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Original Article

Clinical and Electroencephalographic Characteristics of Juvenile Myoclonic Epilepsy in a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the clinical and electroencephalographic features in juvenile myoclonic epilepsy (JME) patients

Study Design: Prospective longitudinal study.

Place and Duration of Study: Department of Neurology, Pak Emirates Military Hospital, Rawalpindi, Pakistan, from Jul to Dec 2022.

Methodology: The participants of this study were diagnosed with JME. Patients with hypoxic brain injury, metabolic diseases, family history of progressive myoclonic epilepsy, and abnormal neurological examination or neuroimaging were excluded from study. Data was recorded from consenting patients on a pre-designed proforma recording various parameters.

Results: Among 135 patients, 84 were females (62.2%) and 51 were males (37.8%). Mean age at diagnosis was 19.38±5.40 years. Positive family history was present in 22.2%. Generalized Tonic Clonic Seizures (GTCS) were most common seizure type (53.3%) at diagnosis where as GTCS + Myoclonic jerks (MJ) were most common types (68.9%) during disease course. Classic JME was present in 81.5% cases. Lack of sleep was most common precipitating factor (51.9%). Spike and polyspike slow wave activity was most common EEG abnormality in 44.5%. Majority were fit free on either valproic acid (42.2%) or levetiracetam (38.5%) whereas 20.7% had refractory seizures. Anxiety was most common associated psychiatric co-morbidity present in 14.1%.

Conclusion: JME can be diagnosed by carefully eliciting history of MJ along with GTCS and finding of spike and polyspike slow wave activity in EEG. Majority achieve remission from fits either on valproic acid or levetiracetam.

Keywords: EEG, Juvenile Myoclonic Epilepsy, Myoclonic Jerks.

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INTRODUCTION

Herpin T first explained JME in 1867 and was recognized by International League against Epilepsy (ILAE) as one of the Idiopathic Generalized Epilepsies (IGEs) in 1989. It is represented by MJ which are arrhythmic and mostly occur within 2 hours after awakening from sleep with typical EEG findings of generalized spike and wave or polyspike wave pattern.[1] Patients are often unable to recognize the MJ and frequently elicited in history by physician on presentation with Generalized Tonic Clonic Seizures (GTCS) . MJ are brief, sudden, symmetric often unilateral and mostly involve upper limbs. Inquiry patients describe dropping objects, spilling or sudden falls in early morning or after nap.[2] The usual trigger for fits is lack of sleep, followed by photic stimulation. Most patients show circadian variation in that they go to bed late and get up late in the morning (evening type) because seizures often occur early morning after awakening.[3] The prevalence of JME is around 4 cases per 10,000 general population and 5 – 10% in epileptic population. It typically presents in adolescence with mean onset age of 14.8 years and female preponderance.[4] The MJ onset prior to 8 years of age makes the diagnosis unlikely. Febrile fits can be elicited in history in about 29% cases. Other seizure types commonly found in JME include GTCS in > 90% and typical absence seizures (TAS) in around 33%. GTCS are almost always preceded by multiple episodes of MJ. GTCS are absent in about <10% patients. TAS are typically brief lasting for 3–8 seconds and often associated with mildly impaired conscious level or eyelid flicker. They usually precede MJ by years when present. Both convulsive and absence status epilepticus are uncommon in JME.[5] Occurrence of focal, generalized tonic or atonic seizures excludes the diagnosis of JME. There are four clinical phenotypes of JME: classic JME, JME with adolescent absence, childhood absence epilepsy (CAE) evolving to JME, and JME with astatic seizures.[6] The background EEG rhythm is normal except for generalized slowing after a GTCS.Interictal EEG often reveals generalized spike or polyspike wave activity

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which can be elicited even with sleep deprivation. Photic stimulation elicits a photo paroxysmal response in more than 1/3 patients.[7] Neuroimaging studies are normal and are not required in typical cases for diagnosis. JME shows a good response to Anti-Epileptic Drugs (AEDs) and majority require lifelong treatment.[8] Valproic acid (VPA) followed by Levetiracetam (LEV) is the most effective AED for all seizure types. Lamotrigine (LMT) and Topiramate(TMP) is other commonly used AED. Breakthrough seizures occur in more than 75% patients after cessation of AED.[9] About 30% patients remain refractory to treatment even on optimal treatment.[10] Juvenile Myoclonic Epilepsy (JME) generally has a good prognosis, yet some patients develop refractory disease. Previous studies suggest that early onset, multiple seizure types, absence-only seizures, psychiatric co-morbidity, type 3 phenotype, and praxis induction may predict poor response.[9] These variations emphasize the clinical and EEG heterogeneity of JME. This study, therefore, aimed to assess the clinical features, EEG findings, and drug responsiveness of patients with JME presenting to a tertiary care hospital.

METHODOLOGY

This prospective longitudinal study was conducted on patients diagnosed with JME who were referred to Neurology Department of PEMH Rawalpindi, Pakistan, from Jul 2022 to Dec 2022. Prior approval from Ethical Review Committee of the institute was taken vide ERC certificate number A/28/185(2)/EC/474/22 Jul 2022. Sample size (n) was calculated keeping confidence level (Z21-α/2) of 90%, margin of error (d) 6% and taking expected percentage of MJ + GTCS (P) in JME as 76.6%.[10] A total of one hundred and thirty-five consenting cases were enrolled using consecutive non-probability sampling.

Inclusion Criteria: All patients aged 10 to 20 years of both genders, with a history of MJ along with GTCS and/ or TAS, mostly within 2 hours of awakening, a normal neurological examination, and normal neuroimaging.

Exclusion Criteria: History or evidence of hypoxic brain injury, metabolic diseases causing MJ, family history of progressive myoclonic epilepsy, abnormal neurological examination, and neuroimaging consistent with epilepsy.

All patients and their parents/guardians were interviewed according to a predesigned proforma recording various parameters, including demographic profile, family history, circadian variation, history of febrile seizures, seizure types at diagnosis and during disease course, phenotype, precipitating factors, seizure-free period, treatment history, proportion of patients with refractory seizures, and associated psychiatric co-morbidities. Data was recorded by consultant and resident neurologists. All patients also underwent 21-channel EEGs to study characteristic changes seen in JME.

Statistical Analysis: Data analysis was done using Statistics Package for Social Sciences (SPSS) version 21.0. Descriptive variables were used to define various characteristics of patients, e.g., gender, family history, circadian variation, seizure type at diagnosis and during disease course, phenotypes, precipitating factors, EEG features, treatment given, and associated psychiatric co-morbidities presented as numbers and percentages. Results for quantitative variables, e.g., age, were presented as Mean±SD. Chi-Square test was used to calculate the *p*-value for different variables, and *p*-values ≤0.05 were considered significant.

RESULTS

A total of one hundred and thirty-five patients were inducted in our study. The total number of males was 51(37.8%) and females were 84(62.2%). There was a slight female preponderance with a male-to-female ratio of 1:1.6. The mean age at onset was 17.38±4.90 years, mean age at diagnosis was 19.38±5.40years. Positive family history was present in 30(22.2%) and a history of childhood febrile seizures in 18(13.3%) patients. There were no significant gender related differences in positive family history and childhood febrile seizures.

GTCS was the most common seizure type at diagnosis, found in 72(53.3%) patients, whereas TAS was the least common type, present in 8(5.9%) patients. MJ and GTCS were the most common seizure types during the disease course, found in 93(68.9%) and MJ and TAS were the least commonly found types, present in 10(7.4%) patients. Classic JME was the most common phenotype, 110(81.5%), and lack of sleep was the most common seizure precipitating factor, 70(51.9%). Anxiety was the most commonly associated psychiatric co-morbidity, 19(14.1%) (Table-I).

Spikes/polyspike and slow waves were the most common EEG findings, present in 60 (44.5%) patients, and focal asymmetry/diffuse slowing was the least common, present in 11(8.1%) patients. Photic stimulation was observed in 38(28.1%) (Table-II).

Valproic acid was most commonly used AED in 57(42.2%) patients whereas 1(0.7%) patient required triple AEDs including VPA, LEV and TMP (Figure-1). Most patients, 89(65.9%) had seizure free period of less than one year, only 7(5.2%) had remission for more than 5 years (Figure-2).

Table-I: Seizure Types, Precipitating Factors, Phenotypes, and Psychiatric co-Morbidities Among JME Patients (n=135)

Feature	Male (n=51)	Female (n=84)	*p*-value
Seizure Type at Diagnosis			
GTCS	28(38.9)	44 (61.1)	0.254
MJ	17(41.5)	24(58.5)	
MJ	2(14.3)	12(85.7)	
TAS	4(50.0)	4(50.0)	
Seizures Type During Disease Course			
MJ	2(14.3)	12(85.7)	0.048
MJ + GTCS	36(38.7)	57(61.3)	
MJ+TAS	7(70.0)	3(30.0)	
MJ+GTCS+TAS	6(33.3)	12(66.7)	
Precipitating Factor			
Lack of Sleep	28 (40.0)	42 (60.0)	0.026
Flashing Lights	12 (54.5)	10 (45.5)	
Fatigue	7(41.2)	10(58.8)	
Stress	4 (30.8)	9(69.2)	
Menstruation	0(00.0)	13(100)	
Phenotype			
Classic JME	45(40.9)	65(59.1)	0.319
CAE evolving to JME	2(15.4)	11(84.6)	
JME with adolescent absence	3(37.5)	5(62.5)	
JME with astatic seizure	1(25.0)	3(75.0)	
Psychiatric Co-morbidities			
None	30 (30.3)	69(69.7)	0.038
Depression	6(60.0)	4(40.0)	
Anxiety	10(52.6)	9(47.4)	
Impulsivity	1(50.0)	1(50.0)	
ADHD	4(80.0)	1(20.0)	

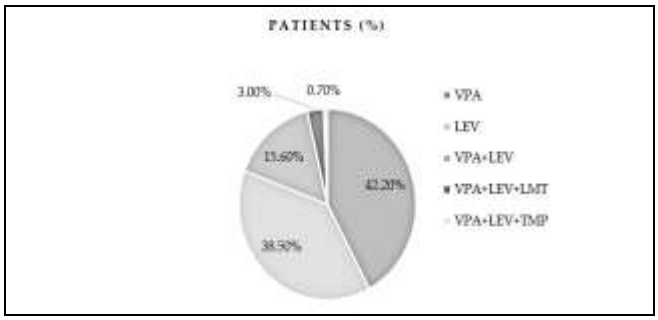

Figure-1: Antiepileptic Drugs Responsiveness Among JME Patients (n=135)

Table-II: EEG Findings in JME Patients (n=135)

EEG Features	Male (n=51)	Female (n=84)	*p*-value
Normal	3(18.7)	13(81.3)	
S/PS-SW > 3.5Hz – 5Hz	24(40.0)	36(60.0)	
S/PS-SW < 3.5Hz	15(40.5)	22(59.5)	0.559
Focal Asymmetry	5(45.5)	6(54.5)	
Diffuse Slowing	4(45.5)	7(54.5)	
Positive Photic Stimulation	19(50.0)	19(50.0)	0.067
Hyperventilation	10(37.0)	17(63.0)	0.929

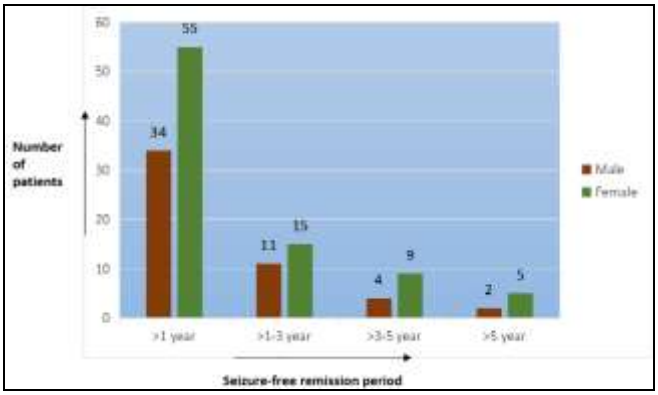

Figure-2: Seizure Remission on AEDs Among JME Patients (n=135)

DISCUSSION

In this study, Juvenile Myoclonic Epilepsy emerged as a condition with substantial long-term implications for patients and their families. It was found that timely and accurate diagnosis plays a critical role in guiding appropriate antiepileptic treatment. Although a majority of patients demonstrated good seizure control, a notable proportion continued to experience refractory seizures. Consistent with existing literature, our findings did not reveal any definitive clinical or electrographic markers that could reliably predict refractoriness.

JME is a common syndrome among genetic epilepsies. The diagnosis is often delayed due to a lack of identification of myoclonus by general medical specialists and sometimes by neurologists as well.[12] An early correct diagnosis is important from a treatment viewpoint as around 80% patients become fit free on appropriate antiepileptics.[13] Females were affected predominantly in this study, with a male-to-female ratio of 0.61, as is also reported by Camfield *et al*.[14] Similar sex differences have been observed by Reddy *et al*., in other types of idiopathic generalized epilepsy (IGE). The cause of this predilection remains poorly understood, though hormonal differences, predisposing genes, differences in brain development, glial and neurotrophic responses have been implicated to affect brain excitability.[15] Thirty patients (22.2%) volunteered a positive family history, whereas Cacao *et al*., showed a positive family history in 28% patients.[6] Circadian variation was observed in 24.4% patients. Patients with JME, like other generalized epilepsies, are "evening types," i.e., going to bed late in the evening and getting up late in the morning.[3] Febrile seizures were noted in 13.3% patients in our study, Haki *et al*., reported in 17.3% patients.[2]

GTCS, along with MJ, were the most common seizure types (68.9%), followed by all three seizure types, including GTCS, MJ, and TAS (13.3%), MJ alone (10.4%), and MJ with TAS (7.4%). The findings of this study are in concord with a study by Pietrafusa *et al*., who reported a combination of GTCS and MJ in 65.6%, a combination of GTCS, MJ, and TAS in 16.4%, MJ alone in 11.5% and MJ with TAS in 6.5%.[4] Reproducible results were obtained for seizure precipitating factors, with lack of sleep being the most common in 51.9%, flashing lights in 16.3%, fatigue in 12.6%, stress in 9.6% and menstruation in 9.6% women.[6]

The overall rate of EEG abnormalities in our study was 88.1% which was in accordance with the study conducted by Shafait *et al*.[16] Our results have shown that 93.7% patients had abnormal EEG. The most common EEG abnormality, spikes/polyspike and slow waves > 3.5Hz – 5Hz, was also found in 44.5% in our study versus 47.6%. EEG was normal in 11.9% in our study, whereas 6.3% in Montalenti *et al*.[17] Positive photic stimulation was present in 28.1% which is comparable to study results of Pietrafusa *et al*., in which 33.3% patients were photosensitive.[4]

Fits were well controlled on monotherapy with valproic acid in 42.2% of patients, followed by Levetiracetam in 38.5%. Comparable outcomes have been reported by Silvennoinen *et al*., in which 42.7% patients responded to valproic acid and 37.1% to Levetiracetam.[18] 15.6% of the patients were on dual antiepileptics (Valproic Acid + Levetiracetam), and 3.7% on triple antiepileptics (Valproic Acid + Levetiracetam + Lamotrigine/ Topiramate). However, in reproductive age group females, valproic acid use is limited due to its teratogenic profile, and alternative options are used, including Levetiracetam and Lamotrigine. Milano *et al*., proved that Levetiracetam showed significantly higher efficacy as compared to Lamotrigine in reproductive age group females previously on Valproic Acid in controlling GTCS and MJ.[19] Majority of patients (65.9%) had less than one year fit-free period, 19.3% between 1 – 3 years, 8.6% >3 – 5 years, and 5.2% for more than 5 years. This finding is contradictory to results of Chowdary *et al*., in which around 90% patients with JME were found to be in remission.[20] It may be due to a referral bias of more drug-resistant cases to a tertiary care hospital.

Refractory seizures were present in 20.7% patients, out of which 71.4% were females and 28.6% were males. Ascoli *et al*., in a recent review, showed that 30% patients with JME had drug resistance.[10] Most common causes of drug resistance were poor drug compliance and pseudo drug resistance owing to getting incorrect drug or insufficient dose of antiepileptics, and lack of sleep. One reason of increased female refractoriness may be related to gender related choices in use of alternative AEDs other than Valproic acid in women of childbearing age as shown by Irelli *et al*.[21] However it might be possible that refractoriness is overestimated due to selection bias of patients from a tertiary care hospital where patients have severe phenotype of disease as compared to those who are treated at primary and secondary care set ups. Furthermore, there is a progressive loss of follow-up of patients with a milder course of the disease at tertiary care setups. Associated psychiatric comorbidities were anxiety (14.1%), depression (7.4%), Attention Deficit Hyperactivity Disorder (3.7%), and impulsivity (1.5%). Similar psychological and behavioral comorbid have been reported by Syvertsen *et al*.[22]

LIMITATIONS OF STUDY

Though our study included a large cohort of patients, data collection is based on patient recall and subject to recall bias. Data collection was from a tertiary care center, which can lead to a false increase in resistant cases due to referrals from primary and secondary care setups. Pseudo-resistance is another factor contributing to refractory seizure control and could not be assessed in our study. Larger studies with a diverse population are required to generalize the results.

CONCLUSION

Juvenile Myoclonic Epilepsy is a lifelong condition that significantly affects patients and their families. Accurate early diagnosis is essential for selecting the most effective antiepileptic therapy. While many individuals achieve adequate seizure control, a subset continues to experience refractory seizures, and reliable predictors of refractoriness remain unclear.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

FA & IA: Data acquisition, data analysis, critical review, approval of the final version to be published.

SS & JL: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

NA & JK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Elmali AD, Auvin S, Bast T, Rubboli G, Koutroumanidis M. How to diagnose and classify idiopathic (genetic) generalized epilepsies. Epileptic Disord 2020; 22(4): 399–420. https://doi.org/10.1684/epd.2020.1192
2. Cemile H, Ozlem A, Ibrahim Hakkae B. Diagnostic difficulties in patients with juvenile myoclonic epilepsy. Sanamed 2020; 15(3): 299–303. http://dx.doi.org/10.24125/sanamed.v15i3.456
3. Xu L, Guo D, Liu Y yan, Qiao D dan, Ye J yi, Xue R. Juvenile myoclonic epilepsy and sleep. Epilepsy Behav 2018; 80: 326-330. https://doi.org/10.1016/j.yebeh.2017.11.008
4. Pietrafusa N, La Neve A, de Palma L, Boero G, Luisi C, Vigevano F, et al. Juvenile myoclonic epilepsy: Long-term prognosis and risk factors. Brain Dev 2021; 43(6): 688–697. https://doi.org/10.1016/j.braindev.2021.02.005
5. Murthy JMK. Juvenile Myoclonic Epilepsy: Myoclonic Status Epilepticus without Coma - Report of Three Cases. J Epilepsy Res 2020; 10(2): 92-95. https://doi.org/10.14581/jer.20015
6. Fayad C, Saad K, Kahwagi GJ, Hallit S, Griffin D, Abou-Khalil R, et al. A systematic review and meta-analysis of factors related to first-line drugs refractoriness in patients with juvenile myoclonic epilepsy (JME). PLoS One 2024; 19(4): e0300930. https://doi:10.1371/journal.pone.0300930
7. Rathore C, Prakash S, Makwana P. Prevalence of photoparoxysmal response in patients with epilepsy: Effect of the underlying syndrome and treatment status. Seizure 2020; 82: 39–43. https://doi.org/10.1016/j.seizure.2020.09.006
8. Stephen LJ, Brodie MJ. Pharmacological management of the genetic generalised epilepsies in adolescents and adults. CNS Drugs 2020; 34(2): 147–161. https://doi.org/10.1007/s40263-020-00698-5
9. Stevelink R, Koeleman BPC, Sander JW, Jansen FE, Braun KPJ. Refractory juvenile myoclonic epilepsy: a meta-analysis of prevalence and risk factors. Eur J Neurol 2019; 26(6): 856–864. https://doi.org/10.1111/ene.13811
10. Ascoli M, Mastroianni G, Gasparini S, Striano P, Cianci V, Neri S, et al. Diagnostic and therapeutic approach to drug-resistant juvenile myoclonic epilepsy. Expert Review of Neurotherapeutics 2021; 21(11): 1265-1273. https://doi.org/10.1080/14737175.2021.1931126
11. Shahnaz, Sher K, Sattar RA. Clinical and EEG characteristics of Juvenile Myoclonic Epilepsy. Pakistan J Med Sci 2014; 30(1): 12–15. https://doi.org/10.12669/pjms.301.4465
12. Abdalla SF, Elmagzoub MS, Babikir HE-H. Clinical Presentations and Factors Responsible for Delays in Diagnosis of Juvenile Myoclonic Epilepsy among Sudanese Patients. J Neurol Neurosci 2017; 8(4): 209. https://doi.org/10.21767/2171-6625.1000209
13. Jayalakshmi SS, Srinivasa Rao B SS. Focal clinical and electroencephalographic features in patients with juvenile myoclonic epilepsy. Acta Neurol Scand 2010; 122(2): 115–123. https://doi.org/10.1111/j.1600-0404.2009.01270.x
14. Camfield CS, Striano P, Camfield PR. Epidemiology of juvenile myoclonic epilepsy. Epilepsy Behav 2013; 28(1): S15–S17. https://doi.org/10.1016/j.yebeh.2012.06.024
15. Reddy DS, Thompson W, Calderara G. Molecular mechanisms of sex differences in epilepsy and seizure susceptibility in chemical, genetic and acquired epileptogenesis. Neurosci Lett 2021; 750: 135753. https://doi.org/10.1016/j.neulet.2021.135753
16. Shafait S, Alamgir W, Ahmad I, Arif S, Liaqat J, Hashmat A. A study on comparative yields of standard short-term electroencephalogram and long-term electroencephalogram recording in suspected epilepsy patients. Pak Armed Forces Med J 2021; 71(5): 1727-1731. https://doi.org/10.51253/pafmj.v71i5.5921
17. Montalenti E, Imperiale D, Rovera A, Bergamasco B, Benna P. Clinical features, EEG findings and diagnostic pitfalls in juvenile myoclonic epilepsy: a series of 63 patients. J Neurol Sci 2001; 184(1): 65–70. https://doi.org/10.1016/s0022-510x(00)00496-2
18. Silvennoinen K, de Lange N, Zagaglia S, Balestrini S, Androsova G, Wassenaar M, et al. Comparative effectiveness of antiepileptic drugs in juvenile myoclonic epilepsy. Epilepsia Open 2019; 4(3): 420–430. https://doi.org/10.1002/epi4.12349
19. Milano C, Turco F, Pizzanelli C, Bonanni E, Siciliano G, Fornai F, et al. Response to levetiracetam or lamotrigine in subjects with Juvenile Myoclonic Epilepsy previously treated with valproic acid: A single-center retrospective study. Epilepsy Behav 2021; 115: 107706. https://doi.org/10.1016/j.yebeh.2020.107706
20. Chowdhury A, Brodie MJ. Pharmacological outcomes in juvenile myoclonic epilepsy: Support for sodium valproate. Epilepsy Res 2016; 119: 62–66. https://doi.org/10.1016/j.eplepsyres.2015.11.012
21. Cerulli Irelli E, Cocchi E, Morano A, Casciato S, Fanella M, Albini M, et al. Valproate impact and sex-dependent seizure remission in patients with idiopathic generalized epilepsy. J Neurol Sci 2020; 415: 116940. https://doi.org/10.1016/j.jns.2020.116940
22. Syvertsen M, Selmer K, Enger U, Nakken KO, Pal DK, Smith A, et al. Psychosocial complications in juvenile myoclonic epilepsy. Epilepsy Behav 2019; 90: 122–128. https://doi.org/10.1016/j.yebeh.2018.11.022