

## GENDER DIFFERENCES IN PATIENTS WITH EPILEPSY CLASSIFIED ACCORDING TO THE INTERNATIONAL LEAGUE AGAINST EPILEPSY CLASSIFICATION

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**Abstract:** Epilepsy is a neurological disorder characterised by recurrent seizures, and it manifests differently across genders. Understanding these gender differences is crucial for tailored treatment and management strategies. **Objective:** To determine gender differences in patients with epilepsy classified according to the International League against Epilepsy (ILAE) classification. **Methods:** This descriptive observational study was conducted at the Department of Medicine, Lady Reading Hospital, Peshawar, from January 2023 to July 2023. The study included 140 patients with epilepsy, comprising 70 males and 70 females aged between 25 to 50 years. Gender differences were examined according to the ILAE classification for epilepsy. Data analysis was performed using SPSS version 23. The Chi-Square test assessed gender differences in epilepsy and its subtypes, with a significance level (p-value) set at < 0.05. **Results:** The mean age of the participants was  $37.74 \pm 7.29$  years. Idiopathic generalized epilepsy was significantly more common in females (42.9%, n=30) than in males (17.1%, n=12). Cryptogenic localization-related epilepsy was also more frequent in females (48.6%, n=34) compared to males (8.6%, n=6). Conversely, localization-related symptomatic epilepsy was significantly higher in males (74.3%, n=52) than in females (8.6%, n=6) ( $p = 0.0001$ ). **Conclusion:** Idiopathic generalized and cryptogenic localization-related epilepsy were more prevalent in females, while localization-related symptomatic epilepsy was more common in males. These findings underscore the importance of considering gender differences in the diagnosis and treatment of epilepsy.

**Keywords:** Epilepsy, Gender Differences, ILAE Classification, Seizures

### Introduction

Epilepsy is a chronic neurological condition characterized by recurring seizures. Epilepsy can affect people of any age, gender, or ethnic background (1). An individual's quality of life can be significantly impacted by epilepsy, particularly their occupation, family life, education, and socioeconomic status as well as cause stigmatization to a person (2). Furthermore, the costs associated with epilepsy can adversely affect patients and their caregivers (3).

Epileptic patients are at a significantly increased risk of suffering injuries as a consequence of seizures (4, 5). Increased prevalence of mood disorders like anxiety and sadness, as well as low self-esteem, are associated with epilepsy. Consequently, patients who suffer from epilepsy have a tendency to acquire a fear of getting hurt and a tendency to isolate themselves socially (5).

Epileptic seizures are divided into focal and generalized types (based on onset in cerebral cortex and presence or loss of awareness) by the International League against Epilepsy (ILAE) classification system, which is presently in its third version (6). In addition, epileptic syndromes are classified according to the age at which symptoms emerged, seizures type and other particular characteristics. It is possible to gain significant insights into the complex presentations of epilepsy and its progression by examining gender differences within the context of this classification paradigm (6, 7).

Epilepsy is a common neurological disorder. In developed countries, the reported cumulative life time risk is 3.1%. However, the prevalence of epilepsy is much higher in

developing countries which can be attributed to the lack of resources, that there is insufficient access to medical care, that there is an elevated rate of infection in the central nervous system and there is exposure to perinatal risk factors (8-10). It was shown that the lifetime incidence of epilepsy was 7.60 per 1,000 people all over the world, while the point incidence for those with epilepsy was 6.38 per 1,000 people (11). The prevalence of epilepsy has been reported to be approximately 2.3 per 1,000 people in a number of Arab nations (12).

There is increasing concern regarding gender differences in the classification of epilepsy and the specific epilepsy syndromes. In the process of determining gender differences in epilepsy patients, a complex interaction between environmental, hormonal, and genetic variables is observed. The recognition of these gender differences are essential for the customization of treatment techniques, the optimization of therapeutic outcomes, prognosis and the enhancement of the general standard of life for persons who are living with epilepsy. A greater awareness of gender-specific patterns associated with ILAE categorization will pave the way for more individualized and efficient approaches to the management of epilepsy. We, therefore, conducted this study to determine the gender differences in patients with epilepsy classified according to ILAE classification.

### Methodology

After obtaining ethical approval from the hospital, we conducted this observation study from January 2023 to July

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2023 at the Department of Medicine, Lady Reading Hospital, Peshawar. We selected 140 patients with epilepsy aged 25 to 50 years of either gender through consecutive sampling methods. Patients with other (provoked) causes for seizures like hypoglycemia, hyponatremia, hypocalcemia, hypomagnesemia, and encephalitis; and those with seizure mimics (syncope, conversion disorder) were excluded from the study. We divided the patients equally into two groups based on gender. Patients provided their consent to be part of the study.

Epilepsy patients who presented to medical out-patients (OPD), as well as indoor patients in medical wards, were assessed for fits regarding their nature (true/pseudo fits), type (focal/ generalized/others), and presence of provoked causes. A focused neurologic and psychiatric examination was carried out. Relevant investigations, including blood glucose, calcium, electrolytes, and magnesium levels, were carried out from the hospital lab. Electro-encephalography (EEG) was done in all patients, while brain imaging (CT/MRI) and ECG were performed in selected patients when indicated. We recorded all the demographic information such as age, gender, education, marital status, substance abuse, employment status, and clinical details on a pre-designed proforma.

Epilepsy was defined as recurrent unprovoked seizures. Epilepsy and its sub-types were classified using ILAE's latest classification of epilepsy. We assessed gender differences according to the ILAE classification for

epilepsy. Mean  $\pm$  standard deviations were calculated for numerical variables like age, and frequency was calculated for categorical variables like gender and epilepsy sub-types. SPSS 23 was used to analyze the variables. The chi-square test was used for the assessment of gender differences regarding epilepsy and its sub-types. The level of significance (p-value) was kept at  $< 0.05$ .

## Results

We selected 140 patients with epilepsy for this study; 70 male and 70 female patients were analyzed. The mean age was  $37.74 \pm 7.29$  years. The demographic data showed that 45 (64.3%) males were married, 39 (55.7%) females were married, 50 (71.4%) male patients were literate, 40 (57.1%) females were literate. Employment status in male patients showed that 56 (80%) were employed, while in female gender, 21 (30%) were unemployed. In male patients, 19 (27.1%) patients were involved in substance abuse, while in female gender, 6 (8.6%) patients were involved in substance abuse, as is shown in Table 1.

According to the ILAE classification of epilepsy, idiopathic generalized epilepsy was present in 30 (42.9%) of the female gender. Cryptogenic localization-related epilepsy was more frequent in the female gender 34 (48.6%), while localization-related symptomatic epilepsy was higher in the male gender 52 (74.3%) ( $P = 0.0001$ ), as shown in Table

**Table 1: Demographics of study participants (n=140)**

Demographics		Gender				P value
		Male		Female		
		N	%	N	%	
Marital Status	Married	45	64.3%	39	55.7%	0.30
	Un-married	25	35.7%	31	44.3%	
Education Status	Literate	50	71.4%	40	57.1%	0.07
	Illiterate	20	28.6%	30	42.9%	
Employment	Employed	56	80%	21	30%	0.0001
	Un- Employed	14	20%	49	70%	
Substance Abuse	Yes	19	27.1%	6	8.6%	0.04
	No	51	72.9%	64	91.4%	

**Table 2: Gender difference according to ILAE classification (n=140)**

Gender	ILAE classification			Total	P value
	Idiopathic Generalized Epilepsy	Cryptogenic Localization-related Epilepsy	Localization-related Symptomatic Epilepsy		
Male	12	6	52	70	0.0001
	17.1%	8.6%	74.3%	100%	
Female	30	34	6	70	
	42.9%	48.6%	8.6%	100%	
Total	42	40	58	140	
	30%	28.6%	41.4%	100%	

## Discussion

Sex and gender disparities in epilepsy have a significant role in epilepsy treatment. The term "sex" pertains to the inherent biological distinctions between males and females,

encompassing genetic composition, hormonal profiles, and reproductive anatomy (12). The hormonal disparities between genders play a crucial role in epilepsy, as they influence the specific therapeutic considerations for female patients at different phases of life. Gender, in contrast, refers

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to the societal influences that differentiate between men, women, and gender-varied individuals. Gender can have an impact on how patients with epilepsy view their lives. An individual's gender identification may diverge from the biological sex assigned at the moment of conception. Despite the specific reporting in the medical literature of the distinctions between sex and gender in recent years, the terms sex and gender are nevertheless commonly used interchangeably (13).

There are an estimated 50 million individuals globally who have epilepsy. Typically, the occurrence and prevalence of epilepsy are almost equal among males and females. Specifically, there is a nearly equal frequency between males and females, which has been primarily observed in localized epilepsies, such as temporal lobe epilepsy (14). There is no notable disparity between sexes about hippocampal sclerosis, which is the prevailing disease linked to temporal lobe epilepsy. Upon further classification of focal epilepsies, a higher occurrence was observed in males in cases where a structural anomaly was identified, particularly among individuals aged 30 to 59 years. Males in this age group have been found to have an increased susceptibility to traumatic brain injuries and post-traumatic brain injury epilepsy, which could partially account for this phenomenon. Men have overall greater exposure to risk factors associated with symptomatic (secondary) epilepsy. Moreover, females may underreport or conceal the occurrence of seizures in some parts of the world due to stigmatization and sociocultural reasons.

Among the generalized epilepsies, genetic generalized epilepsy syndromes, including juvenile myoclonic epilepsy and juvenile absence epilepsy, exhibit a distinct prevalence among females. The specific biological reasons contributing to this distinction have not yet been fully understood, although sex hormones are expected to play a significant role (15). Moreover, there are behavioral differences between male and female genders in some types of epilepsy syndromes, e.g., mesial temporal sclerosis. Females have more frequent auras, while males have a higher frequency of secondary spread of seizure (15).

Identification of gender differences in epileptic patients is crucial to optimize therapeutic goals and choice of anti-epileptics for better control of seizures. The impacts of sex and gender are evident over an individual's lifespan, encompassing the maturation of the brain, childhood, adolescence, pregnancy, and aging. Sex and gender factors have an impact on both diagnostic considerations and crucial therapy decisions (16).

We conducted our study on 140 epileptic patients. The mean age of the patients was  $37.74 \pm 7.29$  years. Fundamental demographics analysis revealed no difference between both genders regarding marital and education status. Employment status showed that most male patients were employed compared to female patients. Substance abuse was more common in the male gender than the female gender. Similar findings have been reported by a study that showed that male patients have a higher frequency of employment as well as substance abuse (17).

Regarding the ILAE classification of epilepsy, we found that idiopathic generalized epilepsy and cryptogenic localization-related epilepsy were notably more common in the female gender (42.9% and 48.6%) than in the male gender (17.1% and 8.6%), respectively. Localization-related symptomatic epilepsy was more common in the male

gender (74.3%) than in the female gender (8.6%), ( $p = 0.0001$ ).

Our findings were in conformity with the study by Kishk N et al 17, which showed that females had a comparatively higher frequency of juvenile myoclonic epilepsy ( $p = 0.01$ ), idiopathic generalized epilepsy ( $p = 0.02$ ), and temporal lobe epilepsy ( $p = 0.02$ ). On the other hand, symptomatic (secondary) epilepsy was more frequent in males ( $p = 0.001$ ). Another study by Christensen J et al. 18 reported similar findings regarding gender differences in epilepsy. It was shown that idiopathic generalized epilepsy and cryptogenic localization-related epilepsy were more frequent in the female gender (57%,  $p = 0.002$  and 58%,  $p < 0.001$ , respectively), while localization-related symptomatic epilepsy was more common in the male gender (55%,  $p = 0.005$ ) (18). We did not consider genetic factors regarding the occurrence of epilepsy and its sub-types in both genders. Further studies with larger sample sizes are needed to assess this association.

### Limitation of Study:

We did not consider genetic factors regarding occurrence of epilepsy and its sub-types in both genders. Further studies with larger sample sizes are needed to assess this association.

### Conclusion

We concluded that according to the ILAE classification of epilepsy, idiopathic generalized and cryptogenic localization-related epilepsy was more frequent in the female gender. In contrast, localization-related symptomatic epilepsy was significantly more common in the male gender.

### Declarations

#### Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

#### Ethics approval and consent to participate

Approved by the department concerned. (IRBE-MAYD\_885 dated 12-05-22)

#### Consent for publication

Approved

#### Funding

Not applicable

### Conflict of interest

The authors declared the absence of a conflict of interest.

### Author Contribution

#### ZEESHAN AYAZ

Coordination of collaborative efforts.

Study Design, Review of Literature. Manuscript revisions, critical input.

Data acquisition, and analysis.

Manuscript drafting.

**ZAFAR ALI** (Assistant professor)

*Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.*

*Conception of Study, Final approval of manuscript.*

*Data entry and Data analysis, drafting article.*

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