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Incidence and Associated Factors of Juvenile Myoclonic Epilepsy among Idiopathic Generalized Epilepsy

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Abstract

Juvenile myoclonic epilepsy (JME) is widely recognized presumed genetic, electroclinical idiopathic generalized epilepsy (IGE) syndrome. The prevalence of JME is about 18% of IGEs. However, there is a considerable variation in different settings.

Aims: to determine the incidence and associated factors of JME among patients with IGEs.

Patients and Methods: This retrospective study included a total of 52 patients with electro-clinical feature of IGE. All enrolled patients were undergone a three-hour video electroencephalography (EEG). JME was diagnosed on the basis of JME consensus definition clinical criteria class II. The demographic and clinical characteristics of the patients were abstracted from their records.

Results: The most common epilepsy syndrome of IGE was generalized tonic-clonic seizure (GTCS) only affecting (32.7%) followed by juvenile absence epilepsy (JAE) (25%), JME and JME only (each 17.3%) and Generalized myoclonic epilepsy and generalized tonic-clonic (GMEGTC) (13.46%). All JME patients were females (100%) compared with 69.77% of the patients in other IGE syndromes with a highly significant difference. According to EEG results, 8 patients (88.89%) of JME patients had generalized polyspikes, and two patient (22.22%) showed generalized spikes and waves (3/second spike and wave complex). One patient (11.11%) two EEG findings (polyspike and generalized spike and waves)

Conclusions: JME can affect adolescents and young adults and it can effect child age group. It is distinguished by the occurrence of myoclonic seizures, characteristic spike-and-wave EEG pattern at 4-6 Hz, and more common in females than males.

الإصابة بالصرع الرمعي العضلي عند الأحـــداث والعوامل المرتبطة به بين الصرع المعـــمم مجـهول الســبب

الخلاصة :

يُعرف الصرع الرمعي عند الأحداث (**JME**) على نطاق واسع بأنه متلازمة الصرع المعمم الوراثي مجهول السبب الكهروكلينيكي (**IGE**). انتشار **JME** حوالي ١٨٪ من **IGEs**. ومع ذلك، هناك تباين كبير في الأوضاع المختلفة.

الأهداف: تحديد مدى حدوث **JME** والعوامل المرتبطة به بين المرضى المصابين بمتلازمة (**IGE**).

المرضى والطرق: تضمنت هذه الدراسة بأثر رجعي ما مجموعه ٥٢ مريضا مع السمة الكهربائية السريرية من **IGE**. خضع جميع المرضى المسجلين إلى تخطيط كهربية الدماغ بالفيديو (**EEG**) لمدة ثلاث ساعات. تم تشخيص **JME** على أساس معايير إجماع **JME** للمعايير السريرية من الدرجة الثانية. تم استخراج الخصائص الديموغرافية والسريرية للمرضى من سجلاتهم.

النتائج: كانت متلازمة الصرع الأكثر شيوعًا لـ **IGE** هي النوبة التوترية الارتجاجية المعممة (**GTCS**) التي تؤثر فقط على (٣٢.٧٪) يليها صرع غياب الأحداث **25) (JAE)**٪) ، **JME** و **JME** فقط (كل ١٧.٣٪) والصرع الرمعي العام والمنشط الرمعي المعمم **(GMEGTC) (13.46%)**. جميع مرضى (**JME**) كانوا من الإناث (١٠٠٪) مقارنة بـ ٦٩.٧٧٪ من المرضى الذين يعانون من متلازمات **IGE** الأخرى مع وجود فرق مهم للغاية. وفقًا لنتائج مخطط كهربية الدماغ، كان لدى ٨ مرضى (٨٨.٨٩٪) من مرضى **JME** نبضات متعددة معممة، وأظهر مريضان (٢٢.٢٢٪) ارتفاعات وموجات معممة (ارتفاع ٣ / ثانية وعقدة موجية). مريض واحد (١١.١١٪) اظهر نتيجتان من مخطط كهربية الدماغ (نبضات متعددة وارتفاعات وموجات معممة).

الاستنتاجات: يمكن أن تؤثر **JME** على المراهقين والشباب ويمكن أن تؤثر على الفئة العمرية للأطفال. يتميز بحدوث نوبات رمع عضلي، ونمط **EEG** مميز بارتفاع وموجة عند ٤-٦ هرتز، وهو أكثر شيوعًا عند الإناث منه عند الذكور.

Introduction

The idiopathic generalized epilepsies (IGEs) constitute nearly a third of all epilepsies [1]. They are genetically determined and affect otherwise healthy people of both sexes and all races [2]. IGEs manifest with typical absences, myoclonic jerks and generalized tonic–clonic seizures (GTCSs), alone or in varying combinations and severity [3]. Seizure-precipitating factors and photo sensitivity are common [4]. Most seizures occur on awakening, particularly after sleep deprivation. Absence status epilepticus is frequent [5]. Syndromes of IGE usually start in childhood or adolescence, but some have an adult onset [6,7].

Juvenile myoclonic epilepsy (JME), previously 'impulsive petit mal,' Janz syndrome, is one of the most common IGE of childhood. It typically occurs in otherwise healthy adolescents and is characterized by the triad of myoclonic jerks, generalized tonic-clonic seizures (GTCS) and absence seizures (also called petit mal). Seizures characteristically occur upon awakening or in association with sleep deprivation, and patients generally respond quickly and completely to standard antiepileptic drugs (AEDs). Seizure frequency often lessens in adulthood but most patients require life-long AED therapy. The underlying cause of JME is not known and there are likely complex underlying genetic defects [8].

Although early reports were in favor of male predominance, most recent case series show that approximately 60% of patients are women [9]. One population-based study also found that females outnumbered males with JME [10]. The literature suggests that JME typically appears in the second decade. However, the age of onset of JME spans a wide range from about 8 to 36 years, with peak onset between 12 and 18 years [11]. Other reports recognize an even wider age range for onset from 2 to 40 years [12,13]. Those with the onset of JME outside the 8- to 36-year age bracket are uncommon and should be carefully evaluated for other diagnoses. It is well documented that about 15% of children with childhood absence epilepsy (CAE) and juvenile absence epilepsy (JAE) progress on to JME [14], usually at the end of the first or early second decade. It is possible that those with CAE plus photosensitive spike–wave on EEG are more likely to develop JME [15].

The present study aimed to determine the incidence and associated factors of JME among patients with IGE.

Patients and Methods

This is a retrospective study which was done over a period from 1st of May 2020 to the end of May 2021. A total of 52 patients with electro –clinical feature of IGE were recruited from the first epilepsy clinic in Baghdad medical city. Data of the patients were collected from the patients recording files through special structured questionnaire form focusing on the (age, sex, family history, consanguinity, age of starting first seizure, neuro-developmental examination, neuroimaging, history of febrile seizure, type of IGE, and characteristics of electroencephalography (EEG)).

All enrolled patients underwent a three-hour video EEG. A 19 channel EEG connected to the patient according to 10-20 international system with recording during wakefulness and sleep. Different montages were used to interpretive the record (double banana montage, average montage, etc.).

Activation procedure was used including 3minute hyperventilation, intermittent photic stimulation (IPS) according to automated program using deferent flash frequencies, sleep deprivation and certain activation methods according to the patients' seizure aggravating factors.

JME was diagnosed on the basis of JME consensus definition clinical criteria class II [1].

These criteria have the following 5 points:

(1) myoclonic jerks occurring predominantly on awakening, (2) myoclonic jerks facilitated by sleep deprivation and stress and provoked by visual stimuli and praxis or GTCSs preceded by myoclonic jerks, (3) EEG showing normal background and at least once interictal generalized polyspikes and wave discharges with or without myoclonic jerks, (4) no mental retardation or deterioration, (5) age at onset between 6 and 25 years.

The study protocol was approved by the local ethics committee in the college of medicine, Tikrit University, Iraq, with verbal informed consent from patients.

Data processing and analysis were performed with SPSS Version 25.0.

Continuous data were expressed as mean ±SD and analyzed with Student t-test. Categorical data were expressed as frequency and percentage and analyzed with Chi square. Significance was defined as *p*-value of ≤0.05.

Results

General Characteristics of the Patients

The mean age of the patients at presentation was 31.26±15.31 years (range 3-48 years). The mean age at onset was 10.36±8.82 years. Females accounted for three-fourth of the patients. Consanguinity marriage was reported in 23.08% of the parents. The family history for epilepsy and febrile seizure was found in 34.62% and 17.31% of the patients, respectively. Abnormal neurodevelopment was reported in one patient, while 3 patients (5.77%) had abnormal neuroimaging. (Table 1)

Table 1: General Characteristics of the Patients (n=52)

Characteristics	Value
Age (years)	
Mean ±SD	31.26±15.31
Range	3-48
Mean age at onset (years)	
Mean ±SD	10.36±8.82
Range	0.5-22
Gender	
Male	13(25%)
Female	39(75%)
Consanguinity	
Yes	12(23.08%)
No	40(76.92%)
Family history of epilepsy	
Yes	18(34.62%)
No	34(65.38%)
Family history of febrile seizure	
Yes	9(17.31%)
No	43(82.69%)
Neurodevelopmental examination	
Normal	51(98.08%)
Abnormal	1(1.92%)
Neuro-imaging (MRI)	
Normal	49(94.23%)
Abnormal	3(5.77%)

SD: standard deviation, MRI: magnetic resonance imaging

Types and Frequency of epilepsy syndromes of IGE

The most common epilepsy syndrome of IGE was generalized tonic-clonic seizure (GTCS) only affecting 17 patients (32.7%) followed by juvenile absence epilepsy (JAE) (13 patients, 25%), JME and JME only (each with 9 patients, 17.3%) and Generalized myoclonic epilepsy and generalized tonic-clonic (GMEGTC) (7 patients, 13.46%). Less common epilepsy syndromes were generalized tonic-clonic and absence seizure (GTCAS) only (5 patients, 9.61%), childhood absence epilepsy (CAE) (4 patients, 7.69%) and finally and juvenile myoclonic epilepsy and generalized tonic-clonic (JMEGTCAS) (3 patients, 5.77%) as shown in figure 1.

Factors Associated with JME

From all included factors, only gender was significantly associated with JME.

All JME patients were females (100%) compared with 69.77% of the patients in other IGE syndromes with a highly significant difference. Although consanguinity marriage was more common among JME patients compared with other IGE syndromes (44.44% vs. 18.6%), the difference was not significant. In contrast, family history of epilepsy was more common among other IGE syndromes than JME (39.53% vs. 11.11%). However, the difference was not significant (Table 2).

EEG Findings in Patients with JME

Regarding EEG findings, 8 patients (88.89%) having generalized polyspike and two patient (22.22%) having generalized spikes and waves (3/second spike and wave complex). One patient (11.11%) two EEG findings (polyspike and generalized spike and waves) as shown in figure 2.

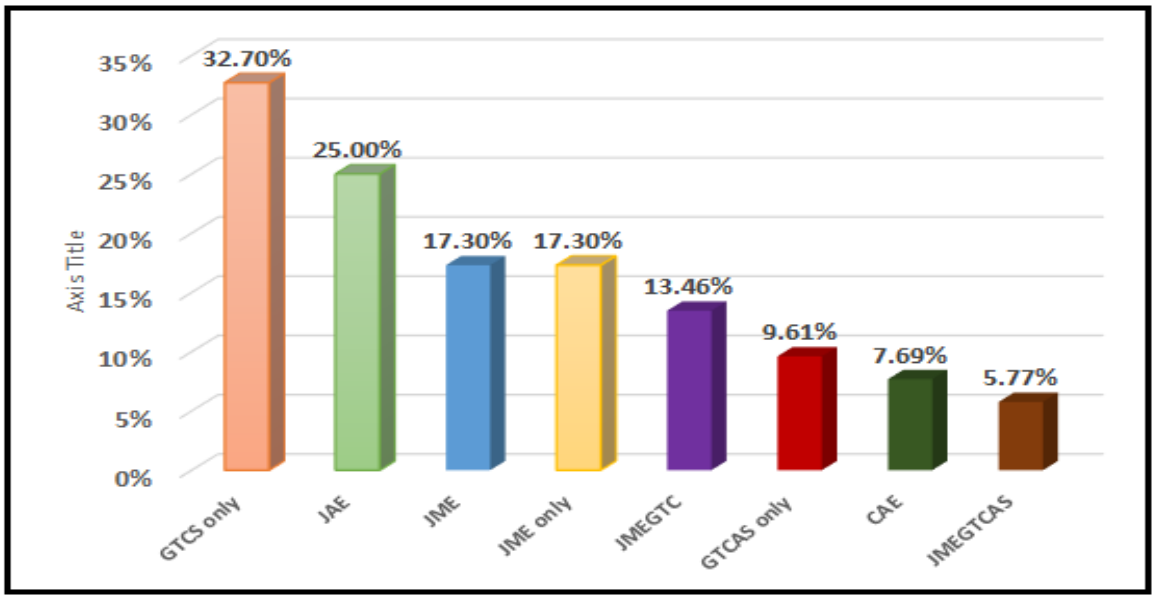

Figure 1: Types and Frequency of epilepsy syndromes of IGE. Patients may have more than one syndrome

Table 2: Factors associated with JME

Characteristics	JME patients (n=9)	Other IGE patients (n= 43)	p-value
Age, (years)			
Mean ±SD	28.2±6.14	33.82±14.7	0.196
Range	3-45	3-48	
Mean age at onset (years)			
Mean ±SD	9.1±4.44	11.22±6.9	0.823
Range	0.5-18		
Gender			
Male	0(0%)	13(30.23%)	**0.005**
Female	9(100%)	30(69.77%)	
Consanguinity			
Yes	4(44.44%)	8(18.6%)	0.094
No	5(55.56%)	35(81.4%)	
Family history of epilepsy			
Yes	1(11.11%)	17(39.53%)	0.103
No	8(88.89%)	26(60.47%)	
Family history of febrile seizure			
Yes	2(22.22%)	7(16.28%)	0.668
No	6(66.67%)	36(83.72%)	
Neurodevelopmental examination			
Normal	0(0%)	1(2.33%)	0.644
Abnormal	9(100%)	42(97.67%)	
Neuro-imaging (MRI)			
Normal	0(0%)	3(6.98%)	0.414
Abnormal	9(100%)	40(93.02%)	

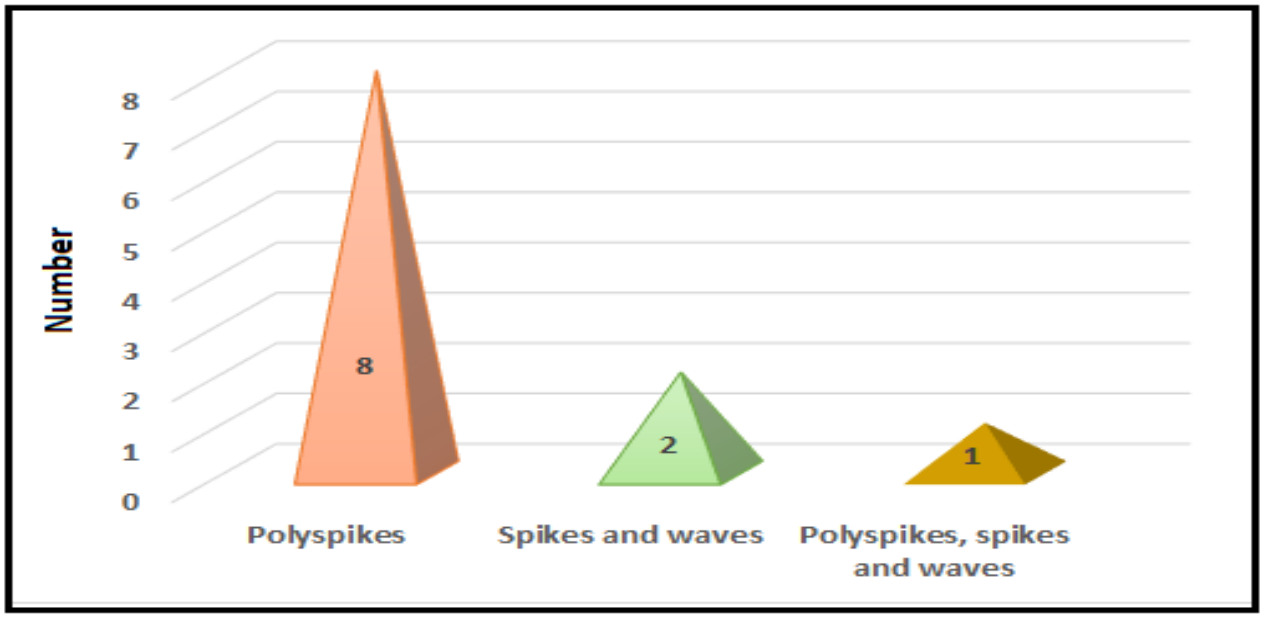

Figure 2: EEG Findings in Patients with JME

Discussion

During this study the percentage of JME in IGE was (17.3%), and it is 10.7% in a study done in the Saudi Arabia [12]. Sennayake and Roman [16] reported JME representing 17-18% of all IGE which is close to our results in other study done in developing. In large cohorts, JME has been estimated to be 18 % of IGEs [17]. The explanation of this deference in frequency among these studies and the exact frequency of JME is often difficult because the diagnosis is often made late and retrospectively confirmed when a tonic-clonic seizure occurs as well as it is misdiagnosed as generalized tonic – clonic epilepsy , because both patient and physician s under estimate the significant of minor myoclonic jerks.

All patients with JME in our study are female 100% while in Desai et al.[18] in India JME affects (male 45.2% female 54.7%). In Saudi Arabia, male and female equally affected [12]. The mean age at referral was 26 year range, which is approximately similar to Desai et al. [18] in India mean age at referral (27year) and range (6- 57 year) while in in Saudi Arabia, the mean age (21.1 year) and range (8- 40 year).

In our study mean age of at seizure onset was 9.1 year, range (0.6 -18 years) while Obeid study, it was 15.5 years. Julia et al. [19] in Germany found the mean age of first seizure to be 13.1 year.

Höfler et al. [20] in Australia, mean age was (15 years). The reason for having low mean age is that we have four patients the onset of their first seizure below twelve years which is the peak of JME and also the small sample of the patient. neurological and mental state of all nine patient (100%) are normal which is similar to Obeid et al. study [12], neuro-imaging was normal in all patients also similar. Interictal EEG findings was abnormal in all nine patients the abnormality included (generalized polyspikes and spike and wave).

This similar to the EEG finding many previous studies worldwide [12, 21, 22, 23].

It can be concluded from these data that although JME is the most common primary generalized epilepsies affecting adolescents and young adults it can affect child age group. It is distinguished by the occurrence of myoclonic seizures, characteristic spike-and-wave EEG pattern at 4-6 Hz, and more common in females than males. Thus, it is recommended that any myoclonic jerk should not be underestimated by the physicians and regarded as benign condition, and patient with myoclonic jerks should undergo video EEG. Genetic and metabolic study is highly recommended in any patient with myoclonus.

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