Prevalence of idiopathic epilepsy among primary school children in Qena City, Qena governorate, Egypt

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Abstract

Background: Epilepsy among children is a common neurological disorder and may have a major impact on children development though epidemiological studies are limited.

Objectives: To estimate the prevalence of idiopathic epilepsy among primary school children in Qena City, Egypt.

Patients and methods: All primary schools were approached; Students were asked to complete prepared validated questionnaires. 4218 children aged 6-12 years old were screened, out of them 1428 males and 1315 females returned the questionnaires thoroughly fulfilled. Positive cases were subjected to detailed history, neurological examination, electroencephalography and neuroimaging.

Results: 21 cases of epilepsy were identified; lifetime prevalence was 7.6/1000, active epilepsy prevalence was 5.8/1000. Epilepsy was more common in males (8.4/1000) than females (6.8/1000). Generalized seizures were significantly higher than focal (76.1%, versus 19%) with prevalence 5.8/1000 and 1.4/1000 respectively. 38% of epileptic children were at 6-8 years. The most common age of onset was 6 to < 12 years. Epilepsy was more common among low socioeconomic class in comparison to the others. The Odd`s ratio for Family history of epilepsy, consanguineous marriage of parents and history of febrile seizures had a significant difference to non-epileptic children. All patients receive anti-epileptic drugs; 81% on mono therapy and 19% on poly therapy.

Conclusions: Prevalence of epilepsy among primary school children in Qena city was 7.6/1000, in line with other Egyptian studies and Arab world studies but much higher than most developed countries. Family history of epilepsy, consanguineous marriage of parents and history of febrile seizures were the main risk factors.

Keywords: Prevalence, Epilepsy, Children.

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Introduction

Epilepsy is one of the most frequent diagnosed neurologic disorders in children and adolescents. Childhood epilepsy diagnosis is a challenging because it has a large array of symptoms and similarities to other non-epileptic conditions with a considerable risk of misdiagnosis (**Chowdhury et al., 2008**). Epilepsy is an important cause of morbidity in children and adolescents and its chronic nature and early onset makes the child vulnerable to developmental, cognitive and social disadvantages. The crude prevalence rate of epilepsy in Europe 4.5-5 per 1000 (**Forsgren et al., 2005**) and in developing countries ranges from 3.8 to 15.4 per 1000 person-years (**Carpio & Hauser, 2009**). In our community the prevalence rate for epilepsy was 12.7/1000 (**Khedr et al., 2013**). To the best of our knowledge this is the first school based study in Qena governorate aimed to estimate the prevalence of idiopathic epilepsy among primary school children and to identify different types of seizures and common risk factors.

Patients and methods

The study was a cross sectional descriptive epidemiological study was carried out to estimate the prevalence of idiopathic epilepsy in primary school children aged 6-12 years in Qena city. Qena city is the capital of Qena governorate located at south Upper Egypt containing 12 primary school. The Minimal sample size calculation according to preliminary idiopathic epilepsy prevalence at Assiut governorate 9.5/1000 (**Khedr et al., 2013)** with level of confidence at 95% was 1369 students (**Daniel, 1999**). The classes for each school were chosen randomly. An official written approval was taken from the vice-ministry of

education to start the research provided that no invasive technique will be done to the students. This consent was given to all school administrators.

Case definitions

Epilepsy was diagnosed when the child had at least two unprovoked seizures more than 24 hours apart or a single seizure or one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years or diagnosis of an epilepsy syndrome (**Fisher et al., 2014**).

Epilepsy classification was according to the operational classification of seizure types by international league against epilepsy 2017 which implies typing to focal onset, generalized onset, unknown onset and unclassified; each type consists of motor and non-motor onset except unclassified group **(Fisher et al., 2017)**

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years (**Fisher et al., 2014)**.

Epilepsy was considered idiopathic in children who had a normal neurological assessment and normal neuroimaging (**Scheffer et al., 2017**).

Lifetime prevalence rate is defined as a diagnosis of epilepsy at some point prior to the prevalence period or date. It includes patients with either active

epilepsy or on remission on the prevalence date (**Hauser et al., 1991**).

Inclusion criteria: includes primary school children aged 6-12 years regularly attending to the schools.

Exclusion criteria: includes single seizure, acute symptomatic seizures, i.e. febrile seizures or seizures related to acute metabolic disorders or toxins. Children with structural brain insult or abnormal neurological status including those with cognitive impairment and deaf-mute children were also excluded.

This study was conducted in three stages:

Stage 1: Screening

All 12 schools were approached with pre-structured clear simplified questionnaires in Arabic terms were completed by the students and their parents. Questionnaire was previously validated in Assiut study with sensitivity and specificity were 95% and 88% respectively **(Khedr et al., 2013)**. The screening questionnaire consisted of two-parts, Part I documenting socio-demographic information and Part II containing modified epilepsy screening questionnaire (**Haerer et al., 1986**) excluding the last question of febrile convulsion, questionnaire was pre-tested in the outpatient clinic of Assiut University Hospital on a group of 25 epileptic patients and 25 age and sex-matched control with joint arthritis without epilepsy. The screening questionnaire consisted of 12 questions requiring answers yes or no. Each query related to the existence or absence of a particular symptom related to epilepsy in the last year or prior years. The completed questionnaires were evaluated by the researcher to identify possibly positive cases.

The socio-economic status was assessed by an Arabic validated scale, It consists of four dimensions: the level of education of the parents, the occupation of the parents, the gross monthly income of the family and the lifestyle of the family. A score of one was given to each item. According to the total score, the socio-economic level was divided into three categories: high, moderate and low (**Abd El-Tawab, 2012**)

Stage 2: Clinical assessment

All possible positive cases were referred to outpatient clinic of neurology department for further assessment which includes:

A) Detailed history taking including developmental history, history of fever related to the attacks or other situation related to epilepsies, age of onset, history of acute central nervous system insults or severe head injury. History of consanguineous marriage, family history of epilepsy of the same or different types and family history of febrile convulsions. Detailed semiology of the seizures, seizure frequency before starting AEDs, history of epileptic emergencies as status epilepticus or serial fits, history of multiple types of seizures, the type of AEDs and the degree of control on treatment; seizures are divided into controlled if there is no seizures for ≥1year and uncontrolled if there is decrease in the frequency or change in the character of seizure from wild picture to mild presentation (**Khreisat, 2011**).

B) General and full neurological examination: For possible motor disabilities, mental sub-normality and speech disorders.

Stage 3: Investigations

A) Electroencephalography (EEG) was obtained for all patients (Nihon Kohden L5-901, 2008), scalp electrodes are mounted according to the international 10-20 system with bipolar and referential montages. EEG record was performed under standard

conditions with eye closed and with provocative maneuvers as photic stimulation and hyperventilation.

B) Magnetic Resonance imaging (MRI) of the brain was occasionally done when indicated clinically.

C) Laboratory investigations were done includes complete blood picture, renal and liver function tests and glycosylated hemoglobin (HgA1c) to exclude secondary causes of epilepsy.

Ethical Considerations: All parents of participant children provided an informed written consent. The local Ethical Committee of Qena faculty of medicine approved the study.

Statistical analysis

Data obtained from this study will be fed into computer by using statistical package program for social science (IBM, SPSS, version 26) to analyze data via simple descriptive analysis (i.e. frequency and percentage). Comparative statistical analysis between variables was done using chi-square for qualitative data. A value of $P < 0.05$ was considered statistically significant. Odds ratio (OR) was calculated to determine the potential risk factors for epilepsy in the studied children.

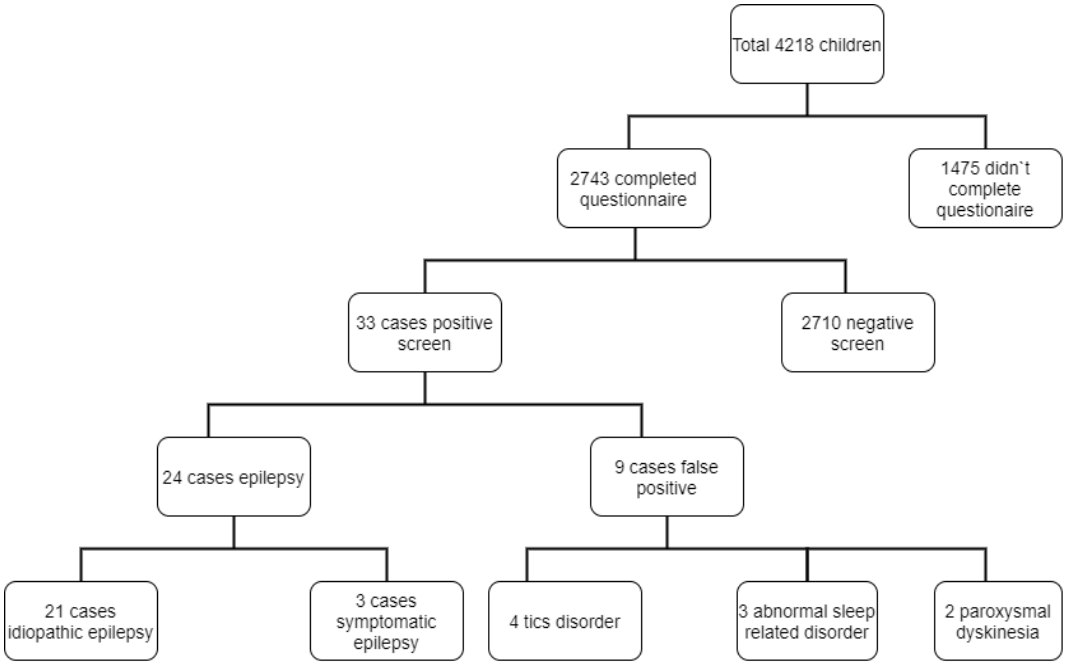

Fig.1. Flow chart for studied children

Results

According to the official document represented by the vice minister of ministry of education, the number of registered primary school students were 4218 (2255 male and 1953 female) of 12 schools in Qena city. All schools were approached, and students were asked to respond by filling questionnaires. 1475 (35 %) didn't return questionnaires or answered it carelessly, therefore they were excluded. 2743 (65%) (1428 male and 1315 female) returned the questionnaires thoroughly fulfilled. In those students we identified 33 cases as positive cases and after reevaluation 24 cases proved to have epilepsy, after reevaluation by neuroimaging and

EEG, 21 cases found to have idiopathic epilepsy. 3 cases proved to be symptomatic epilepsy, 1 case has a congenital cerebral anomaly (schizecephaly) and the other two cases have chronic ischemic lesions related to perinatal insults (cerebral palsy). The remaining false positive 9 cases found to have tic disorder (4 cases), abnormal sleep movement disorder (3 cases) and paroxysmal dyskinesia (2 cases). Active epilepsy was diagnosed in 16 cases; Details illustrated in (**Fig.1**).

The lifetime crude prevalence rate of total cases of idiopathic epilepsy was 7.6/1000 (95% CI: 4.7-11.7) while the active epilepsy prevalence rate was 5.8/1000 (95% CI: 3.3-9.5). The sex specific prevalence rate for males and females 8.4/1000 (95% CI: 4.3-14.7) and 6.8/1000 (95% CI: 3.1-12.9) respectively with insignificant difference between males and females' rates (X^2=*0.22,* P-value =0.64). The most common seizures type was generalized seizures with prevalence rate 5.8/1000 while focal seizures prevalence rate was 1.4/1000. Details illustrated in (**Table 1**).

Table 1. The lifetime crude prevalence rates of idiopathic epilepsy and seizures classification

Number of cases/ Number of populations	**CPR/1000**	**95% CI**
Total number of epileptic children 21/2743	7.6/1000	4.7-11.7/1000
Total number of active epileptic children 16/2743	5.8/1000	3.3-9.5/1000
Sex specific Prevalence rate :		
Total number of epileptic males 12/1428	8.4/1000	4.3-14.7/1000
Total number of epileptic females 9/1315	6.8/1000	3.1-12.9/1000
Seizure types		
Generalized 16/2743	5.8/1000	3.3-9.5/1000
Motor:		
Tonic-clonic 11/2743	4/1000	2-7.2/1000
Myoclonic 1/2743	0.36/1000	0.009-2/1000
Atonic 1/2743	0.36/1000	0.009-2/1000
Non motor		
Absence 3/2743	1.1/1000	0.2-3.1/1000
Focal 4/2743	1.4/1000	0.3-3.7/1000

Motor: Clonic 2/2743	0.7/1000	0.008-2.6/1000
Non motor Cognitive 1/2743	0.36/1000	0.009-2/1000
Focal evolve to bilateral seizures 1/24743	0.36/1000	0.009-2/1000
Unknown onset 1/2743	0.36/1000	0.009-2/1000

N: number, CPR: crude prevalence rate, CI: confidence interval

Electroencephalographic finding and epileptic syndromes

33% of total studied children with idiopathic epilepsy had normal interictal EEG while abnormal EEG with epileptiform changes was recorded in 67%. Abnormal EEG in Children with generalized seizures was 69% while in focal was 75%. Specific epileptic syndromes were recorded in 3 cases with typical absence childhood epilepsy and one case with benign epilepsy of childhood with centrotemporal spikes. Details shown in (**Table 2**).

Sociodemographic status, risk factors and seizures characteristics of studied epileptic children

The mean age of epileptic children ±SD was 9.5±1.8, epilepsy was more common in 6-8 age group representing 38% of total epileptic children. Regarding age of onset the most common age of onset was from 6-≤12 years (47.6%) with significant difference among males and females across all age groups (p-value =0.04). Epilepsy was more common in low socioeconomic level students (71.4%) in comparison to middle and high socioeconomic level students (23.8 and 4.8%). Most of epileptic seizures occur in both day and night 13 cases (61.9%), 5 cases (23.8%) diurnal, one of them occur on awakening, 3 cases (14.3%) at night.

As regard risk factors, 23% of epileptic children have positive family history of epilepsy, 57.1% epileptic children have positive consanguinity of parents while 19% have past history of febrile seizures. The most common drugs in use were levetiracetam and sodium valproate representing 42.8% and 28.6% respectively. All patients received anti-epileptic drugs 17 cases (81%) on mono therapy and 4 cases (19%) on poly therapy. 38.1% with uncontrolled seizures, 14% partially controlled seizures and 47.6% fully controlled seizures. No history of serial fits or status epilepticus found during evaluation. Details in (**Table 3**).

Table 2. Electroencephalographic finding and epileptic syndromes

Parameters	Number (%)
Normal EEG	7(33%)
Focal	1(25%)
Generalized	5(31%)
Unknown	1(100%)

Abnormal EEG Focal Generalized Unknown	14(67%) 3(75%) 11(69%) 0(0%)
Type of Paroxysm Focal Generalized Unknown	 Focal spike and sharp waves (3) Generalized spikes and spike-wave discharge (16) Non
Epileptic syndromes Typical childhood absence epilepsy Benign epilepsy of childhood with centrotemporal spikes	4(19%) 3 1

EEG: Electroencephalography

Table 3. Sociodemographic, risk factors and seizures characteristics of epileptic children

Parameters	Number (%)
Age(years) mean±SD	9.53±1.8
Common age groups 6-8 years/9-10 years/11-12 years	 8(38.1%)/7(33.3%)/6(28.6%)
Age of onset • < 1 year(Males/females) • 1<6 years(Males/females) • 6<12 years(males/females)	 2(9.5%)/0(0%) 7(33.3%)/2(9.5%) 3(14.3%)/7(33.4%)
Social class Low/middle/High	 15(71.4%)/5(23.8%)/1(4.8%)
Family history of epilepsy (positive/negative)	 5(23.8%)/16(76.2%)
Consanguinity history (positive/negative)	 12(57.1%)/9(42.9)
Febrile seizures history (positive/negative)	 4(19%)/17(81%)
Time of seizures Diurnal/Nocturnal/ diurnal and nocturnal	 5(23.8%)/3(14.3%)/13(61.9%)
Prodromal symptom (positive/negative)	 4(19%)/17(81%)
Postictal subjective symptoms • Headache • Sleep • Drowsiness and confusion • Muscle aches • Vomiting	17(81%) 4(19%) 9(42.9) 2(9.5%) 1(4.8%) 1(4.8%)
Type of drug treatment • Carbamazepine • Sodium valproate	 3(14.3%) 6(28.6%)

• Lamotrigine • Levetiracetam	3(14.3%) 9(42.8%)
Degree of seizures control • Uncontrolled • Partially controlled • Fully controlled	 8(38.1%) 3(14.3%) 10(47.6%)

SD: standard deviation

The odd`s ratio and relative risk between epileptic and non-epileptic children

Children with positive family history of epilepsy have 12.8 times to develop idiopathic epilepsy compared to children with negative family history. Also, children with positive past history of febrile seizures have 26.6 times to have idiopathic epilepsy than children without. On the other hand, relative risk of Consanguinity of parents between epileptic and non-epileptic was 2.9. The odds ratio between three above risk factors is highly significant in comparing epileptic and non-epileptic children. Details in (**Table 4**).

Table 4.The Odd`s ratio of epileptic children

Parameter	epileptic	Non-epileptic	OR(95%CI)	RR(95%CI)	P value
Family history of epilepsy (positive/negative)	5/16	60/2662	13.8(4.9-39)	12.8(4.8-34)	0.0001
Consanguinity (positive/negative)	12/9	850/1872	2.9(1.2-7)	2.9(1.2-6.8)	0.011
Febrile seizures (positive/negative)	4/17	20/2702	31.8(9.8-103)	26.6(9.7-73.3)	0.0001

OR: odd`s ratio, RR: relative risk.

Discussion

Epilepsy is one of the most common neurological diseases globally affecting all ages. It has a negative effect on childhood quality of life in comparison to other medical diseases (**Moreira et al., 2013**).

The current study showed that the lifetime prevalence rate of idiopathic epilepsy among children aged 6-12 years in Qena city was 7.6/1000 while active prevalence rate was 5.8/1000. The finding was consistent with two Egyptian school-based studies with prevalence rate 7.2/1000 in 6-14 years children (**Mahmoud, 2009; Alshahawy et al., 2018**). There was a three-representative door to door Egyptian epidemiological studies involving prevalence of epilepsy, first **Farghaly et al. (2012)** found the prevalence among early childhood and adolescent was 10.8/1000 and 7.2/1000 respectively; However, the rate above include both idiopathic and symptomatic epilepsy. The prevalence rates of other two studies by **Khedr et al. (2012)** and **Fawi et al. (2015)** were 9.5/1000 and 9.47/1000 respectively, which was higher than our result due to inclusion of both adult and pediatric population. In Sudan, **Muhammad et al. (2017)** found prevalence rate

among school children 4/1000 which is lower than our results. In Morocco, the prevalence was 11/1000, including both symptomatic and idiopathic epilepsy (**Itri and Khalifa, 1998**). The overall lifetime prevalence rate of epilepsy of adult or children in Arab world was 7.8/1000 (**Bhalla et al., 2016**). In Africa, the prevalence of overall epilepsy including both and adult and children ranges from 10.8-15.4/1000 (**Del Brutto et al., 2005; Medina et al., 2005; Preux, 2005**). The insufficient health care systems and low socioeconomic levels may be responsible for the high figures in Africa. In Europe and eastern world, the figures are much lower than the current study. In a recent Norwegian study, the prevalence in children aged 5-14 years was 6.7/1000 (**Syvertsen et al., 2015**). In Japan, the prevalence was 5.3/1000 (**Oka et al., 2006**). In Western world, A Canadian study found the prevalence of childhood epilepsy 5.26/1000 (**Prasad et al., 2011**). While in less developed Latin America the prevalence is 18/1000 which considered higher than the current and developed countries (**Burneo et al., 2005).** The discrepancies between various studies in case ascertainment, definitions, age and type of population may be accounted for difference in the prevalence rates.

In the current study the prevalence rate of idiopathic epilepsy in males was higher than in females but not reach to the level of significant difference. Our results were consistent with other studies (**Khedr et al., 2012**; **Fawi et al., 2015; El-Tallawy et al., 2013; Muhammad et al., 2017**). In our community (Upper Egypt), the parents may deny the shameful diagnosis of epilepsy for females fearing of delaying or losing her chance for marriage.

The current study revealed that epilepsy is significantly more common in low socioeconomic levels in comparison to high social levels, this in line with other studies finding by **Szaflarski (2014) and Khedr et al (2012)**. Social disadvantage may affect early diagnosis and affordability of treatment initiation and maintenance cost.

In the present study, 52.4% of seizures started during the first 6 years of life. Early infancy and early adolescence were the most common age onset of first seizure which could be related to decreased seizure threshold of the immature brain (**Farghaly et al., 2018; Talaat et al., 2009**).

The most common prevalent seizure in our study was generalized tonic clonic seizures which more common than absence and partial seizures probably due the unforgotten fearful experience of tonic clonic seizure to the parents while other seizures may be passed unnoticed, the finding are consistent with other studies finding (**Shawki, 1995; Bhalla et al., 2016**; **Mahmoud, 2009**)

As a monotherapy, Levetiracetam was the most common drug used in the current study. **Talaat et al. (2009**) found the most common used drug was carbamazepine. The frequent usage of levetiracetam in our study may be attributed to rush prescriptions of the drug to epileptic students by general practitioners at first glance without making effort in classifying seizures.

We observed a significant association between positive family history, consanguinity between parents of epileptic children and febrile seizures and idiopathic epilepsy in the studied children. The inheritance of idiopathic epilepsy is mainly non-mendelian inheritance which involve interaction between multiple genes and

environmental factors. Higher consanguinity in our community attributed to higher prevalence of first cousin marriage and inbreeding within the same family believing in the authenticity of the blood line. The association between consanguinity and family history with idiopathic epilepsy was consistent with other studies across involving our community and Arab world (**Khedr et al., 2012; fawi et al., 2015**; **Muhammad et al., 2017**; **Bhalla et al., 2016; al-Rajeh et al., 1990**).

We found febrile seizures were a risk factor for development of idiopathic epilepsy in the studied children with significant difference to the non-epileptic (**Ogunniyi et al., 1987). Nelson and Ellenberg (1976)** found the risk of association of febrile seizures and subsequent development of afebrile seizures in neurologically and developmentally normal children to be 11/1000 on follow up for 7 years which was significantly higher in comparison to those not experienced febrile seizures.

Limitations

The main limitations of the current study was involving only Qena city which considered an urban sector of the governorate and not including rural areas. The limitations also include the lack of cognitive function assessment between epileptic and non-epileptic children. We also exclude school students of special needs losing the comparison to normal traditional schools.

Conclusions

The idiopathic epilepsy is relatively common in our community, the prevalence was 7.6/1000 among primary school children aged 6-12 years which was consistent with other Egyptian studies and midway between the developed and developing world studies. Positive family history seizure, consanguinity and history of febrile seizures were the most common risk factor for developing subsequent epilepsy in childhood.

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