, all of whom were on antiretroviral treatment; however, four of the five children had evidence of advanced neurological damage related to HIV encephalopathy. Few studies reported HIV data in the paediatric population with seizures. In one retrospective case control study of children aged 10 months to 176 months, Burman *et al.*, [47] reported that 28 (54%) out of their 57 HIV-positive patients with seizures had HIV encephalopathy and 11 had CSE at presentation. We believe that our study has added new data in terms of the low impact of HIV status in the aetiology of paediatric CSE and highlighted that poorly controlled HIV disease is to be avoided as it can lead to HIV encephalopathy which may be associated with CSE.

The introduction of nutritional data in this category of children is important. The study findings have highlighted that children presenting with CSE are not only predisposed to poor nutrition in our setting but other compounding factors such as feeding difficulties and chronic underlying medical conditions further contribute to their poor nutritional status.

Study limitations

As this was a retrospective study, we relied on handwritten medical notes made by attending clinicians during admission for accurate record keeping – medical record documentation was therefore variable. The duration of the seizures and time to seizure arrest affects the pathways to care and planning and were important but challenging to measure owing to variable documentation. Cerebrospinal fluid polymerase chain reaction assays for viruses were performed at a later stage in the ward, hence these data were not available at the time of initial admission. Furthermore, follow-up data were not routinely documented in most of our patients.

Conclusion and recommendations

Future research should include an exploration of aetiological variances in those admitted to the paediatric ICU. In addition, we need to promote future rigorous prospective studies to formally elucidate the impact of CSE, particularly at a vulnerable age, on neurodevelopmental outcomes.

We need to improve pathways to care from home in addition to raising awareness for children with epileptic syndromes who would benefit from early interventions.

It is also necessary to establish the circumstances surrounding non-compliance and sub-therapeutic ASM levels. This can be improved by ensuring drug supply is always adequate and placing emphasis on compliance education. Additionally, since few children had drug levels done, we need to inform the clinicians of the importance of knowing the drug levels in this category of children.

Acute infections were the most common cause of CSE in our setting, with the highest proportion of children presenting in the infantile age range. The age distribution in our cohort was concordant with other studies, however, the present study results revealed a higher percentage of acute infective causes. Improved access to healthcare and timely intervention can reduce insults on the developing brain.

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Conflicts of interest. None.

1. Trinka E, Cock H, Hesdorffer D, et al. A definition and classification of status epilepticus. Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia 2015;56(10):1515-1523. https://doi.org/10.1111/epi.13121
2. Raspall-Chaure M, Chin RFM, Neville BG, Bedford H, Scott RC. The epidemiology of convulsive status epilepticus in children: A critical review. Epilepsia 2007;48(9):1652-1663. https://doi.org/10.1111/j.1528-1167.2007.01175.x
3. Chin RF, Neville BG, Peckham C, Bedford H, Wade A, Scott RCJTL. Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: Prospective population-based study. Lancet 2006; 368: 222-229. https://doi.org/10.1016/S0084-3954(08)70464-0
4. Dham BS, Hunter K, Rincon F. The epidemiology of status epilepticus in the United States. Neurocritical Care 2014;20(3):476-483. https://doi.org/10.1007/s12028-013-9935-x
5. Hayakawa I, Miyama S, Inoue N, Sakakibara H, Hataya H, Terakawa T. Epidemiology of pediatric convulsive status epilepticus with fever in the emergency department: A cohort study of 381 consecutive cases. J Child Neurol 2016;31(10):1257-1264. https://doi.org/10.1177/0883073816652234
6. Hesdorffer DC, Logroscino G, Cascino G, Annegers JF, Hauser WA. Incidence of status epilepticus in Rochester, Minnesota, 1965 - 1984. Neurology 1998;50(3):735-741. https://doi.org/10.1212/wnl.50.3.735
7. DeLorenzo RJ, Hauser WA, Towne AR, et al. A prospective, population-based epidemiologic study of status epilepticus in Richmond, Virginia. Neurology 1996;46(4):1029-1035. https://doi.org/10.1212/wnl.46.4.1029
8. Raspall-Chaure M, Chin RF, Neville BG, Bedford H, Scott RC. The epidemiology of convulsive status epilepticus in children: A critical review. Epilepsia 2007;48(9):1652-1663. https://doi.org/10.1111/j.1528-1167.2007.01175.x
9. Gurcharran K, Grinspan ZM. The burden of pediatric status epilepticus: Epidemiology, morbidity, mortality, and costs. Seizure 2019;68:3-8. https://doi.org/10.1016/j.seizure.2018.08.021
10. Idro R, Gwer S, Kahindi M, et al. The incidence, aetiology and outcome of acute seizures in children admitted to a rural Kenyan district hospital. BMC Pediatr 2008;8:5 https://doi.org/10.1186/1471-2431-8-5
11. Newton CR, Kariuki SM. Status epilepticus in sub-Saharan Africa: New findings. Epilepsia 2013;54:50-53. https://doi.org/10.1111/epi.12277
12. Sadarangani M, Seaton C, Scott JAG, et al. Incidence and outcome of convulsive status epilepticus in Kenyan children: A cohort study. Lancet Neurol 2008;7(2):145-150. https://doi.org/10.1016/S1474-4422(07)70331-9
13. Shinnar S, Pellock JM, Moshé SL, et al. In whom does status epilepticus occur: Age-related differences in children. Epilepsia 1997;38(8):907-914. https://doi.org/10.1111/j.1528-1157.1997.tb01256.x
14. Reddy Y, Balakrishna Y, Mubaiwa L. Convulsive status epilepticus in a quaternary hospital paediatric intensive care unit (PICU) in South Africa: An 8-year review. Seizure 2017;51:55-60. https://doi.org/10.1016/j.seizure.2017.07.016
15. Adhikari S, Sathian B, Koirala DP, Rao KS. Profile of children admitted with seizures in a tertiary care hospital of Western Nepal. BMC Pediatr 2013;13:43. https://doi.org/10.1186/1471-2431-13-43
16. Burman RJ, Ackermann S, Shapson-Coe A, Ndondo A, Buys H, Wilmshurst JM. A comparison of parenteral phenobarbital vs. parenteral phenytoin as second-line management for pediatric convulsive status epilepticus in a resource-limited setting. Front Neurol 2019;10(506). https://doi.org/10.3389/fneur.2019.00506
17. Novorol CL, Chin RF, Scott RC. Outcome of convulsive status epilepticus: A review. Arch Dis Child 2007;92(11):948-951. http: 0.1136/adc.2006.107516
18. Wilmshurst JM. Management of children with status epilepticus. J Int Child Neurol Assoc 2015;1(1). https://doi.org/10.17724/jicna.2015.104
19. Raspall-Chaure M, Chin RFM, Neville BG, Scott RC. Outcome of paediatric convulsive status epilepticus: A systematic review. Lancet Neurol 2006;5(9):769-779. https://doi.org/10.1016/S1474-4422(06)70546-4
20. Scott RC, Surtees RAH, Neville BGR. Status epilepticus: Pathophysiology, epidemiology, and outcomes. Arch Dis Childhood 1998;79(1):73-77. https://doi.org/10.1136/adc.79.1.73
21. Barzegar M, Shiva S, Rahbari-Banaeian G. Etiology and short-term outcome of children with convulsive status epilepticus admitted to Tabriz Children's Hospital, Iran. J Analytical Res Clin Med 2014;2(3):112-117. https://doi.org/10.5681/jarcm.2014.019
22. Lin KL, Lin JJ, Hsia SH, Wu CT, Wang HS. Analysis of convulsive status epilepticus in children of Taiwan. Pediatr Neurol 2009;41(6):413-418. https://doi.org/10.1016/j.pediatrneurol.2009.06.004
23. Hussain N, Appleton R, Thorburn K. Aetiology, course and outcome of children admitted to paediatric intensive care with convulsive status epilepticus: A retrospective 5-year review. Seizure 2007;16(4):305-312. https://doi.org/10.1016/j.seizure.2007.01.007
24. Epstein LG, Shinnar S, Hesdorffer DC, et al. Human herpesvirus 6 and 7 in febrile status epilepticus: The FEBSTAT study. Epilepsia 2012;53(9):1481-1488. doi:10.1111/j.1528-1167.2012.03542.x
25. Rempel G. The importance of good nutrition in children with cerebral palsy. Phys Med Rehabil Clin N Am 2015;26(1):39-56. https://doi.org/10.1016/j.pmr.2014.09.001
26. Wang T, Wang J, Dou Y, et al. Clinical characteristics and prognosis in a large paediatric cohort with status epilepticus. Seizure. 2020;80:5-11. https://doi.org/10.1016/j.seizure.2020.04.001
27. Samia P, Petersen R, Walker KG, Eley B, Wilmshurst JM. Prevalence of seizures in children infected with human immunodeficiency virus. J Child Neurology 2013;28(3):297-302. https://doi.org/10.1177/0883073812446161
28. Kariuki SM, Kakooza-Mwesige A, Wagner RG, et al. Prevalence and factors associated with convulsive status epilepticus in Africans with epilepsy. Neurology 2015;84(18):1838-1845. https://doi.org/10.1212/WNL.0000000000001542.
29. Dhakar MB, Sivakumar S, Bhattacharya P, Shah A, Basha MM. A retrospective cross-sectional study of the prevalence of generalised convulsive status epilepticus in traumatic brain injury: United States 2002 - 2010. Seizure 2015;32:16-22. https://doi.org/10.1016/j.seizure.2015.08.005
30. Annegers JF, Coan SP. The risks of epilepsy after traumatic brain injury. Seizure 2000;9(7):453-457. https://doi.org/10.1053/seiz.2000.0458
31. Abdulaziz ATA, Li J, Zhou D. The prevalence, characteristics and outcome of seizure in tuberculous meningitis. Acta Epileptologica 2020;2(1):1. https://doi.org/10.1186/s42494-020-0010-x
32. Kumar M, Kumari R, Narain NP. Clinical Profile of Status epilepticus (SE) in children in a tertiary care hospital in Bihar. J Clin Diagnc Res 2014;8(7):Pc14-7. https://doi.org/10.7860/JCDR/2014/9288.4579
33. Bohmwald K, Gálvez NMS, Ríos M, Kalergis AM. Neurologic alterations due to respiratory virus infections. Front Cell Neurosci 2018;12:386. https://doi.org/10.3389/fncel.2018.00386
34. Vezzani A, Fujinami RS, White HS, et al. Infections, inflammation and epilepsy. Acta neuropathologica 2016;131(2):211-234. https://doi.org/10.1007/s00401-015-1481-5
35. Talbot HK, Falsey AR. The diagnosis of viral respiratory disease in older adults. Clinical infectious diseases: An official publication of the Infectious Diseases Society of America. 2010;50(5):747-751. Clin Infect Dis 2010;50(5):747-751. https://doi.org/10.1086/650486
36. Kim YO. Benign convulsions with mild gastroenteritis. Ann Child Neurol 2020;28(1):2-7. https://doi.org/10.26815/acn.2019.00248
37. Higuchi Y, Kubo T, Mitsuhashi T, et al. Clinical epidemiology and treatment of febrile and afebrile convulsions with mild gastroenteritis: A multicenter study. Pediatric Neurology 2017;67:78-84. https://doi.org/10.1016/j.pediatrneurol.2016.05.011
38. Mahyar A, Ayazi P, Azimi E, Dalirani R, Barikani A, Esmaeily S. The relation between urinary tract infection and febrile seizure. Iran J Child Neurol 2018;12(4):120-126.
39. Kwak M, Yum MS, Yeh HR, Kim HJ, Ko TS. Brain magnetic resonance imaging findings of congenital cytomegalovirus infection as a prognostic factor for neurological outcome. Pediatric Neurology 2018;83:14-18. https://doi.org/10.1016/j.pediatrneurol.2018.03.008
40. Suzuki Y, Toribe Y, Mogami Y, Yanagihara K, Nishikawa M. Epilepsy in patients with congenital cytomegalovirus infection. Brain Dev 2008;30(6):420-424. https://doi.org/10.1016/j.braindev.2007.12.004
41. Shriyan R, Aggarwal K, Gupta R. G171(P) Aetiological profile and immediate outcome predictors of paediatric convulsive status epilepticus: An Indian perspective. Br Med J 2019;104(Suppl 2):A69-A70. https://doi.org/10.1136/archdischild-2019-rcpch.166

42. Oa O, Sba O, Ta A, et al. Prevalence, aetiology and outcome of status epilepticus in children with convulsions at the Wesley Guild Hospital, Ilesa. J Pediatric Neurol Med 2017;2:1 https://doi.org/10.4172/2472-100X.1000116
43. Nishiyama I, Ohtsuka Y, Tsuda T, et al. An epidemiological study of children with status epilepticus in Okayama, Japan: Incidence, etiologies, and outcomes. Epilepsy Research 2011;96(1):89-95. https://doi.org/10.1016/j.eplepsyres.2011.05.004
44. Uzair M, Ibrahim A, Zafar F, Sultan T. Etiology and outcomes of convulsive status epilepticus in children. Pakistan J Med Sci 2019;35(3):620-623. https://doi.org/10.12669/pjms.35.3.120
45. The Joint United Nations Programme on HIV and AIDS (UNAIDS). The global HIV and AIDS Epidemic 2020. Geneva: UNAIDS, 2020. https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics (accessed 15 March 2022).
46. Burman RJ, Wilmshurst JM, Gebauer S, Weise L, Walker KG, Donald KA. Seizures in children with HIV infection in South Africa: A retrospective case control study. Seizure 2019;65:159-165. https://doi.org/10.1016/j.seizure.2019.01.023

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