

Clinical characteristics of seizures in children admitted to Al-Sadaqa general teaching hospital, Aden (2008-2009)

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Abstract

This study aimed at describing the frequency and clinical spectrum of seizure disorders among hospitalized children and determining the various underline etiologies in this population with reference to age, sex and the overall outcomes. A retrospective analysis of all medical records for children admitted to Al-Sadaqa General Teaching Hospital with seizures, during a period of two years (Jan 2008- Dec 2009) was carried. A total of 318 children were included, 181; (56.9%) were males and 137 (43.1%) were females. The majority of seizures were associated with fever (82.7%), commonly in the age group 6 months- 5 years (66%). Generalized tonic-clonic (GTC) seizure was the most frequent type (57.5%), followed by partial seizures (28.6%). Status epilepticus was present in (10.3%) of the cases. The most common diagnosis were febrile seizure (26.7%), followed by meningitis (16.3%), encephalitis (12.9%) and epilepsy (17.3%). Presenting symptoms beside seizure were fever (82.7%), cough (27.7%), vomiting (21.4%) and diarrhea (19.8%). Loss of conscious was the presenting feature in 20 cases (6.3%). Twenty five children with seizure (7.9%) died in hospital, and higher death rate was observed among those with CNS infections.

The results of this study indicate that seizure is an important cause of hospitalization with significant mortality. Fever was the most common associate and febrile seizure, which is known to have benign prognosis, was peaked at early childhood. Other more serious problems; such as CNS infections, cerebral malaria and status epilepticus, need to be considered as they can possess a real threat for child life or might have long-term detrimental consequences.

Key words: Seizure, convulsion, epilepsy, meningitis, encephalitis, malaria

Introduction:

Seizures are the most common acute neurological disorders in children and constitute an important cause of pediatric hospital admissions (3, 31). A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behavior that results from disturbed cerebral function with abnormal electrical activity in the brain and, it occurs in about 10% of children (17, 21).

The most common type of seizures in pediatric age is febrile seizure, which is described as a convulsion event associated with fever but without intracranial infection or a defined cause and limited to neurologically healthy child typically aged between 6 month - 6 years (19, 39). Febrile seizure occurs in 2-7% of children under 5 years in the developed countries; but, in the tropical regions the frequency is higher ranging from 16% to a maximum 38%, and this is attributed to higher prevalence of acute febrile illness in these areas (7).

Infection of the central nervous system (CNS) is a frequent cause of neurological signs and symptoms associated with fever in children. In general, viral infections of CNS are much more common than bacterial, fungal or parasitic infections (36).

Viral encephalitis in children is frequently associated with seizure, although it has nonspecific feature and difficulties in specific etiological diagnosis, hence an accurate detection of causative agents remains a wide spread problem, mainly in poor resource settings (25).

Aseptic meningitis is the inflammation of meninges with sterile bacterial cultures of the cerebrospinal fluid (26). Viruses are the most common cause of aseptic meningitis, but the list of differential diagnosis is large and includes partially treated meningitis, tuberculosis or fungal meningitis, collagen vascular disease and drug-induced meningeal irritation (34).

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Bacterial meningitis is a serious public health problem demanding early diagnosis with prompt and effective treatment. It is considered as a common cause of seizure and it occurs in about one third of hospitalized children, usually within first 24-48 hours of admission(37). Meningitis is a major cause of morbidity and mortality among infants and children below the age of five years(16, 38), therefore, it is prudent that bacterial meningitis must be excluded in any child presented with acute seizure accompanied by fever.

One of the most common parasitic infection affecting brain is malaria which remains a major problem in many parts of the world; approximately 500 million people are affected annually and about one million deaths each year, most of them are children(42). Children are vulnerable to severe complicated malaria, including cerebral malaria, which is caused mainly by *plasmodium falciparum* species(23). In endemic areas, approximately half of children with malaria infection are showing neurological features and seizures occur not only in cerebral malaria, but also in non-complicated malaria.

Epilepsy refers to the clinical condition of recurrent, unprovoked seizures. The overall incidence of epilepsy is 49 per 100,000, and, in the Arab countries, the estimated prevalence of epilepsy in children is ranging from 3.6 – 10.5/10000(8). Of these patients, approximately 5 to 8% have some form of static neurologic deficit present since birth mostly as a consequence of perinatal complications(20). Higher risk of epilepsy was perceived in patients with combined mental retardation and other neurologic deficits(29), and numerous studies have shown that epilepsy occurs in 15 to 90% of children with cerebral palsy(32).

There are limited information about seizure profile in children in developing countries, like Yemen, thus the aim of this study is to describe the frequency and clinical spectrum of seizure disorders among hospitalized children and to determine the various underline etiologies in this population with references to age, sex and overall outcomes.

Methods:

The study was conducted in Al-Sadaqa General Teaching Hospital, which is a third level hospital in Aden, serving urban and semi urban populations. A retrospective analysis of all medical records for children admitted with seizures during a period of two years (Jan 2008- Dec 2009), was carried. The age range of the included children was >one month to 15 years. Neonates were excluded from the study because they have particular conditions, like hypoxic-ischemic encephalopathy, metabolic derangements and septicemia, which interfere with seizure spectrum, in addition neonatal seizure are usually typical and have subtle manifestation. Many studies evaluating children seizure profile have excluded infant less than one month of age(10).

The following data were collected: age, sex, frequency and type of seizure, associated symptoms (fever, diarrhea and vomiting, rhinorrhea, cough, headache, loss of consciousness), past history, developmental history and family history of febrile or non-febrile convulsion. Results of laboratory investigations were obtained, including complete blood count (CBC), blood film for malaria parasites, blood sugar and serum electrolytes, cerebrospinal fluid (CSF) analysis, CT scan and EEG.

Bacterial meningitis was consider if organism grew or was detected by Gram stain in the CSF, and if CSF culture was negative but showed all of the following in CSF disturbances: > 10 white cells/mm³, protein >0.6g/l, glucose <40mg/dl . Children who did not fulfill these criteria but had evidence of CSF disturbance (white cells >10/mm³) were considered to have viral meningitis. Children who were clinically suspected of having meningitis and their parent's refused to do lumbar puncture were treated empirically as bacterial meningitis. Viral encephalitis was presumed if a child with fever has alteration of conscious or behavior, and focal neurological signs, new onset seizure and mild CSF pleocytosis (more than 5 WBC/mm³) with no alternative cause can be identified(25). Cerebral malaria is defined as a state of un-arousable coma with no identifiable cause of altered conscious and with asexual *Plasmodium falciparum* in the blood detected by light microscopy(42).

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Febrile seizure is based on occurrence of seizure in neurologically healthy children between one month and 5 years of age without evidence of intra-cranial infection or known seizure disorders(28).

Epilepsy was considered if a child had a medical document of epileptic seizure, or a recurrent of two or more unprovoked seizures separated by at least 24 hours(9).

Classification of seizure type, including generalized tonic clonic (GTC), partial seizure, generalized tonic (GT), clonic, secondary generalized, myoclonic and absence was based on that recommended by the International League Against Epilepsy (ILAE)(15).

Status epilepticus is defined as a single epileptic seizure persisted for more than 30 minutes or a series of seizures during which conscious is not regained between ictal events(4).

Statistical analysis:

The data was statistically analyzed using IBM SPSS (the Statistical Package for the Social Sciences version 21, SPSS, Inc., Chicago, IL, USA). Differences between frequencies were tested by Chi Squared and Fisher exact test and means comparison by student t-test. Differences are considered statistically significant when the P value is less than 0.05.

Results:

A total number of 318 children were admitted with seizures during the 2 year period of study. There were 181 (56.9%) males and 137 (43.1%) females with a ratio of 1.4:1, and overall mean age 2.21 ± 2.69 years (table 1).

Table 1. Characteristics of children by type of seizures

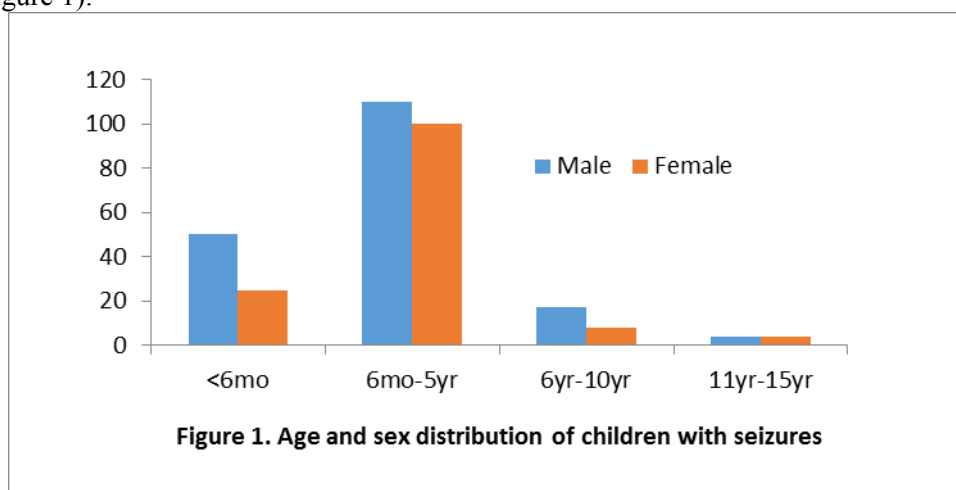
Variables	No fever	Fever	Total	P value
	n (%)	n (%)	n (%)	
	n=55 (17.3)	n=263 (82.7)	n=318 (100)	
Sex				
Male	29 (16.0)	152 (84.0)	181 (56.9)	0.49
Female	26 (19.0)	111 (81.0)	137 (43.1)	
Age				
<6mo	20 (26.7)	55 (73.3)	75 (23.5)	0.026
6mo-5yr	28 (13.3)	182 (86.7)	210 (66.1)	
6yr-10yr	4 (16.0)	21 (84)	25 (7.8)	
11yr-15yr	3 (37.5)	5 (26.5)	8 (2.6)	
Seizure type				
GTC	32 (17.5)	151 (82.5)	183 (57.5)	0.007
Partial	20 (22.0)	71 (78.0)	91 (28.6)	
GT	17 (22.0)	60 (77.9)	77 (24.2)	
Status epilepticus	9 (27.3)	24 (72.7)	33 (10.3)	
Clonic	5 (13.9)	31 (86.1)	36 (11.3)	
Secondary generalized	1 (14.3)	6 (85.71)	7 (2.2)	
Myoclonic	0 (0.0)	11 (100.0)	11 (3.4)	
Absence	0 (0.0)	1 (100.0)	1 (0.3)	

The majority of children with seizures were presented with fever 263(82.7%) and 55 (17.3%) were none febrile, and high proportion of seizures 285 (89.6%) occurred in less than 6 years of age with no significant sex differences ($p=0.49$). Non-febrile seizure was common in the age group older than 11 years (37.5%) and in those younger than 6 months of age (26.7%). GTC was the most frequent type of seizures 183(57.5%), and it occurred more frequently in association with fever ($p=0.007$). This is followed by partial seizures (28.6%). Status epilepticus was present in (10.3%) of the cases.

Table 2. Distribution of seizure diagnosis by sex of children

Diagnosis	Male n(%)	Female n(%)	Total n(%)
Febrile	45 (52.9)	40 (47.1)	85 (26.7)
Epilepsy	30 (53.5)	26 (46.5)	56 (17.6)
Meningitis	29 (55.8)	23 (44.2)	52 (16.3)
Encephalitis	26 (65.0)	14 (35.0)	40 (12.6)
Status epilepticus	20 (60.6)	13 (39.4)	33 (10.4)
Cerebral palsy	18 (72.0)	7 (28.0)	25 (7.8)
Malaria	7 (46.6)	8 (53.4)	15 (4.7)
Others	6 (50.0)	6 (50.0)	12 (3.7)

Males outnumbered females in almost all seizure types (Table 2), and differences were observed mainly in the age groups less than 6 months (66.7% vs 33.3%) and at 6-10 years (68.0% vs 32%)(Figure 1).



The most common admitting diagnosis was febrile seizure 85 (26.7%), 45 (53%) males, majority of these 74 (87%) occurred between (6 months- 5 years), followed by CNS infections (meningitis 16.3% and encephalitis 12.9%) and epilepsy (17.6%) (Table 3). Family history of febrile seizure was reported in 26 (30.6%) of children with febrile seizure, while the family history of non-febrile seizure was noted in 16 (28.6%) of the children with epilepsy and in 9 (27.3%) of the cases with status epilepticus.

Table 3: Analysis of children with seizure based on age groups

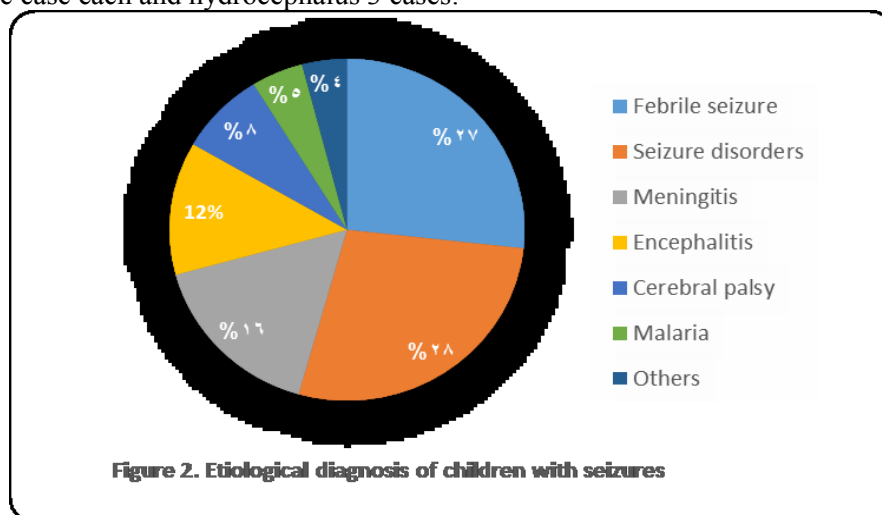
Variables	<6mo n (%)	6mo-5yr n (%)	6yr-10yr n (%)	11yr-15yr n (%)	Total n (%)
Sex					
Male	50 (66.7)	110 (52.8)	17 (68.0)	4 (50.0)	181 (56.9)
Female	25 (33.3)	100 (47.6)	8 (32.0)	4 (50.0)	137 (43.1)
Diagnosis					
Febrile	9 (12.0)	74 (35.2)	2 (8.0)	0 (0.0)	85 (26.7)
Epilepsy	13 (17.3)	32 (15.2)	8 (32.0)	3 (37.5)	56 (17.6)
Meningitis	19 (25.3)	30 (14.3)	2 (8.0)	1 (12.5)	52 (16.3)
Encephalitis	20 (26.7)	20 (9.5)	0 (0.0)	0 (0.0)	40 (12.6)
Status epilepticus	6 (8.0)	20 (9.5)	5 (20)	2 (25)	33 (10.4)
Cerebral palsy	3 (4.0)	15 (7.1)	6 (24)	1 (12.5)	25 (7.8)
Malaria	2 (2.6)	12 (5.7)	1 (4.0)	0 (0.0)	15 (4.7)
Others	3 (4.0)	7 (3.5)	1 (4.0)	1 (12.5)	12 (3.7)

Beside fever as the most common symptoms, associated with seizure (82.7%), cough (27.7%), vomiting (21.4%) and diarrhea (19.8%), were frequently reported. Loss of conscious was presenting symptoms in 20 cases (6.3%). Table 4

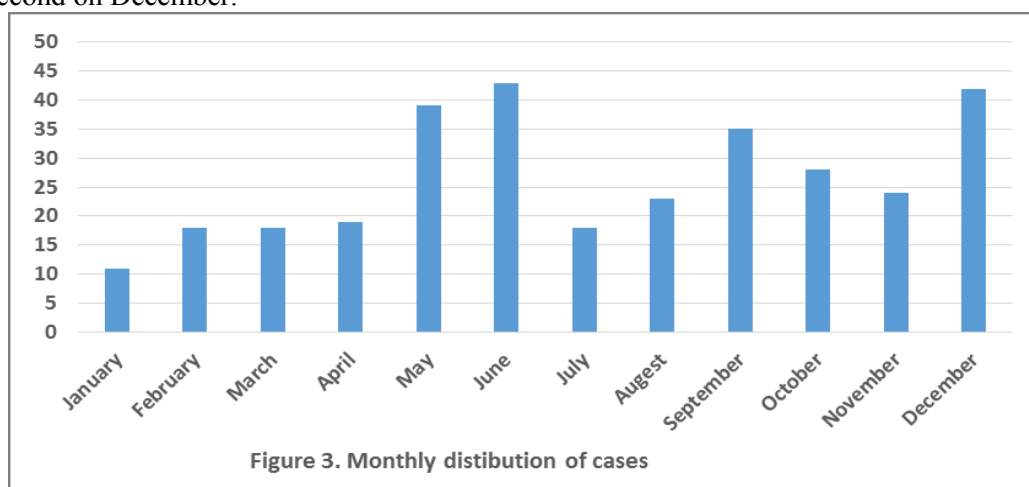
Table 4: Frequency of presenting symptoms associated with seizure events

Symptom	No fever n (%)	Fever n (%)	Total n=318 (%)
Cough	11 (12.5)	77 (87.5)	88 (27.7)
Vomiting	8 (11.7)	60 (88.3)	68 (21.4)
Diarrhea	7 (11.1)	56 (88.9)	63 (19.8)
Rhinorrhea	4 (7.4)	50 (92.6)	54 (17.0)
Loss of conscious	3 (15.0)	17 (85.0)	20 (6.3)
Headache	1 (33.3)	2 (66.7)	3 (0.9)

Figure 2 illustrates etiological diagnosis, into which seizure disorder represented (28%), febrile seizure (27%), meningitis (16%) and encephalitis (12%), cerebral palsy (8%) and malaria infection (5%). Other diagnosis include tuberculosis, brain tumor, neurodegenerative disease, intracranial hemorrhage, neurocutaneous syndrome, head trauma, Karrabe disease, cerebellar tumor, drug toxicity, one case each and hydrocephalus 3 cases.



Monthly distribution is shown in Figure 3, two peaks were observed; the first on May-Jun and the second on December.



The overall outcomes are shown in Table 5. Twenty five children (7.9%) died in hospital, 16.2% left hospital against medical advice, (7.5%) absconded, (1.1%) were referred and the remaining (66.6%) were discharged after recovery. Higher death rate was observed among those with meningitis (21.2%) and encephalitis (17.5%). Of the 33 cases with status epilepticus, 2 cases (6%) were died.

Table 5: Outcomes of children with seizure in relation to sex, fever and diagnosis

Variables	Total (n=318)	Discharge n (%)	DAMA n (%)	Absconded n (%)	Transfer n (%)	Died n (%)	P value
Sex							
Male	181	127 (70.1)	29 (16.3)	13 (7.3)	2 (1.1)	10 (5.6)	0.24
Female	137	89 (64.9)	22 (16.2)	11 (8.1)	0 (0.0)	15 (11)	
Fever							
Yes	263	177 (67.3)	43 (16.6)	19 (7.3)	2 (0.8)	22 (8.5)	0.76
No	55	39 (70.9)	8 (14.5)	5 (9.1)	0 (0.0)	3 (5.5)	
Diagnosis							
Febrile	85	61 (71.8)	16 (18.8)	8 (9.4)	0 (0.0)	0 (0.0)	0.01
Epilepsy	56	39 (69.6)	9 (16.1)	6 (10.7)	0 (0.0)	2 (3.6)	
Meningitis	52	28 (53.8)	8 (15.4)	5 (9.6)	0 (0.0)	11 (21.2)	
Encephalitis	40	24 (60.0)	8 (20.0)	1(2.5)	0 (0.0)	7 (17.5)	
Status	33	24 (72.7)	5 (15.2)	2 (6.0)	0 (0.0)	2 (6.0)	
Cerebral palsy	25	19 (76.0)	3 (12.0)	2 (8.0)	1 (4.0)	0 (0.0)	
Malaria	15	12 (80.0)	2 (13.3)	0 (0.0)	0 (0.0)	1 (6.7)	
Others	12	9 (75.0)	0 (0.0)	0 (0.0)	1 (8.3)	2 (16.6)	

Discussion:

Seizure is a frightening event for child and parents and is alarming for health care providers (41). There are many reasons to make children more susceptible to seizure attack. Brain development (e.g. neuronal proliferation, migration, organization, myelination) may make a child vulnerable with lowering of seizure threshold at younger age. Furthermore, many of these developmental processes (e.g. organisation, and myelination) in central nervous system continue after birth through infancy and childhood making developing cortex more sensitive to provoked seizures(13).

Febrile convulsions are an age related disorder characterized by generalized or occasionally partial seizures occurring during an acute febrile illness(6).Most febrile convulsion occurs within the first 24 hours of illness, often as a first sign of fever. In our study, we found febrile convulsion commonly occurs at age 6 months to 6 years (87%), and the rate is decline with increasing age which is similar to study done in Saudi Arabia(30).Our documented male predominance in almost all seizure types, including febrile seizure, is consistent with previous studies(2, 12).

Seizure is an important neurological complication of bacterial meningitis, especially in young children.Suspected bacterial meningitis is a medical emergency that requires early diagnosis and immediate administration of empirical antibiotic therapy as mortality in untreated cases may approach 100%, and even with optimal management neurological damage are still occur (26).Meningitis morbidity and mortality may vary with age, type of causative agent and geographical location, and the risk of permanent neurological sequel ranges from 10-30%(33).The introduction of more effective antimicrobials and immunization against the most common causative organisms produces a decrease in the incidence of bacterial meningitis,nevertheless mortality and case fatality rate did not change(40).

There is no specific diagnostic signs for encephalitis and, due to limited laboratory facilities for detection of etiological agents in our situation, the diagnosis remains presumptive. Viruses are the most common causative agent of encephalitis, some are worldwide in distribution such as herpes and enteroviruses, while others are dominant in certain geographical regions. However, even in the

Clinical characteristics of seizuresWagih Azazi, Abdul-Wahab Al-Saqladi, Mariam Binyahia developed countries, despite the extensive investigations to detect causative agents, up to 60% of cases with encephalitis the etiology remains unknown(24).

We found that approximately one quarter of both meningitis and encephalitis have occurred in infants aged less than 6 months which is similar to the result of a study done in Oman(14).The total mortality from meningitis and encephalitis was approximately 39% which is nearly similar to study done in India(35).

Of the estimated 3.5 million people who develop epilepsy each year, 40% are children and more than 80% live in developing countries(18).In the Arab world, with a total population of about 315 millions, the estimated number of epilepsy cases is approximately 724,500, the highest rate is reported in children(8).Many epileptic patients have received inadequate treatment therefor poorly control and increase treatment gap, furthermore a large proportion of these patients even receive no treatment at all, especially in rural areas(11).Generalized seizures is found to be more common than partial seizures in the current study and this is in agreement with that reported from the Arab countries, Asia and Africa(8).

Brain damage, caused by cerebral palsy, is associated with high rate of symptomatic epilepsy in this group of children. Low perinatal care and the high prevalence of consanguineous married in our society which, is similar to other Arab communities, could be partly explain this association(8). Status epilepticus account for approximately 10.3% in our study which is exactly similar to the figure of 10% reported in children with seizures presenting to the pediatric emergency department in Taiwan (12).Young children had the highest rate of status epilepticus with fever, the most common triggering factor and the short term mortality of 6% in our sample is an acceptable outcome as it is in the lower range of 20% reported by others(27).

Seasonal changes in seizure frequency may be attributed to the epidemiology variation of common infectious illness in children such as viral respiratory, gastrointestinal infections and malaria. In Yemen, summer months begin in April-September, meningioencephalitis is more common in these months which is similar to a study done in Kuwait(22). Malaria has variable transmission activities and it increases in winter in coastal areas, but becomes more active in the summer at the high mountainous areas; and most cases of cerebral malaria was referred from rural area where the weather during these months is usually rainy and summer(1).This is comparable to Saudi Arabia, where malaria cases increase during the rainy season between November and March(5).

New epidemiologic measures need to be taken to diminish the serious situation. In our study, the death still stay high probably because most of the parents bring their children late to hospital and many refuse lumbar puncture, in addition to the lack of neuro-imaging and other diagnostic facilities hindering accurate etiological diagnosis. In resource- limited settings, poverty, low education and bad sanitation have contributed to the increase of CNS infections(11), and many seizures can be preventable through the improvement of perinatal care, control of infection by adherence to immunization and optimizing the overall health care of peoples(10).

Conclusions

Seizure attacks in children are one of the most common cause of pediatric hospitalization and carry a significantly high mortality. Febrile seizures are the most common type, particularly in early childhood. Meningitis and encephalitis account for the majority of death cases. Preventive measures through promotion of immunization, control of infectious disease, good perinatal care and effective treatment of specific etiology of CNS infection with proper timing of intervention are strongly recommended.

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الخصائص السريرية للاختلاجات في الأطفال المرقدين في مستشفى الصداقة

التعليمي العام، عدن (2008-2009م)

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الملخص

هدفت هذه الدراسة لوصف معدل التكرار والطيف السريري للاضطرابات الاختلاجية وتحديد مسبباتها المختلفة لدى الأطفال الداخلين للمستشفى بالرجوع إلى السن والجنس والمآلات العامة.

تم القيام بالتحليل الاستعادي لجميع سجلات الأطفال الداخلين إلى مستشفى الصداقة التعليمي العام والمصابين بنوبات اختلاجية خلال فترة عامين (يناير 2008 - ديسمبر 2009). ضمت هذه الدراسة 318 طفلاً، 56,9% من الذكور، 43,1% من الإناث. وقد كانت معظم الاختلاجات مصحوبة بالحمى (82,7%) وبالذات في الفئة العمرية بين 6 أشهر - 5 سنوات (66%). وكانت الاختلاجات التوتيرية - الرمعية العامة هي الأكثر شيوعاً (57,5%) تليها النوبات الجزئية (28,6%)، وظهرت الحالة الصرعية لدى (10,3%) من الأطفال.

كان التشخيص الأكثر شيوعاً هو الاختلاجات الحموية (26,7%)، يليها التهاب الدماغ (16,3%) والتهاب السحايا (12,9%) ثم الصرع (17,3%)، أما الأعراض المصاحبة للاختلاجات فهي الحمى (82,7%)، السعال (27,7%)، التقيؤ (21,4%) والإسهال (19,8%)، وكان فقدان الوعي في 20 حالة (6,3%). توفي 25 طفلاً من هذه العينة (7,9%)، كان معظمهم من المرضى المصابين بالتهابات الجهاز العصبي المركزي.

تشير نتائج هذه الدراسة إلى أن الأطفال المصابين بالاختلاجات يشكلون نسبة عالية بين المدخلين إلى المستشفى وكذا بين حالات الوفاة، وقد كانت الحمى أكثر الأعراض مصاحبة للاختلاجات، ومع أن الاختلاجات الحموية الحميدة بلغت ذروتها في الطفولة المبكرة ولا يوجد لها مضاعفات مستقبلية ملحوظة لكن هناك مشاكل أكثر خطورة مثل التهابات الجهاز العصبي المركزي، الملاريا الدماغية وحالات الصرع والتي تحتاج ان توضع بعين الاعتبار كونها تشكل تهديداً حقيقياً لحياة الطفل وقد يكون لها عواقب ضارة على المدى الطويل.

الكلمات المفتاحية: الاختلاجات، التشنج، الصرع، التهاب السحايا، التهاب الدماغ، الملاريا.