

Prevalence and risk factors of psychogenic non-epileptic seizures (PNES) among adult Sudanese epileptic patients who attend Dauod charity clinic, Sudan, 2021

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Abstract

Background: Seizures can present in many diseases like epilepsy which is in the list of the commonest neurological diseases. Some seizures can present as psychogenic seizures. Epilepsy can also be associated with psychogenic non-epileptic seizures.

Objectives: To assess prevalence and risk factors of psychogenic non-epileptic among adult Sudanese epileptic patients.

Methodology: A descriptive cross-sectional facility-based study was conducted during Jan-Feb 2021 at Daoud Charity Clinic in Omdurman city, Sudan. Data collection was conducted through an interview-based structured questionnaire and there was a total number of 99 participants who were included in this study.

Results: Overall, in this study there were 99 epileptic patients. 57% were females, 79% of the patients reside in Khartoum, and 32% reached secondary school. The main type of epilepsy was generalized tonic clonic (68%) followed by focal with impairment (11%). The majority of patients have been diagnosed with epilepsy for more than three years (65%). Psychogenic non-epileptic seizures history was found in 29 (29%). The PNES prevalence was significantly higher in patients with social problems and depression (p value 0.005, 0.00 respectively). Patients with depression were having 14 times risk to have psychogenic non-epileptic seizures than patients without depression (CI 95%: ##-##). Most of the participants had no sexual or physical abuse history, school/university/work refusal, and/or absence (94%, 84%, and 63% respectively).

Conclusion: A considerable high prevalence rate of PNES can be found among adult epileptic patients. Epileptic patients suffering from social problems or/and depression and poor economic status have a higher tendency to develop psychogenic non-epileptic seizures especially after two to three years of treatment and above.

Introduction

Background:

Epilepsy is considered a disease which has a persistence tendency for patients to experience epileptic seizures and also by the neurobiological, psychological, cognitive, and social sequel of this condition. An epileptic seizure is the signs and/or symptoms that occur transiently due to abnormal synchronous or excessive neuronal activity that occurs in the brain. A seizure can be characterized as an event and that epilepsy as the disease that involves recurrent unprovoked seizures.[1] International league against epilepsy(ILAE) named six etiologies for epilepsy which include: structural causes, genetic causes, infectious causes, metabolic causes, immune causes and unknown causes. The ILAE also classified the etiologies of seizures in (2017) into: Generalized onset, Focal onset and unknown onset. The ILAE divided epilepsy into four categories: generalized epilepsy, focal epilepsy, combined generalized/focal epilepsy

and an unknown category. [10] Epilepsy diagnosis is mainly clinical and largely depends on a careful history taken from the good eyewitnesses. The EEG may help in epilepsy classification, but normal EEG may be observed in patients with epilepsies and abnormal findings in patients without epilepsy.[2] Magnetic resonance imaging should be the imaging investigation of choice and is particularly important in those who have epilepsy that occurred before two years or in adulthood, who have a focal onset as suggested by history, from the examination, or by electroencephalography (unless it is clear that it is a benign focal epilepsy) and in whom there are still seizures despite using first line medication.[3] The plan of management for patients with epilepsy (PWE) focus on three main goals: to control seizures, to avoid the side effects of the drug, and to maintain the quality of life (QOL) or to restore it.[4] Immediate anti-seizure drug therapy is usually not necessary in individuals after a single seizure and is typically reserved for individuals who are at high risk of recurrent seizures or patients who developed more than one unprovoked seizures.[4]

Psychogenic non-epileptic seizures (PNES) are conditions that clinically resemble epileptic seizures, but don't have physiological dysfunction of central nervous system but instead can be determined psychogenical.[7] Many Psychosocial stressors may result for those who are vulnerable to have emergence of PNES, include bereavement, unwanted pregnancy and ongoing abuse; physically, verbally, or sexually.[7] Duration that is prolonged, course that is fluctuating, movements that are asynchronous, movements of the head or the body that are from side-to-side, thrusting of the pelvis, crying during the ictal phase, ictal eye closing, memory recall, and postictal confusion absence were the most reliable signs in distinguishing PNES from epileptic seizure. What is important to recall is that there is no exact feature that is either specific or sensitive for PNES.[7] Manifestations of PNES include unresponsive behavior with motor manifestations mimicking a generalized convulsion or a complex partial type is the manifestation that is most common of a PNES.[7] PNES most likely don't occur during sleep but epileptic seizures can occur during sleep. There are many convulsive-like motor activities that can occur in PNES. Motor activities of the epileptic seizure usually present as a brief tonic posturing or a synchronized convulsion within which motor activity progression is defined; in PNES movements are more often variable, asynchronous and waxing and waning over the ictus course. Movements that can suggest PNES include thrashing, writhing, opisthotonus (arched back), pelvic thrusts and jactitation or side to side rolling. Rapid alerting and reorientation is common after PNES but uncommon with epileptic seizures.[7] The best diagnostic tool available is Video-EEG.[8] Consistent history with PNES and typical event recording of typical semiological PNES features with electroencephalogram (EEG) recording showing absence of epileptiform activity before the attack, during it, or thereafter is the best measure to reach the diagnosis. History, semiology and video EEG suggesting PNES combination gives the "documented" PNES level. However, recognizing PNES even in situations with very low levels of certainty is important, because not everyone in the world has video EEG access and clinicians and patients may need to adjust treatment choices (maybe about tapering inappropriate antiepileptic drugs or starting psychological treatment) when the diagnosis is not completely certain. Such uncertainty levels can be characterized in descending order as "clinically established," "most likely," and "possible".[9] Prevalence estimates of

concurrent epilepsy in patients diagnosed with PNES vary from 5 to 56 percent, in part because of differing diagnostic criteria used to determine when both conditions have occurred together.[7]

Stigma is a status which found when components of labeling, categorizing, disconnection, discrimination and loss of status occur together in a situation of power that permits them to unfold. In other words stigma is the bearing the disease burden and also the heaviness of labeling as lower or being infected by those who are not diseased and in better power or situation to label the diseased person and losing them their status in the community.[6] Stigma perceived by the PWE patient can be classified into four major types, Enacted, Felt in patients, and coaching and courtesy in their families. Enacted stigma refers to real discrimination events towards PWE because of their disease, i.e. it happens when others –because of many reasons- label, naming, or act in discriminative ways towards PWE. Mainly it is because of misconceptions and/or lack of knowledge of the disease. Many fear from PWE as they are thought to be in sin or with demonic possession, others believe epilepsy is infectious. Felt stigma is explained as the shame from having an epilepsy and the repressive fear of contracting Enacted stigma. Coaching stigma occurs in ashamed parents who tend to teach their sons that epilepsy is an unsought uniqueness or moral weight they have to bear. Courtesy stigma on the other hand is when stigma is extended from labeled individuals to their relatives. [6]

Problem statement:

Co-existence of epilepsy and psychogenic non-epileptic seizure places an even greater challenge for both psychiatrists and neurologists in following up their patients, as PNES also may lead to being misdiagnosed as a true seizure by some neurologists. Almost all patients' relatives consider PNES as a true seizure before consulting their neurologist, which may create some sort of stress and loss of hope in relatives (as the patients may be already on drugs and well controlled) and create or increase epilepsy stigma in patients and their families. Misunderstanding PNES as true seizure by either the patients and/or their family may lead them (especially in Sudan) to lose hope in medical therapy and seek help from a traditional healer (ex. herbal remedy and Sheikh). PNES is not uncommon where the estimates are 2-50/100,000 in the general population [11], but it is much larger in patients having epilepsy where 20–40% of those in inpatients in monitoring units of epilepsy and between 5% to 10% of those in outpatients in epileptic clinics have PNES.[12] The lack of appropriate diagnosis of PNES among epileptic patients can results in the increase of an anti-epileptic drugs dose in a potentially harmful way as well as the diagnosis of refractory epilepsy.[3] Patients who are admitted to monitoring units of video-EEG because of a diagnosis of drug-resistant epilepsy one among every five of them are found later to be suffering from PNES; the PNES coin is pseudo-refractory epilepsy.[13] Psychogenic epilepsy is among the top 10 critical neuropsychiatric conditions according to the International League Against Epilepsy (ILAE).[13] According to the reports PNES presence is usually due to financial, interpersonal and psychiatric problems.[14] Depressive, anxiety disorders and relationship problems are more prevalent among PNES patients in comparing them to the general population and even to those with epilepsy which has a strong impact on the QOL.[11] Stigma is another problem encountered in both types, but the perceived stigma risk experience is 42% higher in PNES patients than in patients with epilepsy.[15] Despite of all this most

researchers have studied PNES alone while few studies have conducted on the subgroups of patients having both PNES and epilepsy and on the relation between PNES and its associated co-morbidities.

Justification:

As far as we know there is not enough data regarding the PNES prevalence, factors increasing its risk and the associated co-morbidities; so our study aim is to measure the PNES prevalence among adult epileptic patients and to formulate a relationship between PNES and multiple different factors. Globally this area of co-existence between epilepsy and PNES is not that clear and not researched thoroughly. Also in Sudan there is no available literature. By the end of this research I expect to find an estimated prevalence of PNES among Sudanese adult patients who have epilepsy, and a relation between other independent variables and the PNES prevalence among adult epileptic patients. There must be a clear base of literature regarding the relation between PNES and epilepsy, so to avoid mixing between the two conditions by patients or their relatives, and to further prevent misdiagnosing by the neurologists.

Objectives:

General objective:

To assess the PNES prevalence among adult Sudanese epileptic patients who are attending Daoud charity clinic, 2021.

Specific objectives:

- 1- To find out the PNES prevalence among Sudanese adult patients with epilepsy.
- 2- To study the relation between psychogenic non-epileptic seizures and the type of epilepsy.
- 3- To demonstrate the relation between psychogenic non-epileptic seizures and epilepsy duration.
- 4- To identify the relation between psychogenic non-epileptic seizures and the type of anti-epileptic drugs.
- 5- To illustrate the relation between psychogenic non-epileptic seizures and the number of anti-epileptic drugs.
- 6- To measure the relation between psychogenic non-epileptic seizures and treatment duration.
- 7- To estimate the relation between psychogenic non-epileptic seizures and the stigma of epilepsy.

Literature review:

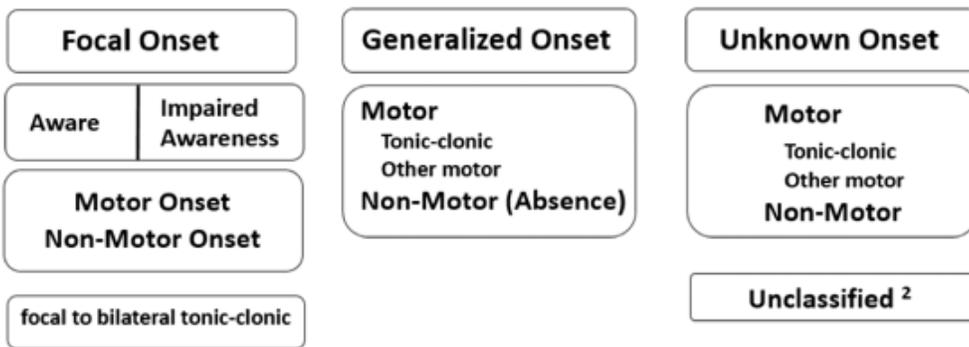
Definitions:

In 2005 epilepsy conceptually was defined as a brain disorder that can be characterized by a persistence tendency to experience epileptic seizures, the application practically of this is routinely defined as having more than one unprovoked seizures >24h apart. Then in 2014 the task force of ILAE considers epilepsy to be a brain disease characterized if any of these conditions has been found: two unprovoked seizures at least occurring >24h apart, one seizure that is unprovoked and at least there is a 60% probability of having another seizure as the general risk following two unprovoked seizures, happening during the next ten years, epilepsy syndrome diagnosis. [16,17,18]

Classification of epilepsy informs many risks of comorbidities like intellectual disability, learning difficulties, and some psychiatric features “like autism spectrum disorder”, and risk of mortality such as unexpected sudden death in epilepsy. Classification has three levels starting with type of seizure (seizures first must be differentiated from convulsive syncope, parasomnias, movement disorders, and the other non-epileptic events), then epilepsy types which are generalized epilepsy, focal epilepsy, combined generalized and focal epilepsy, and unknown epilepsy group, and the last level is epilepsy syndrome (it’s a collection of features often has age-dependent, seizure triggers, diurnal variation, and sometimes prognosis), also epilepsy may has comorbidities such as psychiatric dysfunction and intellectual dysfunction.[17]

ILAE 2017 operational classification Instruction manual of seizures types [50]:

ILAE 2017 Classification of Seizure Types Basic Version ¹

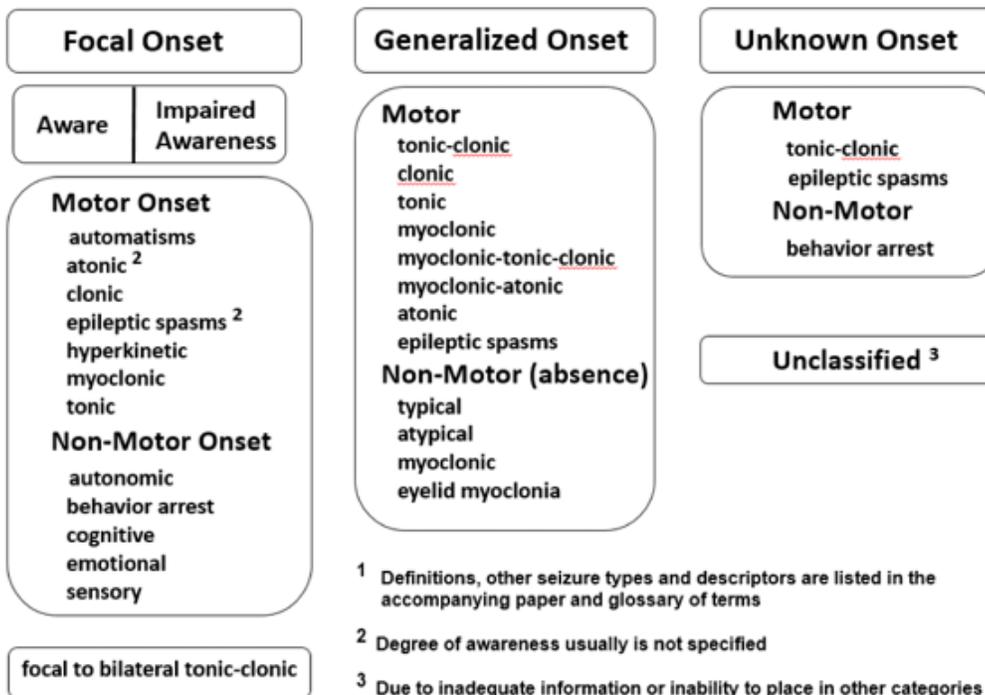


¹ Definitions, other seizure types and descriptors are listed in the accompanying paper & glossary of terms

² Due to inadequate information or inability to place in other categories

ILAE 2017 operational classification Instruction manual of seizures types [50]:

ILAE 2017 Classification of Seizure Types Expanded Version ¹



¹ Definitions, other seizure types and descriptors are listed in the accompanying paper and glossary of terms

² Degree of awareness usually is not specified

³ Due to inadequate information or inability to place in other categories

According to the anatomical origin of epileptic focus epilepsy has been classified into four categories:

- **Temporal Lobe epilepsy:**

Is the type that is most common of localized epileptic seizures to occur. Patients with this type of seizures can hallucinate visions, sounds, tastes and smells for the period of the seizure, as well as feel an inability to explain their sensations afterwards.[19]

- **Frontal Lobe epilepsy:**

This site is the commonest after temporal lobe of localized epilepsy, seizures within the frontal lobe can cause uncontrollable muscle twitching. Patients with this type of seizures may have asymmetrical kicking movements or legs' movements such as riding a bicycle, because of certain muscle control centers over-stimulation in the brain.[19]

- **Occipital Lobe epilepsy :**

Epilepsy affecting this site account for about five and ten percent of total cases of epilepsy, patients with this type typically will have visual hallucinations in form of flashing or repeated images, involuntary movements of the eye, or partial blindness.[19]

- **Parietal lobe epilepsy:**

Most patients with this type of localized epilepsy have aura which is somatosensory that can present as painful dysesthesias, aphasia and though vertigo, disturbances of body image also occur. If supplementary motor area propagation occurs, hyper motor manifestations will be noted. Complex hallucinations auditory or visual in addition to automatisms may appear when temporo-limbic propagation occurs. [20]

General principles of anti-epileptic drugs (AEDs) treatment (NICE, 2012):

1-It is recommended that children, young people and adults should be treated with a single AED (mono-therapy) whenever that is possible.

2-If the initial mono-therapy is not successful, then mono-therapy using another drug or a treatment with a second drug can be added. Caution is needed during the change-over period. Failure of an AED either due to continued seizures or adverse effects, another drug should be commenced (which is either another first-line or instead second-line drug) and increasing to an appropriate or maximum dose that can be tolerated and then slow tapering of the first drug may be done.

3-If the latter AED is not helpful; one of the two drugs may be tapered, depending on their relative efficacies, side effect profiles and drugs tolerability before starting another drug. Some patients will need more than 2 AEDs.[5]

4- The recommendations are that two drugs combinations either as an adjunctive or 'add-on' therapy must be considered only when mono-therapy trials with the tolerated dose of AED have not aborted the seizures. If attempts at combination do not give the desired effects, treatment should be reverted to the regimen (mono-therapy or combination) that showed to be the most acceptable to the patient, that is to provide the best balance between effectiveness in decreasing seizure occurrence and tolerability of adverse effects.

5- When choosing combination therapy, considerations about interactions of AEDs and comorbidities should be sought.

6- If there is no improvement after two adequate trials of AEDs, the patient should be referred for epilepsy surgery evaluation.[5]

PNES:

Psychogenic non-epileptic seizures are a functional neurological disorder/ subtype of conversion disorder, which are neurobehavioral disorders at the neurology and psychiatry interface. [21]

The definitions adopted in the literature to describe psychogenic non-epileptic seizures (PNES), include the following:

1. An observed sudden, usually time-limited paroxysmal change in behavior or consciousness looks like phenomenologically (semiologically) an epileptic seizure.
2. There are no characteristic changes seen in electrophysiology that occur with an epileptic seizure (i.e., the absence of ictal or postictal electroencephalography [EEG] changes).
3. No evidence of other causes for the episodes.
4. Evidence or strong suspicion of psychogenic processes as causative factors. [22]

Clinical features of PNES:

Differentiating Epileptic seizures (ES) from PNES could be clinically challenging. A review detailing signs retrospectively that can distinguish PNES suggested that favoring a PNES diagnosis for events that show a course that is fluctuating, movements that are asynchronous or side-to-side, a long duration, crying at the or eye closure at the onset of the ictal phase, ictal crying and post-ictal recall of information when presented ictally. In addition, urinary incontinence and tongue biting do not reliably distinguish between ES and PNES. A study done prospectively of 120 seizure attacks in 35 consecutive subjects showed that preserved consciousness documented by the video, eye twitching, and the attenuation of the intensity of the event by eyewitnesses reliably predicted PNES; sudden onset, ictal eye-opening and confusion/sleep post-ictally reliably suggests ES. It is also important to know that apart from all of the above, additional diagnoses should also be checked and ruled out including panic attacks, paroxysmal movement disorders and physiologic non-epileptic events that includes cardiac arrhythmias and other disorders.[21] Although there is no definitive single clinical feature that can distinguish PNES from ES, PNES diagnostic suggestive features including duration that is longer, pre-seizure anxiety, negative emotion (i.e., fear) that occurs throughout the events, ictal dissociation, and post-seizure weeping. Fewer reports of ictal self-injury and post-seizure aches and amnesia may also favors the possibility of PNES. [23]

Risk factors:

PNES and physical brain injury may be associated; the latter could have a role in their development: pathogenesis of PNES may be contributed by head injury. There are documented cases of resective surgeries of epilepsy or other intracranial neurosurgery followed by psychogenic seizure. Recent studies found associations between psychogenic seizure disorders and right hemisphere pathologies, non-specific interictal electroencephalography abnormalities, neuropsychological deficits and MRI changes. [24] The most common psychiatric mechanism is thought to be a conversion disorder. And there are some evidences from neuroimaging studies that suggest PNES may actually reflect sensorimotor alterations, cognitive control, emotional regulation/processing and integration of neural circuits. [21]

In a study that was conducted in 2017 in Puerto Rico, on clinical records of PNES patients, a secondary analysis was done for 34 records of PNES patients. 76% (n=26) of those patients were females, in agreement with the hypothesis of PNES being more prevalent among females. Trauma history related to sexual, physical, or emotional abuse (reported by 47%), and stressful life events (reported by 94%), in addition to symptoms of depression (reported by 50%) were among the reported risk factors. [25] A similar study was conducted in India in 2020 to understand the dissociative experiences and stressors related to patients of PNES. A total of 89 patients were screened. Assessment for history of abuse revealed physical abuse in childhood in 7 (10%) patients, 9 (12.6%) patients gave history of being physically eaten, and 6 (8.5%) had been abused sexually as adults. Using the dissociative scale of experiences (DES), the total mean score was noted to be 38.14 ± 14.1 (scores above 30 = high dissociation), indicating a high level of dissociation. The mean score regarding stressful life events was noted to be 98.28 ± 87.1 , indicating that the majority of patients complained of stressful life events, especially marital and family conflicts. In addition, the analysis of various types of stressors revealed that 40% of patients experienced a stress prior to the PNES. [26]

Diagnosis and treatment:

Although PNES is a common differential for epilepsy, misdiagnosis or delay in diagnosis is common with up to 75% of patients being first diagnosed with epilepsy, and an average delay of seven to ten years making a significant burden on the patient's family and health system. [29,30]

Diagnosis of PNES may be challenging due to difficulty in availability of comprehensive neurological and psychiatric assessment plus EEG monitoring at the same setting. Sometimes seizure of interest may be not detected in initial video EEG requiring long term monitoring. [31] Due to these factors non-epileptic seizure task force of ILAE design staged approach for diagnosis based on history witnessed event and EEG with different level of certainty. [32]

The mainstay effective treatment of PNES is psychotherapy with cognitive behavioral therapy (CPT) being the most efficient. If there is no benefit of an antiepileptic drug it should be tapered. Pharmacologic intervention is used for treatment of comorbid illness. [31] An exploratory study in Brazil in 2018, of patients whose age was more than 16 years had been admitted to prolonged monitoring by video-electroencephalogram were evaluated for the features related to demographic, epileptogenic and psychiatric. Detailed psychiatric assessment was performed by M.I.N.I.-plus 5.0, Beck Depression

Inventory, Beck Anxiety Inventory, and the Childhood Trauma Questionnaire (CTQ) was conducted. Data collection was done before reaching the final diagnosis and patients were compared.[33] 86 total patients were included from which 25 (29%) were with PNES. Twelve (14%) were with only PNES, 13 (15%) with ES and PNES and the rest of the 61 (71%) were with ES-only, Out of 122 patients that had been admitted to the epilepsy monitoring unit. Two or more seizure types ($p \leq 0.001$), past psychiatric disorder history and nonspecific hyperintensities of the white matter on MRI ($p < .001$) were associated with ES and PNES coexistence. Also, significantly higher emotional neglect and abuse had been found among these patients ($p < .002$ and 0.001 , respectively). Somatization, which includes conversion disorder, constituted the most commonly diagnosed disorder in PNES- only patients (83%) and patients with co-both PNES and ES (69.2%), distinguishing both of them from patients with ES-only ($p < .001$). This high prevalence of the co-existence PNES/ES in this study reinforced the need to investigate properly PNES in depth.[33] Another similar study conducted in Italy in 2020 with the aim to explore psychopathological features in a sample of referred youth with PNES either alone or with ES, compared with ES control group. Thirty-four patients were between 12 years to 21 years, 15 males and 19 females, were found in the study, 7 of them had both PNES and ES, 15 of them had PNES and 12 patients had ES. Then comparison of the three groups was conducted according to psychiatric diagnoses, life stressors, psychopathological dimensions and personality traits that include interpersonal reactivity, alexithymia and resilience, the assessment was done with structured measures. Patients with PNES with ES or PNES alone were found to have a greater mood disorder incidence, had increased frequency of lifetime traumatic experiences, were impaired more severely, and lower level resilience. All of the above groups presented alexithymic traits and emotional dysregulation.[34] A review done systematically of all published observational studies (from inception to Dec. 2016) was done in order to determine the correlates, frequency and outcomes of dual diagnosis. All of the studies that were reporting a diagnosis of any age of both PNES and epilepsy were included. Observational study designs had been included with the exception of all case reports as well as case series with less than 10 participants.

The mean epilepsy frequency in PNES patients across those studies was noted to be 22% (95% confidence intervals range between 20% to 25%,: 0% to 90%) also the mean PNES frequency in those epileptic patients was noted to be 12% (95% CI range from 10% to 14%, range: 1% to 62%). That means caution should be taken when viewing this high heterogeneity of such pooled estimates. A number of correlates of dual diagnosis also had been reported. Some studies described the differences in seizures semiology in patients with both diagnoses vs. patients with either PNES alone or epilepsy alone. However, the majority of these correlates were found to be inconclusive. Outcomes had been examined in a few of these studies in dual diagnosed patients. In clinical practice dual diagnosis is common, especially in those patients who had been referred to specialized services, and needs careful diagnosis and management.[35] In a study conducted in Sudanese adult patients with epilepsy by **Khabab Abbasher** and his colleagues 40 out of 720 patients had PNES with the most commonly affected age group being those between ages 18 to 25 . It was observed that PNES is more common among patients with idiopathic epilepsy, and is more common in women (75%) than in men which was said to be due to the more cultural stressors among Sudanese epileptic women. It's important to note that all PNES patients

(40) had normal EEG.[36] Markus Reuber and Christian E. Elger (Psychogenic non-epileptic seizures: review and update 2003) concluded if PNES are managed to be recognized early patients will do better if, outcome was found also to be better among children and younger adults . More intelligent patients and people in higher socioeconomic classes do better. There is a relationship found between PNES semiology and outcome had been found with less dramatic seizures had been linked to better prognosis (no tonic clonic like seizures; no tongue biting history, ictal incontinence, or PNES status). Finally, there were an associations found between maladaptive personality dissociative tendencies or wider somatization and poor prognosis.[37] A systematic review done by Gislaine Baroni et.al (2016) mentioned that epilepsy may act as a 'risk factor' for PNES, for high prevalence of psychiatric disorders and due to psychosocial factors. Although psychiatric symptoms usually occur with temporal lobe epilepsy, they point out that they are also found in other epileptic conditions and that abnormalities in brain structure may increase risk not only for ES, but also for other cognitive and psychiatric disorders. When both of them co-exist, PNES onset almost always preceded by ES as in raising important issues for an underlying psychiatric comorbidities of epilepsy that are related to physiopathological mechanisms.[38] In a German study conducted by Reuber and his colleges (2003), out of 329 patients in whom PNES diagnosis had been established 68 women and 22 men had additional epilepsy. 26.8 years was the mean age of PNES onset. In all cases PES started after epileptic seizures. The PNES semiology in 61.1% was convulsive, in 23.3% was tonic, in 10.0% was flaccid and in 5 % was sensory. In 64.4% of patients there was clear loss of consciousness. In 40.0% the semiology and the epileptic seizures of these patients were similar. They conclude that in epileptic patients, female gender, visual memory deficits, global NPS impairment and lower IQ these all are associated with higher PNES risk. Other factors that are organic or biological, especially the epileptogenic lesion lateralization and epilepsy onset age are not found to be associated with a greater PNES risk.[39] According to study conducted by Robert Hopner at Germany (2014) ESs are a common comorbidity in patients with PNESs, being present in one-third of the patients with PNES. There is a significant difference at onset; PNES only patients are significantly older than those with PNESs with epilepsy. A very theoretical explanation for this difference in onset might be because patients with ESs are already familiarized with a paroxysmal attacks of the organic disorder and, thus, tend to gain psychogenic paroxysmal disorder more easily.[40] According to American study done by Jagan A. Pillai and Sheryl R. Haut (Patients with epilepsy and psychogenic non-epileptic seizures 2011) non-epileptic seizures have been noted to follow epileptic seizures immediately, suggesting that seizure experience in susceptible individuals can provoke PNES. A possibility has subsequently been raised that disorders like epilepsy that can impair self-monitoring or emotional functions may contribute to conversion disorder and thereby PNES. The study suggests that the more commonly noted seizure type in epileptic patients with PNES in comparing to those with just epilepsy during EEG video recording are frontal seizures.[41]

Stigma:

Few studies addressed the issue of stigma attached to PNES. A 2017 exploratory study, conducted in the United Kingdom, compared the perceived stigma nature in PNES patients (n=47) against individuals with epilepsy (n=78). Greater stigma level was reported in patients who had PNES than epileptic patients

($p=0.04$). The study indicated that in PNES patients the perceived stigma risk development was 42% greater than in epileptic patients. These findings can suggest that most of the patients who had PNES (87.2%) reported a degree of perceived stigma. [27] The same exploratory analysis done previously about the perceived stigma nature in PNES patients compared to epileptic patients. Recruitment for 78 epileptic and 47 PNES patients was done from a hospital of the United Kingdom or membership organizations for persons living with seizures. All of them were asked to have a questionnaire series about health-related components for quality-of-life (NEWQOL-6D), anxiety (GAD-7), depression (NDDI-E), seizure frequency and severity (LSSS-3), and illness perception (B-IPQ). There was just one question that had been taken from the NEWQOL-6D was measuring perceived stigma. A higher perceived stigma level was reported in PNES patients than epileptic patients ($p = 0.04$). The results showed that the perceived stigma risk in PNES patients was 42% greater than the risk of having it in epilepsy. Seizure frequency, anxiety and depression and perceived stigma were highly associated in epilepsy but not in PNES. In the two conditions, self-control and stigma were associated ($\rho \geq 0.34, p \leq 0.01$). Findings indicated that most(87.2%) of persons having PNES reported some degree of perceived stigma, which indicates greater risk than that in epilepsy.[27]

Another study on stigma among PNES patients was conducted in 2020 in the USA. 43 individuals with PNES and 165 individuals with epilepsy were recruited. Compared with epileptic patients, there is a shorter duration of the disease, higher seizure frequency, poorer psychosocial health, normal diagnostic data and fewer anti-seizure medications among individuals with PNES. There was a higher stigma level in PNES patients compared to epileptic patients. In addition to that, 28 PNES caregivers and 99 epileptic caregivers were recruited. Caregiver stigma was also higher among caregivers of PNES patients, and this was associated negatively with QOL of patients and positively with the anxiety of the patient and caregiver. [28]

Methods And Materials

Study design:

Descriptive cross-sectional facility based study design has been applied.

Study area:

The study was conducted in Daoud charity clinic which was founded in 1985 in Banat. Banat is located in the eastern part of Omdurman, the 2nd biggest city in Sudan in terms of population. Omdurman is home for 2.5 million (2010 census) people of different ethnic backgrounds. The city has 5 hospitals, with only 3 specialized neurological clinicians.

The clinic was commenced as a Neurological clinic in 1995, serving 150-200 epileptic patients per week from all over Sudan. It is supervised by a senior consultant neurologist, under which registrars work and medical students attend the neurological history and examinations part. A senior psychiatrist is also involved and is consulted in cases of PNES.

Study population:

In this study, the population is Sudanese adult patients with epilepsy who attended Daoud charity clinic with different demographic characteristics.

Inclusion criteria:

1- All Sudanese adult patients with epilepsy who attended Daoud charity clinic at the data collection time.

2- Patients who accepted participating in the study.

Exclusion criteria:

1- Epileptic patients less than 18 years old.

2- Those who refused to participate.

Sampling:**Sample frame:**

All adult Sudanese epileptic patients who attended Daoud charity clinic at the data collection time which was from January to February, 2021.

Sample size:

Sample size was taken as total coverage in a period from January to February, 2021.

Sampling technique:

Convenience sampling technique was applied to this study to recruit the suitable patients.

Data collection:**Variables:**

1-Dependent variable:

The prevalence of psychogenic-non epileptic seizures

2-Independent variables:

Age, gender, residency, occupation, marital status, monthly income, educational level, type of psychiatric illness (depression, anxiety, etc..), type of anti-epileptic drugs, number of anti-epileptic drugs, type of epilepsy, duration of epilepsy, stigma of epilepsy, scoring systems (coping with epilepsy + coaching + ...etc)

Data collection tools:

Data was collected by a well-constructed, highly confidential, close ended questionnaire. The questionnaire consists of 7 sections; Socio-demographic, History of epilepsy, Social history, Stigma, History in favor of PNES, Psychiatric history respectively and investigations' findings (MRI, EEG).

Data collection technique:

The data collected include:

1. Demographic data

Age, gender, occupation, residency, educational level, monthly income

2. Full detailed history of epilepsy including:

Date of first attack, Date of last attack, Seizure type, Frequency of attacks, Seizure free period, past medical history social and drug history

3. History of PNES:

Stress, Time between the attack and stress, Description of the attack in favor of PNES, Duration of the attack, Sexual abuse and physical abuse.

4. Social history

5. Type and duration of epilepsy

6. Type and number of antiepileptic drugs.

7. Stigma among participants (by using Standardized scoring system for assessing the felt score, has 3 Yes or No type of questions; yes to be considered 1 and no zero points. Scores 0 and 1 were considered to be felt-stigma free patients, and scores 2 or 3 were considered felt- positive patients. 6, 8, 9, 10 Enacted score that had been designed by the author, consists of 7 questions, by which enacted stigma was assessed by the community towards each patient. The range of the score was from zero point to 7 points, (zero to 2 will be considered as not contracting Enacted stigma, but 3 or more as having positive enacted stigma).

8. Relevant available investigation findings (brain MRI and EEG).

All the included cases were assessed by a senior neurologist and a psychiatrist

Data analysis:

Data was analyzed using the statistical package of social science version 26 (SPSS 26) and Microsoft office excels in forms of tables and graphs. Chi square test was used to determine association between PNES and other variables with P value < 0.05 considered significant. Binary logistic regression was used

to determine the relationship between occurrence of PNES and other factors with CI=95% and P value less than 0.05 considered significant.

Ethical considerations:

It has been sought from the Community Medicine Department at University of Khartoum. Both privacy and protection of the participant's files and information were of the highest priority. Written and verbal consent were taken from the participants.

Results

4.1. Demographic characteristics

The enrolled samples consisted of 99 adult epileptic patients with variable types of epilepsy. The mean age was 31 years with standard deviation of 13.6, 57% were females and the majority of patients reside inside Khartoum and reach secondary school (79%, 32% respectively). Majority of participants were single (63%) and their monthly income is less than 5000 SDG (table1) (figure 1, 2). Participants are of different occupations (figure 3). 29 (57.7%) of the participants have a psychogenic non-epileptic seizures history.

4.2. History of epilepsy

The main type of epilepsy was generalized tonic clonic (68%), followed by focal with impairment (11%). The majority of patients have been diagnosed with epilepsy for more than three years (65%). 80% of participants didn't complete a period of three years free of attacks, from patients who had completed three years free of attacks 61% had recurrence after this period (table 2) (figure 4). Most of participants hadn't known risk factor (60%) .72% had no family history of epilepsy. 67% of participants are on sodium valproate either alone or as a part of treatment with 50% on it alone. 39% are on carbamazepine. Rest of the patients are on Levetiracetam or lamotrigine. 51% of participants are on treatment for three years or more (figure 5).

4.3. Psychiatric, Social problems and stigma of epilepsy

Majority of patients did not have a history of depression or anxiety (72% 82% respectively). Majority of patients were found to not have social problems (63%), from those who are complaining of social problems; problems with school, university or work were the main problem (55%) followed by problems with friends and relatives (43%). 34% had problems with social activities. Regarding stigma 62% of patients were found to not have enacted stigma. Regarding Courtesy and Coaching stigma 74% have no stigma, 16% has moderate stigma and 10% have severe stigma. Regarding coping ability score 63% has poor coping ability. (table 3)

4.4. Psychogenic non epileptic seizure association with demographic characteristics

No significant relation between PNES and gender nor marital status, patients residing in Khartoum state have significantly high frequencies of PNES (p value 0.02). As monthly income decreases based on category frequencies of PNES significantly decrease (p value 0.03). (Table 1)

4.5. Relationship between characteristics of epilepsy and PNES

Most patients who have been treated with antiepileptic drugs for two years and not more than three years have no PNES. (table 2)

4.6. Psychogenic non-epileptic seizures association with social and psychiatric problem and stigma

Prevalence of PNES was significantly higher in patients with social problems and depression (p value 0.005, 0.00 respectively). Patients with depression were 14 times more likely to develop PNES than patients without depression (CI 95%), no significant relation between any type of stigma and PNES. (table 3)

4.7. History in favor PNES

Most of participants have no history of sexual abuse, physical abuse or school/University/work refusal and/or absence (94%,84% and 63% respectively), while 69% have traumatic brain injury history . No significant relation between history of school/University/work refusal and/or absence neither history of traumatic brain injury and PNES was found (p value 0.7 for both).

Table 1: Demographic characteristics and its association with PNES

Demographic characteristics		History of PNES freq(%)		total	P value
		No	Yes		
Gender	Female	38(67.9%)	18(32.1%)	56 (56.6)	0.4
	male	32(74.4%)	11(25.6%)	43(43.4)	
Residency	Khartoum state	51(65.4%)	27(34.6%)	78 (78.8)	0.02*
	Outside Khartoum state	19(90.5%)	2(9.5%)	21(21.2)	
Marital status	Divorced	2(66.7%)	1(33.3%)	3(3.0)	0.9
	married	24(70.6%)	10(29.4%)	34(34.3)	
	Single	44(71%)	18(29%)	62(62.6)	
Monthly income	Less than 5000	27(58.7%)	19(41.3%)	46(46.5%)	0.03*
	5000 and less than 10000	23(76.7%)	7(23.3%)	30(30.3%)	
	10000 and more	20(87%)	3(13%)	23(23.2%)	

Table2: Relationship between characteristics of epilepsy and PNES:

Variable		PNES		P-value
		No n (%)	Yes n (%)	
Types of epilepsy	One type	69 (98.6)	27 (93.1)	0.20
	More than one type	1 (1.4)	2 (6.9)	
Duration of epilepsy	Less the one year	7 (10)	1 (3.4)	0.36
	One year and less than two years	12 (17.1)	2 (6.9)	
	Two years and less than three years	43 (61.4)	21 (72.9)	
	Three years and more	8 (11.4)	5 (17.2)	
Treatment Free attack for three years	No	53 (75.7)	26 (89.7)	0.09
	Yes	17 (24.3)	3 (10.3)	
Recurrence of epilepsy after Treatment Free attack for three years	No	7 (100)	10 (76.9)	0.09
	Yes	0(0)	3 (23.1)	
Known risk factors of etiology for epilepsy	No	42 (60)	17 (58.6)	0.89
	Yes	28 (40)	12 (41.4)	
Family history for epilepsy	Yes	50 (71.4)	21 (72.4)	0.92
Drug history	No	20 (28.6)	8 (29.3)	0.61
	One drug	54 (77.1)	21 (72.4)	
	More than one drug	16 (22.9)	8 (27.6)	
	Less than one year	16 (22.9)	0 (0)	0.017

Duration of treatment	One year and less than two years	11 (15.7)	4 (13.8)	
	Two years and less than three years	33 (47.1)	17 (58.6)	
	Three years and more	6 (8.6)	6 (20.7)	
	None (did not start treatment yet)	4 (5.7)	2 (6.9)	
MRI finding	Normal	37 (17.8)	8 (82.2)	0.12
	Abnormal	13 (65)	7 (35)	
EEG finding	Normal	23 (79.3)	6 (20.7)	0.26
	Abnormal	17 (68)	8 (32)	

Table 3: Psychogenic non-epileptic seizure association with social and psychiatric problems

social and psychiatric problem		History of PNES freq(%)		Total	P value
		No	Yes		
Presence of Social problems	No	50(50.5%)	12(12.1%)	62(62.6%)	0.005*
	Yes	20(54.1%)	17(45.9%)	37(37.4%)	
history of depression	No	60(84.5%)	11(15.5%)	71 (71.7%)	0.00*
	Yes	10(35.7%)	18(64.3%)	28(28.3%)	
history of anxiety	No	60(75%)	20(25%)	80 (80.8%)	0.054
	Yes	10(52.6%)	9(47.4%)	19 (19.2%)	

Table 4: Psychogenic non epileptic seizure association with History favor PNES

History in favor of PNES		History of PNES freq(%)		Total	P value
		No	Yes		
history of school/University/work refusal and/or absence	No	43(69.4%)	19(30.6%)	62(62.6%)	0.7
	Yes	27(73%)	10(27%)	37(37.4%)	
history of traumatic brain injury	No	48(71.6%)	19(28.4%)	67 (67.7%)	0.7
	Yes	22(68.8%)	10(31.2%)	32 (32.3%)	

Table 5: predictors of PNES

Physical abuse	0.514	0.38	0.11	2.33
Sexual abuse	0.896	0.92	0.09	8.9
depression	14.102	0.00*	3.8	52.3
Anxiety	1.548	0.54	0.37	6.4
psychosis	0.863	0.87	0.14	5.17

Exp(B)	P value	95% CI for EXP(B)
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Discussion

This study was directed to determine the PNES prevalence and its associated bi- psychosocial aspects among known epileptic patients. 99 patients were recruited who were assessed by an epileptologist and consultant psychiatric using full detailed history and examinations supported by imaging, EEGs and laboratory investigations.

Out of the 99 patients 19.19% showed a positive history of PNES which coincides with the existing literature that supports the coexistence of PNES and epilepsy. According to A systematic review done by Gislaine Baroni et.al (2016), patients whom were diagnosed as having PNES had a history of epilepsy that preceded the PNES, thus epilepsy may act as a predisposing factor for PNES, due to high psychiatric disorders prevalence and psychosocial factors. Although psychiatric symptoms and temporal lobe epilepsy are usually associated, they point out that they can also be found in other epileptic conditions and that abnormalities in brain structure may increase risk not only for ES, but also for other cognitive and psychiatric disorders. [42,43]

Although 57% of the patients that were in our study were females yet the relationship was not statistically significant between the gender and psychogenic non-epileptic seizure unlike to what had been found in the literature. In a study that was conducted in 2016 by Asadi-Pooya which found that the PNES prevalence is more among females which he attributed to their biological composition.[44] Similarly marital status has not been implicated to be related to PNES. Most of the enrolled patients reside in Khartoum state, among those patients 34.6 % of them showed positive history which generates a relationship of statistical significance between living in Khartoum state and PNES with a p-value of 0.02. This attribute could be because of the state urbanization. Interestingly patients who live in low socioeconomic conditions with less than 5000 SDG per month have significantly higher frequency of PNES with (p value 0.03).

If the epilepsy history is to be considered generalized tonic clonic has been found to be the main type with 68% followed by focal with impairment in 11% of the patients, predominant number of these patients have not completed three years free of fits.

With regards to the psychiatric and social problems there was no history of depression or history of anxiety disorders among the enrolled epileptic patients which are known to co-exist with epilepsy.[45] Social problems similarly were not implicated in most of the patients, and among those who do have social problems, issues with school, University ,work, friends and relatives were mainly faced .

With respect to courtesy and coaching stigma 16% of the patients suffered from moderate stigma while 10% have severe stigma with 63 of the total 99 patients showed poor coping score, this findings coincide with another Sudanese experience conducted in 2017.[46]

In our current study we found no association between PNES and type of epilepsy, duration of epilepsy, neither the family history nor the drug history. But there was an association between experiencing PNES and the treatment duration (P-value =.007). 58.6 % of those who experienced PNES are in 2-3 years of treatment. Those who are in the first year in treatment are unlikely to have PNES. However treatment free attack for 3 year or recurrence of epilepsy after treatment free attack for 3 years were noted to not having an association with experiencing PBES in epilepsy.

Another important finding was that there is no association between MRI finding and EEG finding and experiencing PNES. Non-specific changes in EEG are usually misconceived as an evidence for epilepsy. Improved understanding of the PNES symptomatology is needed to allow PNES to be diagnosed earlier and more accurately.[47]

The mentioned prevalence of stigma in the epileptic patients in previous literature can be contributing to the possible high prevalence of PNES among epileptic patients. In a study conducted by Abbasher Hussien et al. (2012) in Sudanese epileptic patients and their relatives, those with a positive felt stigma score were found to be 16.3%. Almost half of those with PWE experienced courtesy stigma, and coaching stigma was found to affect half of PWE. Poor coping score was found in one fifth of PWE. A determinant factor that is important for epileptic patients for coping with epilepsy also with courtesy stigma was age

below forty. More than 3 seizures per month reduces the coping score of PWE.[6] An exploratory study found that the risk in PNES patients to develop perceived stigma was 43% in PNES which is greater than that in epilepsy. Seizure frequency, depression, anxiety, and many sequels of the condition were associated significantly with perceived stigma in epilepsy but not in PNES.[48] This is not the same as the finding of our study which shows no significant relation found between stigma and PNES.

The prevalence of PNES was high among patients who have depression and social problems ($p < 0.05$). We suggest that this prevalence may be explained by the poor coping ability of the patients (63%). A study reported that the PNES patients tend to utilize significantly more escape– avoidance and also distancing coping strategies in comparison to the control healthy group. The study also indicated that this avoidance coping by PNES patients had a significantly negative effect on the HRQOL. Thus, our findings support the notion that PNES patients do not prefer to approach stressful situations instead of that prefers to avoid them and this avoidance behavior may result for them to be more endangered for developing PNES.[49]

Our study found that 28% of epileptic patients with a history of depression, 18% with a history of anxiety, and 37% of patients complain of social problems especially in school and work (55%). Also, 26% have a stigma of epilepsy and 10% of them have a severe stigma. Epilepsy is among the commonest stigmatizing diseases in our community and this stigma affects the lifestyle and mental health of patients especially. As the direct association between PNES and stigma was not significant in this study, and this may be due to the Islamic religious and cultural background of the Sudanese community as they see disease as a test from God, yet stigma can be a great contributor to the previous mentioned depression and anxiety as risk factors for developing PNES among epileptic patients.

Limitations of the study:

There are some limitations that the study has within which the findings need careful interpretation. Some limitations of this study should be mentioned. First is the duration of data collection was short which resulted in small sample size so did not allow us to properly determine if there any association between PNES and the duration of epilepsy or its treatment. The Second limitation is the respondents of this study denying any history of physical or sexual abuse which limit the result to find the relation between the PNES and this factor, which may be also due to the small sample size. Video EEG was not used to diagnose PNES.

Conclusion

Returning to the question posed at the beginning of this study, it is now possible to state that a high prevalence rate of PNES among adult epileptic patients (29%), can be highly associated with depression, anxiety and the last two years of treatment. When treating epileptic patients, stigma must be put into consideration as a predisposing factor for developing PNES. The present study has shed light that PNES should be recognized by the treating doctor and should therefore be considered as it has a high rate of occurrence and should not be overlooked.

Recommendations:

- From what was mentioned above, we strongly suggest the decision-makers to provide psychological health services to all patients of epilepsy especially those who are on chronic use of medication and including the follow up by psychologists routinely to pick up early risk factors of PNES and treat them earlier.
- We also recommend to include epileptic patients in social programs (e.g. : health insurance, rehabilitation programs, developing epilepsy associations ,... etc.).
- Since this research is the first research conducting the relationship between Epilepsy and PNES, we suggest to conduct more studies in the same topic, especially in developing countries, due to the absence of awareness in both epilepsy and psychological and psychiatric support of epileptic patients, their relatives and surrounding community.

Declarations

Conflicts of interest:

All authors declare that there are no conflicts of interest.

Funding:

There are no funds.

Informed consents:

Both written and verbal consents were taken from each patient.

Ethical approval;

It has been sought from the Community Medicine Department at University of Khartoum. Both privacy and protection of the participant's files and information were of the highest priority. Written and verbal consent were taken from the participants.

Authorship:

All authors fulfilled authorship criteria.

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Figures

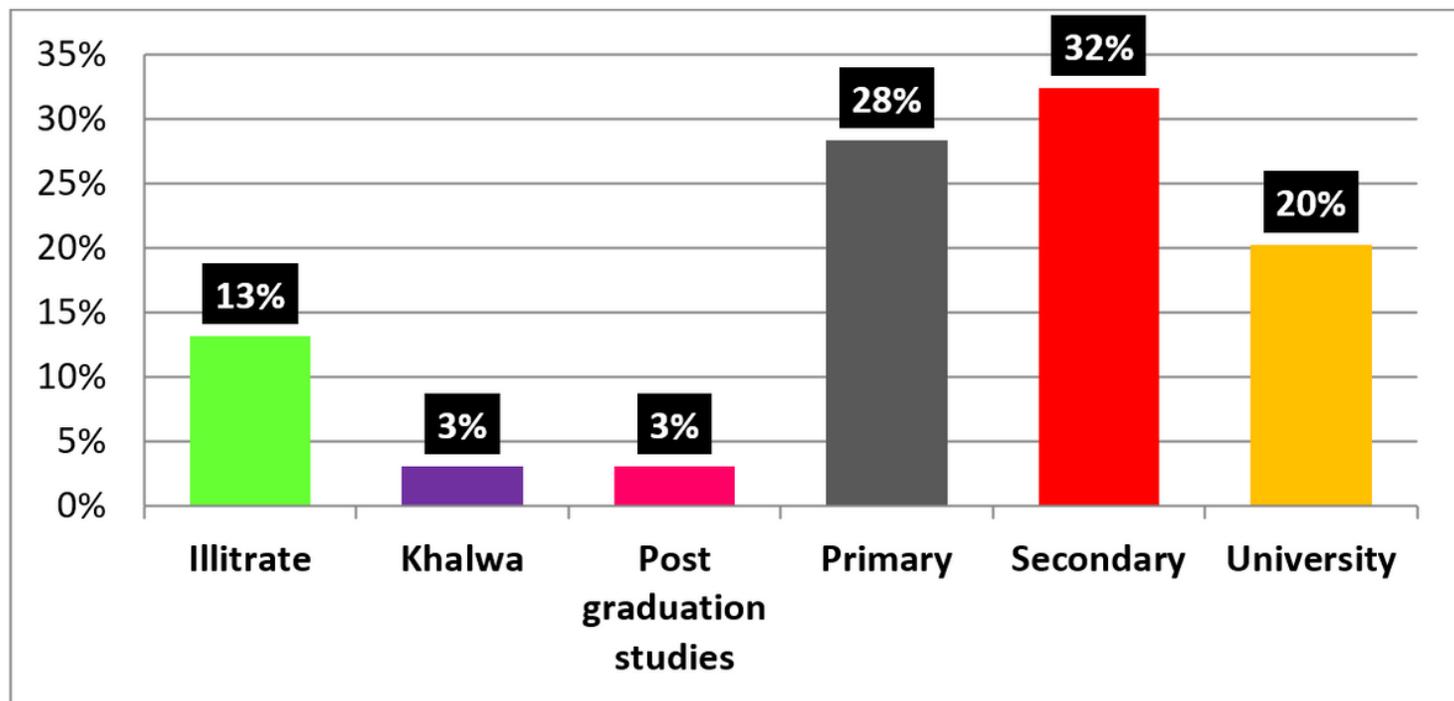


Figure 1

educational level

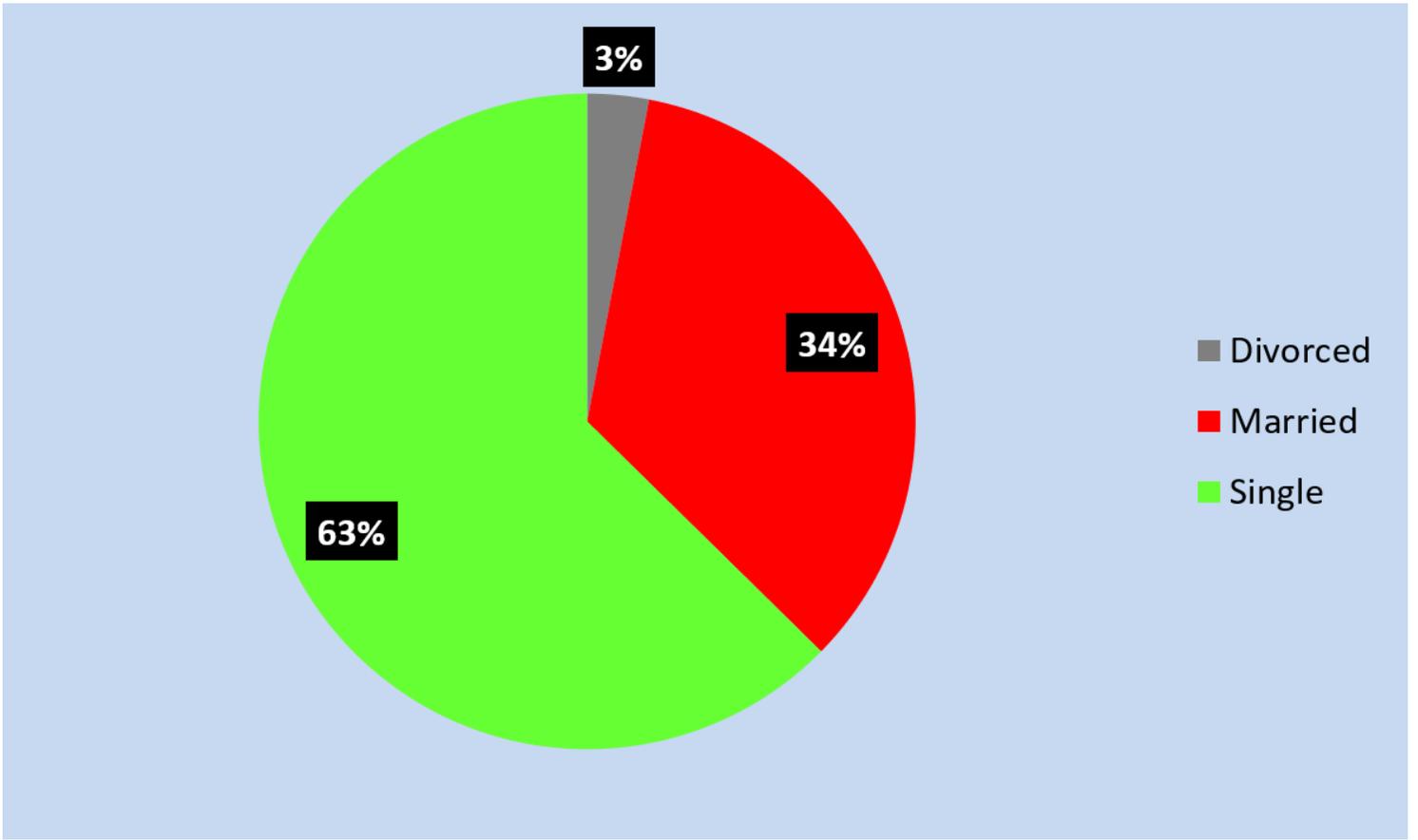


Figure 2

Marital status

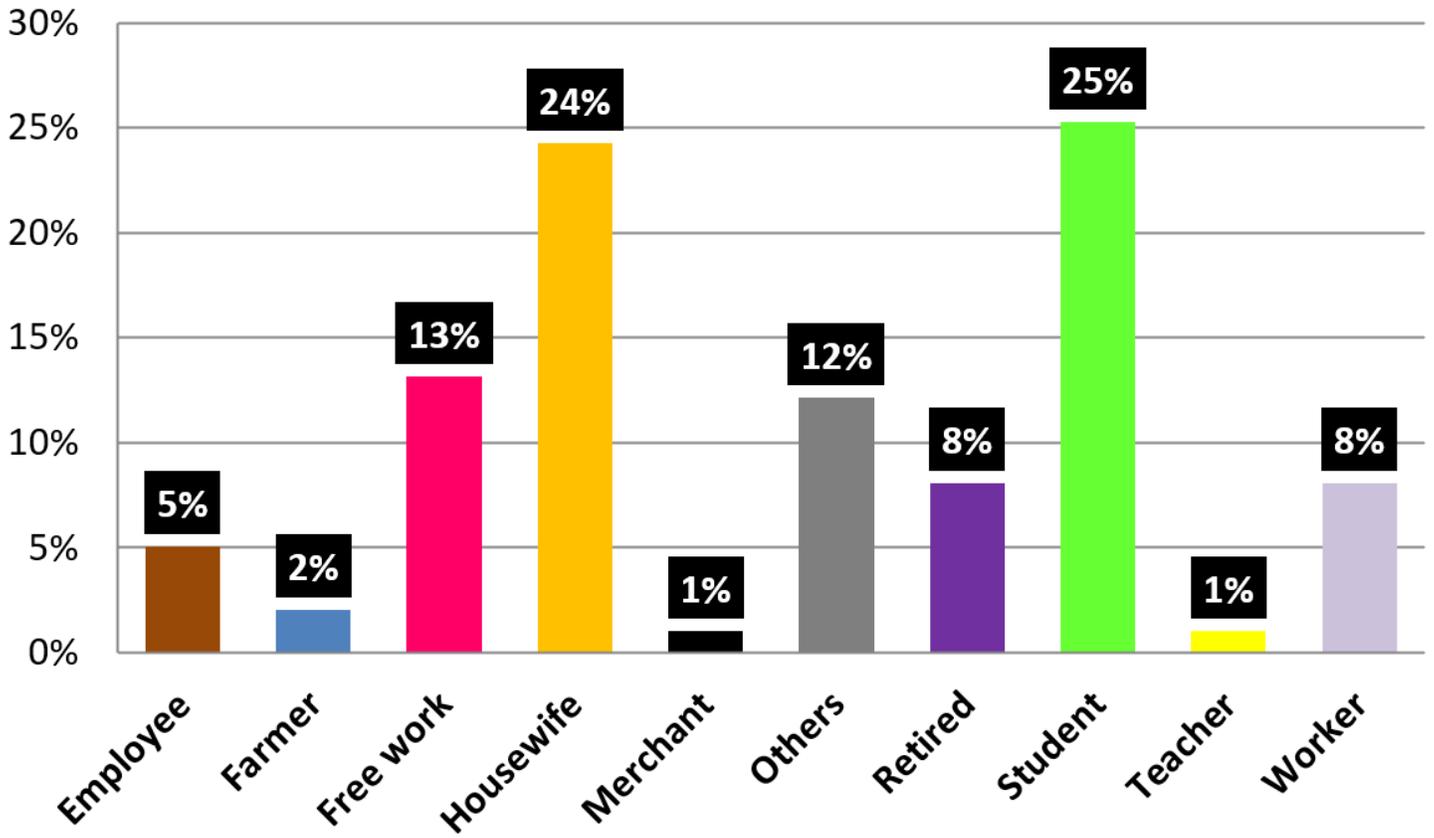


Figure 3

Occupation

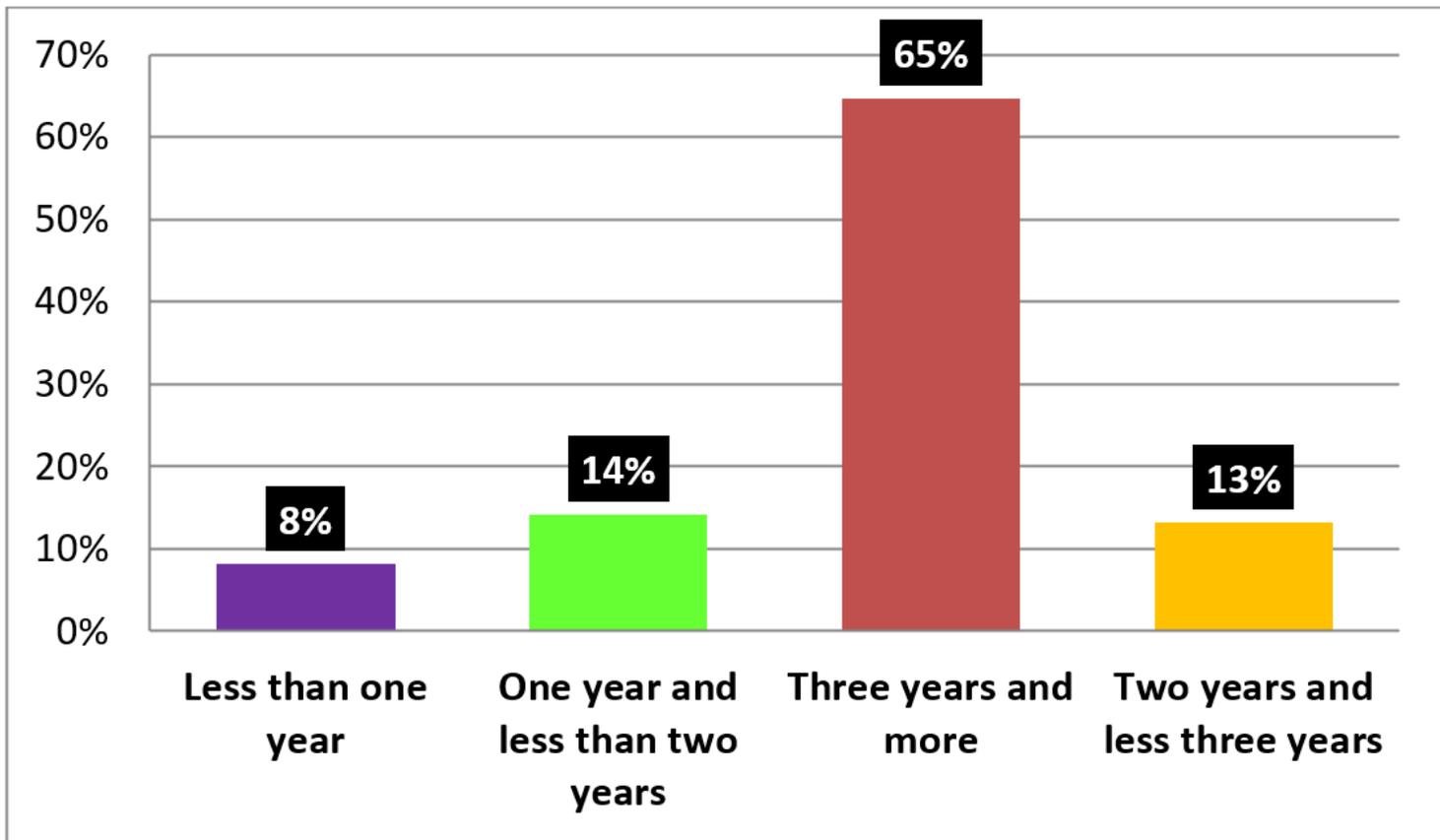


Figure 4

Duration of epilepsy

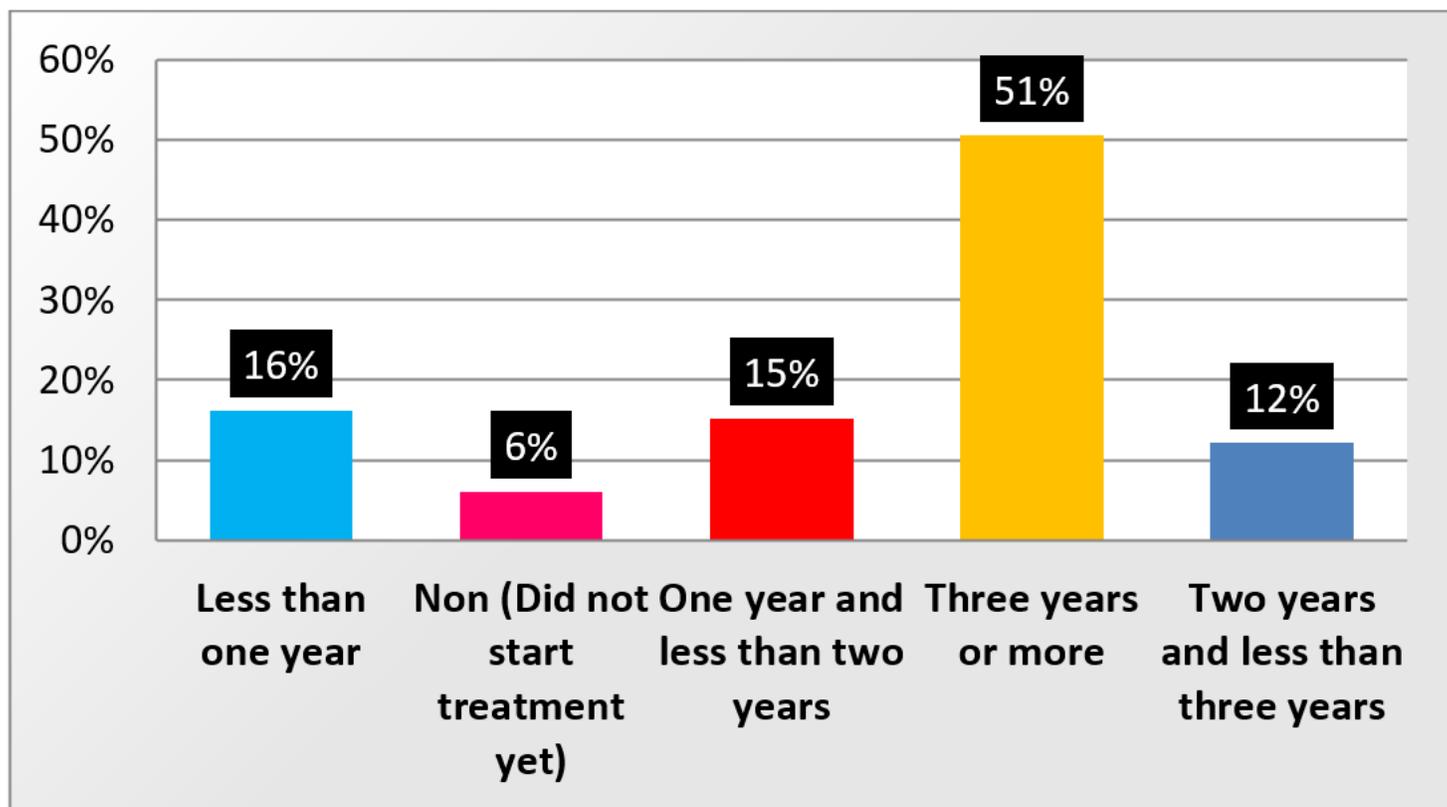


Figure 5

Duration of treatment