

Febrile seizures in an urban Tanzanian population: lessons learned from a community-based random cluster survey

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Abstract

OBJECTIVE To analyse the cumulative incidence of febrile seizures, to evaluate the accuracy of our screening questionnaire and to describe clinical characteristics of children with febrile seizure in an urban population in Tanzania.

METHODS A large random cluster sampled population was screened for a febrile seizure history as part of a larger epilepsy study using a standardised questionnaire in a two-stage door-to-door survey in Tanzania. A subset of screen positive participants was further examined for confirmation of diagnosis and evaluation of clinical characteristics.

RESULTS Overall, 49 697 people were screened for a febrile seizure history of whom 184 (0.4%) screened positive. Women more commonly screened positive than men (112 [0.4%] *vs.* 72 [0.3%]). There was no marked difference between age groups or education. The positive predictive value of the screening tool was 37% (95% CI 24–51%) but its accuracy varied with the age of interviewed individuals. Cumulative incidence rates were estimated between 1.1% and 2.0% after adjusting for the inaccuracy of the screening tool. Most febrile seizures occurred before the age of two (65%) and most children had more than one episode (80%). A large proportion of children had complex febrile seizure (65%), often caused by malaria or respiratory infections.

CONCLUSIONS The community-based cumulative incidence of a febrile seizure history in an urban Tanzanian population was similar to rates reported from other rural populations after adjusting for the inaccuracy of our screening tool. Based on the integrated nature of the febrile seizure questionnaire, screening positivity rates may have been too low. This has implications for the design of future studies. The majority of cases had complex febrile seizures often associated with malaria. This has implications for clinical case management.

keywords febrile seizures, Tanzania, epidemiology, malaria

Sustainable Development Goals (SDGs): 3, 3.2, 3.4

Introduction

Febrile seizures (FS) are the most common convulsions among children and are defined as epileptic seizures accompanied by a fever but without evidence of a central nervous system infection, which predominantly occurs in infants and children between the age of six months and five years [1]. The burden of neurological disorders in low-income and middle-income countries (LMIC) is

large, especially in children, and prevalence, concomitant diseases and complications differ from those of high-income countries (HIC) [2–4]. Other than intracranial infections, seizure disorders like FS account for a large number of neurological disorders in children [3–5]. Data from HIC suggest that in a small proportion of cases, epilepsy and psychiatric disorders can develop, and thus, early detection is crucial [6–9]. Cumulative incidence rates of FS are reported to be between 2 and 4%, with

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incidence peaking between 16 and 20 months of age [6,10–12]. However, studies differ significantly in methods (e.g. different study designs: prospective or retrospective) and definitions applied (e.g. different age limits for diagnosis of FS). There is also evidence that clinic-based studies report much higher incidence rates of FS than population-based studies [13–15]. To date, population-based studies in LMIC, particularly in sub-Saharan Africa, are lacking.

In addition to the greater burden of FS observed in LMIC, incidence appears to be even higher in rural than urban regions. For example in Nigeria, incidence of FS was 11.6% in rural regions *vs.* 8.1% in urban regions [12]. Several reasons may be at play. Malaria is a major cause of fever in children and is more common in rural than urban areas [12,16]. Furthermore, poor medical services specifically in rural areas contribute to delayed diagnosis and treatment of fever-causing diseases.

Moreover, the presentation of FS varies greatly, as demonstrated by an African study in which 71% of FS diagnoses were complex, *vs.* 20% ascertained in a British survey and 16% in a Chinese study [17–19]. Complex FS increases the risk for future epilepsy [20]. In order to appropriately plan and allocate healthcare services and inform parents about the nature of the disease, reliable estimates for FS incidence are crucial. Whilst FS prevalence in rural regions of Tanzania has previously been assessed [21], no community-based studies have been conducted in urban populations of Tanzania. This population is particularly important to assess as recent evidence shows disadvantages in health outcomes compared to rural counterparts [22].

The aims of this population-based study were to report the cumulative incidence of FS in an urban population in Tanzania, to evaluate the accuracy of our screening questionnaire and to report clinical characteristics, treatment and outcome of children with clinically confirmed FS. Furthermore, we describe the lessons learned with data collection on FS specific to an LMIC context.

Methods

The study took place in Kinondoni District, Dar es Salaam (Tanzania) between May and July 2010. Kinondoni is one of three districts of Dar es Salaam and is the industrial centre of Tanzania and therefore considered representative for an urban population. The study was conducted in the context of a large population-based survey on neurological disorders that included questions on epilepsy, FS and Restless Legs Syndrome (RLS). The study design and questionnaire have been described previously in detail [23]. In short, this study was divided into two phases. First, a

door-to-door survey was conducted. Every district in Tanzania is divided into wards consisting of villages and sub-villages that are further divided into so called ‘ten-cells’; ten-cells are the smallest administrative unit in Tanzania and comprise around 10 to 20 households. In this study, the population of the Kinondoni district was divided into 2886 clusters each consisting of 5 to 10 ten-cells. The study was primarily designed to assess community-based lifetime prevalence of epileptic seizures. For this, a sample size of 300 patients with epileptic seizures was defined necessary. A prevalence of 12/1000 people for epileptic seizures was assumed, and the target sample size was doubled to account for drop-out. The target sample size for our study was therefore 50 000 people. For the sampling, 137 clusters were selected following the probability-proportional-to-size method. In each cluster, all households were visited, and all people present were interviewed. The list of households was obtained from the Tanzanian National Bureau of Statistics. As the flow chart in Figure 1 shows, 13 759 households comprising 49 697 people were recruited. In case of minors, parents or guardians were interviewed. Screening was conducted by 15 enumerators trained in general aspects of the diseases, data collection and the conduct of an interview using the questionnaire that was provided in English and Swahili. The question specifically addressing FS or a history of FS was: *Was there a fever with seizures when you were/your child was between 1 month and 7 years of age?* Additional information on demographics and living situation such as education status was also obtained.

In phase two, people who screened positive for FS history in phase one were clinically examined by a

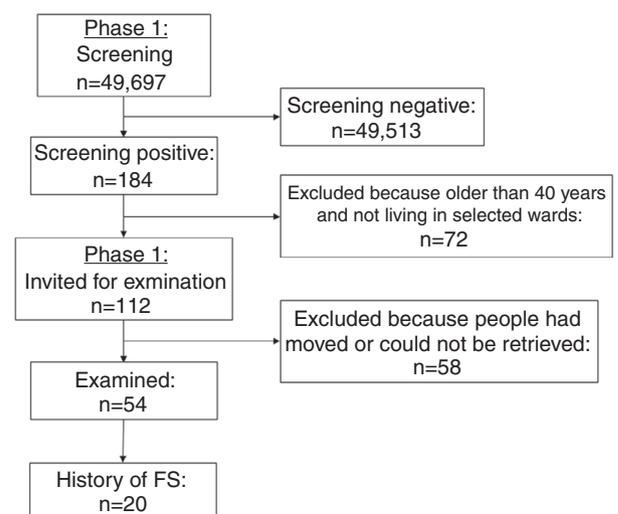


Figure 1 Flow chart of the study.

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neurologist to confirm diagnosis and to assess clinical characteristics of FS. As screening for FS is prone to recall bias, which increases with age, only people aged ≤ 40 years were included for phase two of this study.

Phase two: Confirmation of diagnosis and assessment of clinical characteristics

After the first screening phase, all individuals with a possible history of fever-associated epileptic seizures were identified. Due to limited funding and time at site, we further restricted phase two to only 17 of the original 23 wards (Figure 1). All individuals were either invited to Muhimbili National Hospital in Dar es Salaam or re-visited at their homes for clinical evaluation. Phone calls, home visits or letters of invitation delivered by district administrators were used to reach each individual.

Those who were successfully reached underwent a clinical examination by the study neurologist, and a detailed medical history was taken using an in-depth questionnaire to identify individuals with an actual FS history. FS was defined as epileptic seizure events accompanied by a fever in children between the age of 6 months and 7 years [19]. Individuals with central nervous system infections or neurological abnormalities were excluded by definition.

Among individuals with any FS history, details on clinical characteristics, treatment and outcome were collected. All minors (<18 years) were examined in the presence of a parent or guardian. Parents of adults who could not recall the characteristics of their FS were also invited to the study and provide further details. For participants with several episodes of FS, only the characteristics of the first episode were noted. Complex FS were defined as epileptic seizures with a fever during certain age span with focal features and/or duration of more than 15 min and/or recurrence within 24 h [24]. All other seizures were considered as simple FS.

Data collection and statistical analyses

Data were collected using Microsoft Excel and analysed using R version 3.6.1. Individuals screening positive for fever-associated epileptic seizures within the phase one questionnaire were defined as screen positive, and clinical diagnosis of FS was based on clinical examination and medical history (phase two). Overall rate for screening positive was age- and sex-standardised according to Kinondoni census data to account for unequal probability of selection and to adjust

estimates for representativeness of the district. Positive predictive values, that is the proportion of participants with clinical diagnosis of FS (phase two) among all screen positives of the screening questionnaire (phase one), were calculated by age group using R package 'epiR' having included a dummy variable for those who screened negative [25]. 'True' FS cumulative incidence rates were estimated by a Bayesian method for which we used the observed screening positivity rates and applied the observed positive predictive value and assumed negative predictive values of 99%, 99.5% and 99.9% [26].

Ethics statement

Ethics approval was granted by the National Institute of Medical Research in Dar es Salaam. Ethical approvals were also obtained from the Directorate of Research and Publications, Muhimbili University of Health and Allied Sciences Dar es Salaam as well as from the Ethical Committee of Ludwig-Maximilians University Munich, Germany. Informed consent was obtained from all participants or the legal guardian (for under-aged children) before inclusion in the study.

Results**Phase one: Screening for fever-associated epileptic seizures**

In phase one, 49 697 individuals were screened for FS (Table 1). The median age in our study sample was 23 years (interquartile range: 11–35) years *vs.* 22 years (interquartile range: 11–33) from the census data for Kinondoni. 51.7% were females *vs.* 51.4% reported in the census data of Kinondoni. Most participants had no formal (21%) or only primary education (54%).

In total, 184 screened positive for FS. This corresponds to cumulative incidence of 0.4% which did not change after age and sex standardisation according to census data for Kinondoni district. Women more commonly screened positive than men (112 [0.4%] *vs.* 72 [0.3%]). No marked difference was observed by age group, but screening positivity varied by ward between 0% and 1.3%. (Figures 2 and 3). Less educated people more often screened positive (Table 1).

Phase two: Confirmation of diagnosis and clinical characteristics of febrile seizures

Of the 184 people who screened positive in phase one, 112 were selected for phase two based on our age and

Table 1 Baseline characteristics and people screening positive for fever-associated epileptic seizures in phase one of the study

		Febrile seizures screening questionnaire		
		All <i>n</i> (%)	Negative <i>n</i> (%)	Positive <i>n</i> (%)
Study participants	All	49 697	49 513 (99.6)	184 (0.4)
	≤40 years	40 686	40 686 (99.6)	146 (0.4)
Sex	Females	25 689 (51.7)	25 577 (51.7)	112 (60.9)
	Males	24 008 (48.3)	23 936 (48.3)	72 (39.1)
Age in years	median (interquartile range)	23 (11–35)	23 (11–35)	23 (11–35)
Relation to household head	Head of household	12 697 (25.5)	12 663 (25.6)	34 (18.5)
	Spouse	8279 (16.7)	8241 (16.6)	38 (20.7)
	Child/stepchild	18 664 (37.6)	18,598 (37.6)	66 (35.9)
	Other relative	8873 (17.9)	8831 (17.8)	42 (22.8)
	No blood relationship	991 (2.0)	987 (2.0)	4 (2.2)
	Missing	193 (0.4)	193 (0.4)	0 (0.0)
Education	No formal	10 311 (20.7)	10 254 (20.7)	57 (31.0)
	Primary	26 865 (54.1)	26 766 (54.1)	99 (53.8)
	Secondary	9396 (18.9)	9378 (18.9)	18 (9.8)
	Tertiary	2839 (5.7)	2830 (5.7)	9 (4.9)
	Missing	286 (0.6)	285 (0.6)	1 (0.5)

ward exclusion criteria. 54 of those were clinically examined and received an in-depth questionnaire relating to their symptoms, treatment and other health outcomes. The proportion of participants who were clinically examined differed by age and was smallest for adults aged ≥ 25 years (Figure 4a). Of the 58 people who could not be examined, 17 (29%) had moved, 30 (52%) did not respond to our repeated invitations and 11 (19%) could not be reached by the information we had (Figure 1). Those who could not be examined were older than those who were examined (median age 22 years [IQR 9–29 years] *vs.* 17 years [IQR 10–24 years]) and were more commonly female (60% *vs.* 52%). Overall, only 20 participants were diagnosed with FS; 19 were diagnosed with epilepsy, a further 4 had a single episode of epileptic seizures and no history of convulsions was reported in 11 participants (Figure 4b). This corresponds to a positive predictive value of 37% (95% CI 24–51%) for our screening question. The positive predictive value was highest for children ≤ 7 years (60%, 95% CI 26–88%) and decreased with age (Figure 4c). Using our positive predictive value of 37% and assuming a negative predictive value of 99%, 99.5% and 99.9% to estimate community-based incidence yielded true FS cumulative incidence rates of 2.0%, 1.5% and 1.1%, respectively.

Characteristics of febrile seizures

The clinical and demographic characteristics of the 20 individuals with a proven history of FS are summarised

in Table 2. Thirteen (65%) of the 20 cases with confirmed diagnosis of FS were male. 13 cases had complex FS, mostly due to the duration of seizure episodes, and 7 had simple FS. The median age at first FS was 1.5 years (IQR 8 months–2.5 years) and for children with simple FS incidence occurred earlier than for children with complex FS. In our study, all children experienced their first FS before the age of four.

A history of fever-causing diseases could be determined in 15 of 20 cases (Table 2). The most common causes were malaria ($n = 8$) and respiratory infections ($n = 5$), followed by gastrointestinal infections ($n = 2$). Malaria was more common among children with complex FS (54% *vs.* 14%). Children with complex FS had more median episodes than children with simple FS (6 [2–10] *vs.* 4 [1.5–7]). Usually, FS occurred within the first day of fever.

Treatment and outcome

Fourteen of the 20 individuals with FS sought medical treatment; more among those with complex compared to simple FS (85% *vs.* 43%). Ten were treated with pharmaceuticals and 8 received traditional medicine. Treatments prescribed included antipyretics ($n = 5$), antimalaria medication ($n = 3$) and anti-epileptic drugs ($n = 3$).

Between the occurrence of FS and the interview, two of the 14 cases older than 7 years at time of interview had developed epilepsy, one with simple and one with

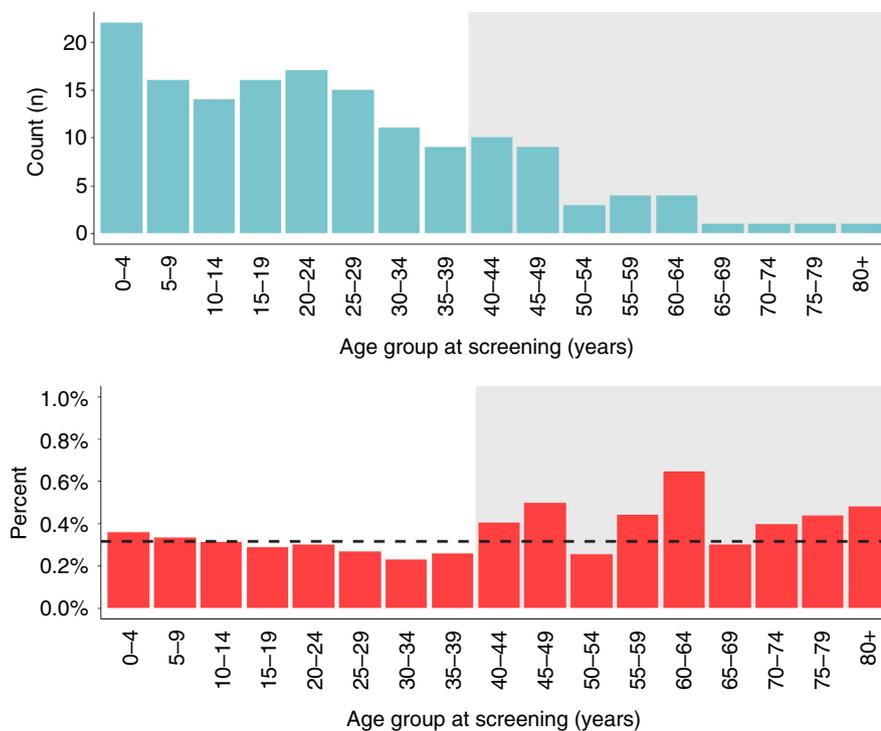
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Figure 2 Distribution of people who screened positive in the questionnaire for febrile seizures (total number and per cent), by age group. Note: People in the age groups of the shaded area were not included in phase two of this study. Dotted line: weighted mean for screening positivity for febrile seizures. [Colour figure can be viewed at wileyonlinelibrary.com]

complex FS (Table 2). None of the individuals had developed neurological sequelae other than epileptic seizures.

Discussion

In this large population-based study, we screened nearly 50 000 people in the urban Kinondoni district of Dar es Salaam, Tanzania, for a history of FS and found a community-based positivity rate of 0.4%. The clinical examination of those who screened positive yielded a positive predictive value of the screening questionnaire that depended on the age of the participant and therefore also on the person who answered the questionnaire. The positive predictive value was highest in children ≤ 7 years of age, for whom a parent or guardian answered, and it decreased as age increased. Upon examination of participants who screened positive, more than half did not have a history of FS by the clinical definition. People with a history of FS mostly experienced their first FS before the age of two, suffered from several episodes and often had complex FS. The most common underlying fever-causing diseases were respiratory tract infections and malaria.

Evaluation of the screening question and cumulative incidence estimates

Case ascertainment of FS in a large population-based study using a single integrated screening question yielded interesting results. In very young children ≤ 7 years of age, a clinically diagnosed history of FS was found in 60% of FS screen positives and this decreased to 19% in adults aged ≥ 25 years. This shows that if a parent or guardian answered for a child and if the FS episode had occurred only a short time before, the questionnaire was quite useful. The longer ago the FS episode occurred, and when people answered themselves and not their parents, the lower the accuracy of the questionnaire. This may be due to recall bias or lack of reporting about FS episodes by participant's parents, likely due to lack of knowledge or consideration of FS as harmless.

Additionally, the screening cumulative incidence we found for FS (0.4%) is considerably lower than expected. The reasons can be manifold. Patients who have epileptic seizures or epilepsy are often stigmatised and discriminated against, as reported in several studies from Africa where aetiology of seizures is commonly conceived as

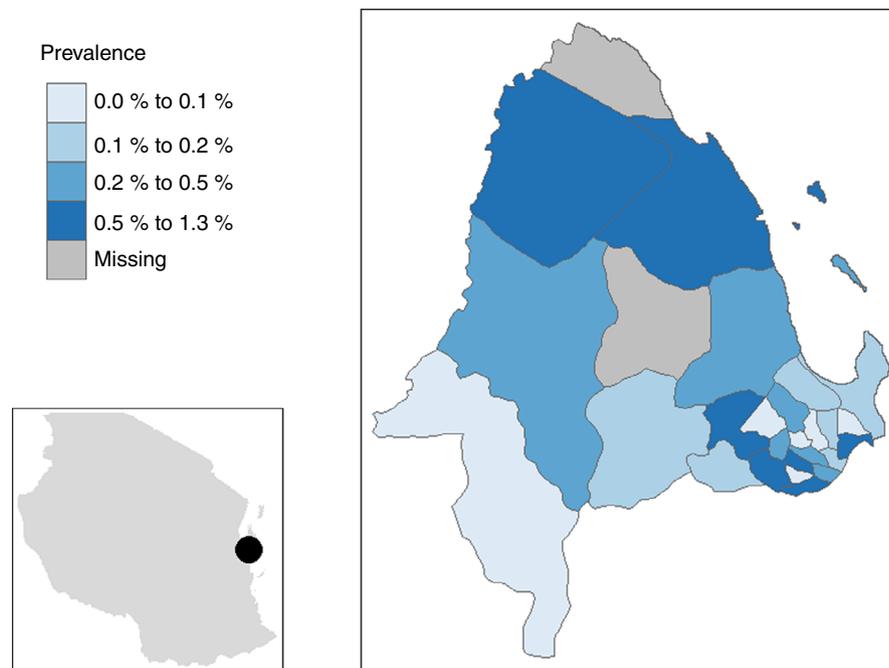
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Figure 3 Screening positivity rate for febrile seizures in Kinondoni district, by ward. [Colour figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.com)]

supernatural [27–30]. This is likely to have influenced the responses to the screening questionnaire as well as uptake of clinical examination. Using Bayesian methods to estimate the ‘true’ cumulative incidence of FS yielded rates that are comparable to those reported in other studies (1.1–2.0%). Unfortunately, we could not examine a subset of those screening negative due to funding and time restraints. However, even if a negative subset had been recruited, it is likely that very few cases of FS would have been detected as there are no objective criteria for retrospective diagnoses of FS. Additionally, higher cumulative incidence estimates among younger individuals could reflect recall bias that increases with time since the event, rather than a recent increase in incidents. Presumably, most who experienced an epileptic seizure as a young child will be completely unaware of the event, but parents whose child recently had FS might be more likely to better recall the incident. Conversely, older age groups screened positive more commonly than younger counterparts; however, this may again be due to recall biases rather than increases in FS incidence over time. Furthermore, there may be a tendency to better recall more severe events, which may explain the predominance of complex FS that we observed. This was also demonstrated in a study from Finland, in which researchers compared prospective with retrospective data on FS and found large differences within the same cohort [31].

Therefore, the actual cumulative incidence estimate may be higher.

Another reason for under-reporting may have been due to the integrative nature of the survey itself, that is several neurological disorders were investigated at the same time. The FS question as described under Methods was not asked in isolation but at the end of an epilepsy questionnaire. This may have led to misclassification of epileptic seizure events, or enumerators may have paid less attention to the final questions or enumerators were not sufficiently medically trained to distinguish between seizure types. The integration of questions on several different diseases into one questionnaire is a commonly used technique in global health epidemiology. For example, Demographic and Health Surveys (DHS) cover various diseases ranging from infectious to non-communicable. In the case of FS and epilepsy, however, this may not be a valid method and may require more specific questions only directed at FS. In addition, adjusted study designs, for example triangulation of different data sources using a mixed-method approach such as medical records from healthcare facilities, community-based disease surveys and key informant interviews with heads of households or community leaders, may yield more realistic estimates for cumulative incidence of FS. However, this may not be feasible in all LMIC settings [32]. In addition, innovative methods such as digital recording of an epileptic seizure

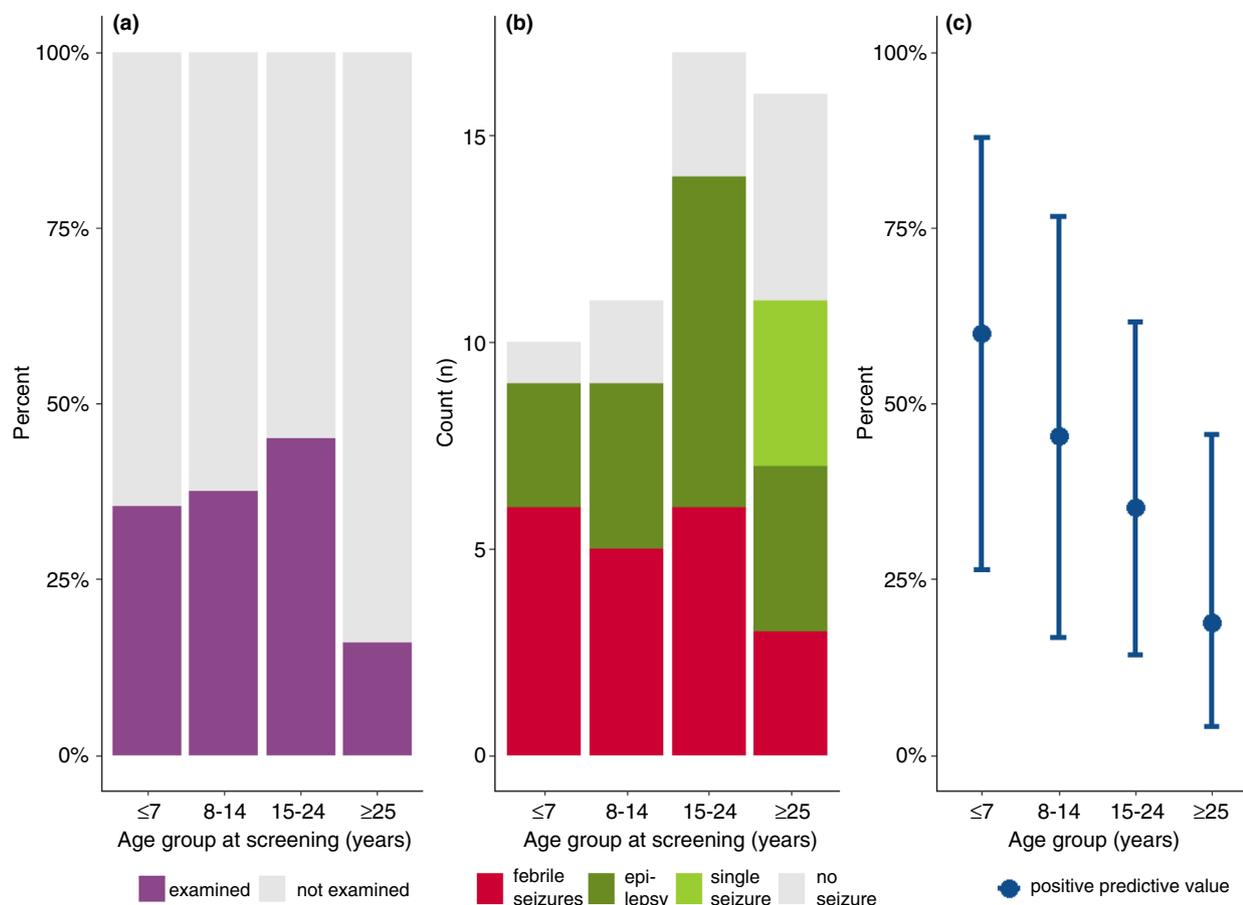


Figure 4 Recruitment percentages in phase two (a), diagnoses of recruited patients in phase two (b) and positive predictive values (c) of the screening question, by age group. [Colour figure can be viewed at wileyonlinelibrary.com]

event through a mobile phone app, which generates automated messages for immediate medical action, can be applied. Those are important lessons learned from our study and future studies should consider these issues, but also be mindful about cultural sensitivities and stigmatisation around epileptic seizures in order to produce better cumulative incidence estimates.

Overall, incidence estimates of FS from the very few studies from LMIC differ greatly. In a community-based study in rural Tanzania, a cumulative incidence of 2.1% was determined, but the sample size of this study was considerably smaller and also children who lost consciousness while having fever were considered as screening positive [21]. Several studies from urban and rural areas in India observed incidences ranging from 0.2% to 1.3% [5,33].

Whether FS are more common in rural than urban Tanzania is difficult to assess because of discrepancies in accessibility of healthcare services and health information

systems and differences in health seeking behaviour. Data collected through DHS, however, can provide an indication [34-36]. Based on all Tanzanian household surveys after 2010, no difference in recent fever prevalence among children < 5 years was detected between urban and rural areas. However, differences were observed for underlying diseases. Prevalence of acute respiratory infections tends to be higher in urban areas, possibly because of higher degree of air pollution. On the contrary, malaria prevalence is substantially higher in rural areas. The most recent data suggest that 9.2% (95%CI 7.2–11.2%) of children < 5 years in rural areas had malaria, but only 2.1% (95%CI 0.8–3.5%) of children in urban areas [35]. Although many countries in sub-Saharan Africa have made great progress towards malaria elimination in the context of the Sustainable Development Goals, the number of malaria cases in Tanzania has unfortunately increased to nearly seven million in 2018 [37]. Therefore, in the future, malaria will likely remain an important

Table 2 Clinical characteristics of patients with a history of febrile seizure(s)

		Overall n (%)	Simple n (%)	Complex n (%)
Number		20	7 (35)	13 (65)
Sex	Female	7 (35)	2 (29)	5 (71)
	Male	13 (65)	5 (38)	8 (62)
Age group (years)	≤7	6 (30)	2 (29)	4 (31)
	8–14	5 (25)	2 (29)	3 (23)
	15–24	6 (30)	2 (29)	4 (31)
	≥25	3 (15)	1 (14)	2 (15)
Age at first febrile seizure (years)	≤1	8 (40)	4 (57)	4 (31)
	1–2	5 (25)	0 (0)	5 (39)
	2–7	7 (35)	3 (43)	4 (31)
Age at first febrile seizure (years)	Median [IQR]	1.5 [0.7–2.5]	0.7 [0.6–2.5]	1.5 [0.8–2.5]
Age at last febrile seizure (years)	Median [IQR]	4.5 [3.5–5.5]	4.5 [3.5–5.5]	4.5 [3.5–5]
Febrile seizures per episode	1	18 (90)	7 (100)	11 (85)
	2	2 (10)	0 (0)	2 (15)
Number of episodes	Median [IQR]	6 [2–10]	4 [1.5–7]	6 [2–10]
Duration of febrile seizure (minutes)	≤15	8 (40)	7 (100)	1 (8)
	16–30	5 (25)	0 (0)	5 (39)
	>30	7 (35)	0 (0)	7 (54)
Side of convulsion	Bilateral	19 (95)	7 (100)	12 (92)
	Unilateral	1 (5)	0 (0)	1 (8)
Loss of consciousness		8 (40)	4 (57)	4 (31)
Duration of fever before febrile seizure	few hours	6 (30)	2 (29)	4 (31)
	less than one day	8 (40)	4 (57)	4 (31)
	1–2 days	5 (25)	0 (0)	5 (39)
	>2 days	1 (5)	1 (14)	0 (0)
Fever-causing diseases	Gastrointestinal infection	2 (10)	0 (0)	2 (15)
	Respiratory infection	5 (25)	2 (29)	3 (23)
	Malaria	8 (40)	1 (14)	7 (54)
	Unknown	5 (25)	4 (57)	1 (8)
Family history of febrile seizures		4 (20)	2 (29)	2 (15)
Problem of mother during pregnancy or delayed development		4 (20)	2 (29)	2 (15)
Medical attention for febrile seizure(s)		14 (70)	3 (43)	11 (85)
Treatment	Pharmacological treatment	10 (50)	2 (29)	8 (62)
	Antipyretics	5 (50)	1 (50)	4 (50)
	Antimalaria medication	3 (30)	1 (50)	2 (25)
	Antiepileptic medication	3 (30)	0 (0)	3 (38)
	Traditional medicine	8 (40)	2 (29)	6 (46)
Neurological sequelae other than epileptic seizures		0 (0)	0 (0)	0 (0)
Outcome	No more epileptic seizures	12 (60)	4 (57)	8 (62)
	Epilepsy at adolescence	2 (10)	1 (14)	1 (8)
	So far no epilepsy*	6 (30)	2 (29)	4 (31)

*Patients ≤ 7 years at time point of examination; IQR = interquartile range.

contributing factor to the burden of FS, particularly to complex FS, as was the case in our study. Likewise, we believe FS rates will neither decrease, nor increase as they likely have remained stable in the preceding decades.

Clinical characteristics

Although our clinical sample size was very small and we primarily aimed to determine FS cumulative incidence,

we were able to ascertain information about characteristics and the outcome of FS in 20 cases. The average age of onset was 1.5 years, and FS occurred typically at initial increase of fever, which is in accordance with results from previous studies [6,38]. The cumulative incidence of FS was higher in boys than in girls, even though females screened more often positive and the sex distribution of the 54 re-interviewed participants was almost equal. Although there is so far no clear explanation for this

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circumstance, many previous studies reported the same observation [2,27,39,40]. Reasons could be genetic factors, differences in sex hormones or immunological differences which may also be associated with overall better survival rates among girls [41–43].

Sixty-five per cent of the former patients had experienced complex FS. This is higher than results from HIC, where about 20% of the FS are complex [18]. On the other hand, our data are similar to findings from previous studies conducted in Tanzania, where a proportion of 42% (community-based) and 65% (hospital-based) with a history of complex FS were reported [16,21]. Hospital-based rates are often higher, because naturally more severe cases are brought to the hospital, whereas mild cases often stay at home [44]. For a similar reason, the proportion of complex FS could be an overestimation as well, because parents are likely to remember complex cases. FS were mainly characterised as complex, because of their long duration, reported by the witnessing parents. This perception is of course highly subjective and might be in fact shorter than parents perceived. Apart from their long duration, most of the seizures had been generalised (95%) and did not recur within 24 hours (90%).

In western countries, FS is usually associated with infections of the respiratory and auricular system, followed by gastrointestinal infections [38,40]. In our study, malaria and respiratory infections were observed as the main cause of FS. It should be mentioned that for the clinician it is often not easy to differentiate between FS due to malaria and epileptic seizures in the context of early stage cerebral malaria [16,21,27–29]. Hence, children in whom the underlying diagnoses is not clear have to be hospitalised and appropriate treatment needs to be initiated without delay.

The risk for developing epilepsy after FS depends on characteristics of FS. Particularly people with complex and recurrent FS have an increased risk of epilepsy later in life [45]. In our cohort, two cases had developed epilepsy after their 15th birthday – one with simple and one with complex FS. This is a higher rate than reported by, for example Van den Berg *et al.* (3%), Ross *et al.* (6%) or Nelson *et al.* (1–10%) [28,38,40,44], but needs to be interpreted with care in our small sample.

Concerning treatment, most of the cases received biomedical treatment. Seven out of ten were brought to the hospital, and in 25% of the cases, pharmaceutical treatment was given. The use of anti-epileptic medication in 15% of children seems rather high as it is not generally recommended.

Limitations

Our study had several limitations. As described above, our screening questionnaire seems to have some drawbacks because of its integrative nature and the retrospective diagnosis of FS, which relies on good recall of the interviewees or, in case of children, of their parents. This has been critically discussed in the above section and ways forward for future study designs have been suggested. Furthermore, for phase two, we only selected 17 wards and were only able to reach half of our study population. This might be due to people in Dar es Salaam changing place of residence commonly, as we noticed during our investigations. A further reason might be that our invitations were indeed received, but people may have had no interest in making the effort to come to the hospital, because FS were no longer of concern to most of the previous interviewees. Consequently, our sample for determination clinical characteristics was very small and prone to selection bias. The participants who could not be re-visited differed from those who we visited. They were more often female and less educated. This might have affected positive predictive values and clinical characteristics of FS. We think that the inverse association between the positive predictive value and age holds true, nonetheless. We cannot rule out survivor bias, but we do not believe this would impact our estimates considerably since only a small excess mortality rate will have occurred due to FS. As observed, in the long term, mortality does not appear to be increased in children with FS [46]. Although the focus of this study was on the lifetime FS prevalence and the screening questionnaire and not on the clinical characteristics of the patients with FS, we believe our results still give a useful insight into clinical characteristics, underlying diseases, treatment and outcome of FS in urban Tanzania, a LMIC.

Conclusion

In this large-scale, population-based study in Dar es Salaam, Tanzania, we found a relatively low screening positivity for FS, which may be due not only to recall bias but also to the way the study was conducted, that is the integrated investigation of FS as part of a larger study on neurological disorders. Our study also highlights possible pitfalls and challenges when such a study is conducted in an urban, highly mobile population within a resource-poor context, but also contributes valuable insights into the cumulative incidence of FS in an under-researched setting. We critically discuss lessons learned from our community-based study within an LMIC urban area and

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give clear suggestions for an improved study design with a potential mixed-method approach.

Our study hints that the majority of FS are complex in nature with an increased risk of developing epilepsy later in life. We found that malaria is the most common and respiratory infections the second most common cause of FS, even in urban areas. Delivery of education on FS to caregivers needs to be emphasized and could potentially be integrated in Mother and Child Clinics in order to diminish stigmatisation and encourage biomedically based management of affected children.

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