

Quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy

Jothipriya^{1,*}, Jasmin Anand¹, Alice Suresh², Vivek Mathew³ and Mahasampath Gowri³

¹ College of Nursing, CMC, Vellore, Tamil Nadu, India.

² Department of Neuromedicine, CMC, Vellore, Tamil Nadu, India.

³ Department of Biostatistics, CMC, Vellore, Tamil Nadu, India.

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Abstract

Epilepsy is the second most common neurological disorder which affects 70 million individuals worldwide. The study assesses the quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy (PWE). A quantitative descriptive correlation study design was adopted. The investigator used simple random sampling technique to select 100 patients with epilepsy, who fulfilled the inclusion criteria. Quality of sleep was assessed using “Pittsburgh Sleep Quality Index”, fatigue with “Modified Fatigue Impact Scale” and adherence of antiepileptic medications with “Adherence in Chronic Disease Scale” by Self reporting technique. The study revealed that the quality of sleep was poor in 64% of the subjects, while the remaining, 36% had good quality of sleep. Majorities (83%) of the epileptic patients were found to have no fatigue, 12% had mild fatigue and the remaining 5% had moderate fatigue. Majority (81%) of the subjects were adherent to antiepileptic medications, 18% were moderately adherent and only 1% of them were non-adherent. The study depicts a negative correlation $r = -0.099$ ($p = 0.338$) between fatigue and adherence to antiepileptic medications which is not significant ($p > 0.01$) and shows no correlation ($r = 0.0295$) ($p = 0.771$) between the quality of sleep and adherence to antiepileptic medications. The study highlights a positive correlation ($r = 0.2831$) ($p = 0.004$) between fatigue and the quality of sleep, which is significant ($p < 0.05$). The study concludes that attention related to sleep in patients with epilepsy has important implication for diagnosis, seizure control and a better quality of life.

Keywords: Quality of sleep; Fatigue; Adherence; Antiepileptic Medications; Epilepsy

1. Introduction

Epilepsy is one of the commonest neurological disorders. The word epilepsy is derived from a Greek word means to “seize” or “take hold of”, indicating the persons having a seizure, is possessed or at least out of control. Epilepsy is characterized by “a brief disruption in normal brain activity and this interferes with functioning of the brain resulting in a seizure. Epilepsy can be classified in various ways depending on the type and degree of severity. The average incidence of epilepsy each year is 150,000 or 48 for every 100,000 people (Epilepsy foundation, 2016) or at a given time between 4 – 10 per 1000 people (WHO, 2019).

Sudden Unexpected Death in Epilepsy (SUDEP) is defined as a sudden, unexpected, witnessed or unwitnessed, non-drowning and non-traumatic death in patients with epilepsy with or without evidence for a seizure and excluding documented status epilepticus in which post-mortem examination does not reveal a toxicological or anatomic cause for death. The mechanism responsible for SUDEP remains unclear but the role of sleep has been suspected. [11].

*Corresponding author: JOTHIPRIYA A

However since the relationship of seizures to sleep has not been well characterized and it is still not very well understood because of the multiple aspects involved in its analysis, as well as its reciprocal and intrinsic influences, the investigator found the need to assess the quality of sleep and factors affecting sleep and to improve sleep hygiene for a productive life of patients with epilepsy.

Hernandez-Ronquillo et al, 2015 indicated that little is known about the severity, impact and phenomenology of fatigue among people with epilepsy.

Antiepileptic drugs (AED) are effective in the treatment of epilepsy, such that about 70% of people with epilepsy can be seizure-free, but poor adherence to medication is major problem to sustained remission and functional restoration (4). A number of clinical and demographic features have been associated with poor adherence to antiepileptic medications allowing clinicians to identify those at greatest risk (12). More than one-third of people with epilepsy were not compliant with their AEDs. Giving health information about epilepsy and its management and consequent reduction in stigma will help for medication adherence (4).

By going through the records it was found that more than 500 patients are being newly diagnosed with epilepsy every year and the investigator also found that their quality of life was found to be affected. So the investigator was interested to study their quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy which has a role to play in their quality of life and which would result in an improved treatment outcome.

Objectives

- To assess the Quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy.
- To determine the relationship between the Quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy.
- To determine the association between Quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy, with their selected demographic and clinical variables.

2. Material and methods

2.1. Patients

A quantitative research approach with correlation study design was adopted in a private hospital, in South India for 6 weeks. The subjects were recruited based on adults >18yrs of age, who attend the Neuromedicine OPD and the Epilepsy clinic, diagnosed with epilepsy for more than 6months, and those who could understand read and respond in English, Tamil and Hindi. Persons suffering from mental and cognitive disorders and diagnosed with sleep disorder were excluded from the study. Informed consent was obtained and Simple random sampling technique was used to select the subject, and a total of 100 subjects participated in the study. The target population was 100. Study was conducted for a period of 6 weeks.

2.2. Self reporting questionnaire

Standardized tools were used to assess Quality of sleep using “Pittsburgh Sleep Quality Index”, fatigue with “Modified Fatigue Impact Scale” and adherence of antiepileptic medication with “Adherence in Chronic Disease Scale”. Self reporting technique was used to collect data. Confidentiality was maintained throughout the study. The anonymity of the subjects was maintained to ensure the reliability of data. The instrument used for data collection was a structured self- reported questionnaire, and the instrument had four parts. The first part with two section constituted the demographic profile which included their age, gender, education, employment, total family income, area of living, type of Co-morbidity, type of family and clinical profile which includes the age at onset of the disease, duration of illness, kind of seizures, frequency of seizures, type of seizure, duration of seizure free, provocative factor for seizure, type of AED, side effects of AED, regularity of drugs.

The second part is an effective instrument used to measure the quality and patterns of sleep in the adult. It differentiates “poor” from “good” sleep by measuring seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, and sleep disturbances, use of sleep medication, and daytime dysfunction over the last month. The content reliability coefficient (Cronbach’s alpha) is 0.83.

The third part was a self-reported questionnaire to assess fatigue, which consist of 40 items, providing a continuous scale of 0–160. The scale was divided into tertiles, as there were no standard cut points. The scoring ranges from 0-84.

It is computed by adding scores on the physical, cognitive and psychological subscales. The internal consistency was high for overall scores and the three subscales (Cronbach's $\alpha \geq 0.87$). Test-retest reliability is high (0.72–0.83).

The fourth part is a self-reported questionnaire to assess the adherence of antiepileptic medications, with 8 items and with proposed 5 sets of answers. The total score ranges from 0 to 32 points. Since Most of them scored more than 25 in adherence scale, we divided into two as ≤ 27 – No adherence/ incomplete adherence, >28 – Complete adherence. The reliability and homogeneity of the questionnaire were confirmed by a-Cronbach's coefficient (0.739).

2.3. Data analysis

Data analysis was done using SPSS package software version 17.0. Categorical variables were summarized using counts and percentages. Quantitative variables were summarized using mean and standard deviation or median and IQR. Spearman ranks correlation was used to identify relationship between the quality of sleep, fatigue and adherence to antiepileptic medication among patients with epilepsy. Chi-square test was used based on the cell counts to identify the association between quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy.

3. Results and discussion

Table 1 Distribution of subjects based on their Socio Demographic variables N=100

Variables	n	%
Gender		
Male	57	57.0
Female	43	43.0
Marital status		
Single	42	42.0
Married	57	57.0
Widow / Widower	1	1.0
Education		
Primary	14	14.0
Secondary	43	43.0
Graduate	38	38.0
Post-Graduate	5	1.0
Religion		
Hindu	89	89.0
Christian	5	5.0
Muslim	6	6.0
Employment		
Unemployed	43	43.0
Employed	46	46.0
Own business	4	4.0
Student	6	6.0
Pension	1	1.0
Total family income		
Rs5001- Rs10,000	31	31.0

Rs10,000 - Rs20,000	40	40.0
>Rs 20,000	39	39.0
Area of living		
Urban	46	46.0
Rural	54	54.0
Co morbidity		
Hypertension	4	4.0
None	96	96.0
Type of family		
Nuclear	21	21.0
Joint	79	79.0

Table1 shows that 57% were males and a similar percentage (57%) were married and holding secondary grade education (43%). Majority (89%) of them were Hindu, 46% were employed and had a monthly family income of Rs 10,000- Rs 20,000 (40%). Similar distribution was seen between urban and rural (54%, 46%) in joint type of family (79%) and a high percentage (96%) of the subjects reported with no history of any co morbidity conditions.

Table 2: Distribution of subjects based on their Clinical variables N=100

Variables	N	%
Age at onset		
<10	29	29.0
10-17	41	41.0
18-28	23	23.0
>28	7	7.0
Duration of illness		
< 5 yrs	10	10.0
>5yrs	90	90.0
Frequency of seizures		
6 Months-1 year	34	34.0
3-6 Months	20	20.0
1-2 Month	30	30.0
1 Week	16	16.0
Type of seizures		
Partial	15	15.0
Generalized	76	76.0
Symptomatic	9	9.0
Duration of seizure free		
6 Months-1 year	35	35.0
3-6 Months	21	21.0
1-2 Month	30	30.0

1 Week	14	14.0
Provocative factors for seizure		
Lack of sleep	14	14.0
Stress	26	26.0
Changes in Antiepileptic medications/ irregular medication	9	9.0
No reason	39	39.0
Others	12	12.0
Type of AED		
Mono pharmacy	31	31.0
Poly pharmacy	69	69.0
Side effect of AED		
Yes	17	17.0
No	83	83.0
Regularity of medication		
Regular	98	98.0
Missed Weekly	1	1.0
Missed Monthly	1	1.0

Table 2 illustrates that majority (41%) of the subjects developed epilepsy between the age group of 10yrs -17 yrs, most of them being diagnosed for >5yrs (90%) with generalized type of seizures (74%) and treated with varied AEDs (69%) . Only 17% reported with side effects, majority (98%) were regular in taking the medications. 34% of them presented with seizure every 6month-1yr, where most (34%) of them were seizure free for 6month-1yr, however majority (39%) of them reported that, there has been no reason as the pro active factor to develop seizure.

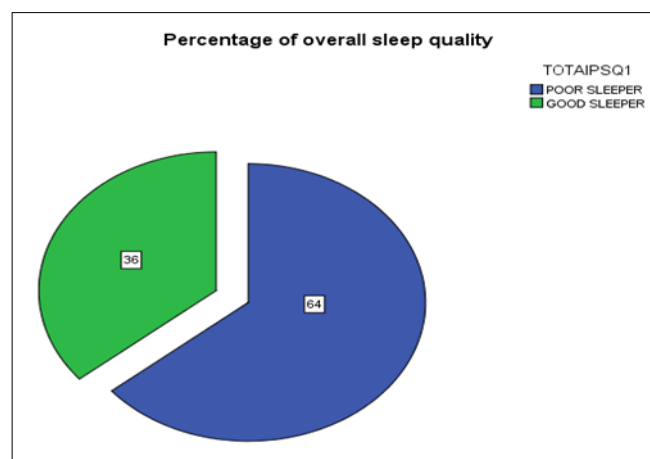


Figure 1 Distribution of subjects based on overall sleep quality

In this study (Figure 1) highlights that 64% of them had poor quality of sleep while 36% of them have good quality of sleep explaining that lack of adequate sleep can cause a gradual decrease in the quality of life of patients with epilepsy.

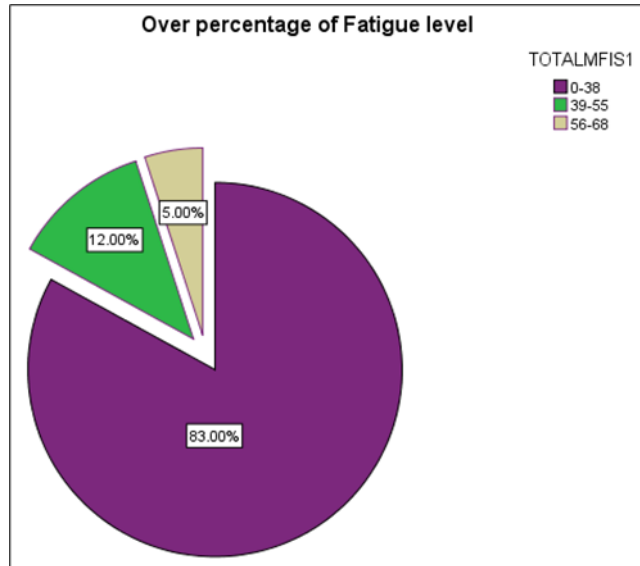


Figure 2 Overall distribution of subjects based on their fatigue level

Figure 2 communicates that majority (83%) of the subjects had no fatigue, 12% of them had mild fatigue and remaining 5% had moderate fatigue.

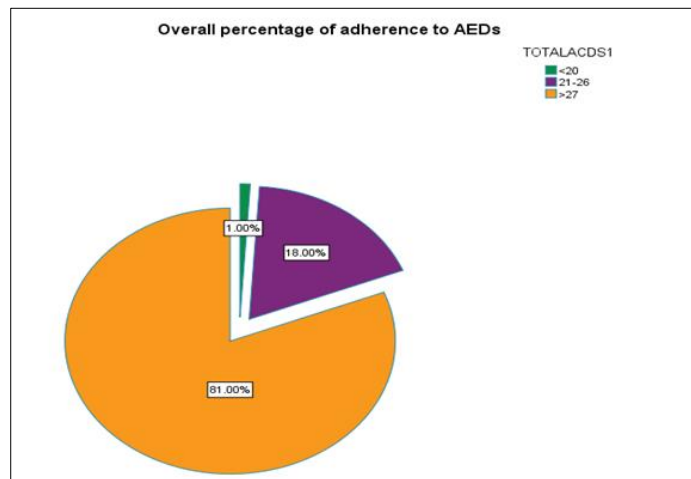


Figure 3 Distribution of subjects based on their overall adherence to AEDs

Figure 3 Illustrates that most (81%) of the subjects were adherent to antiepileptic medications, 18% were moderately adherent and only 1% of the total population were non-adherent.

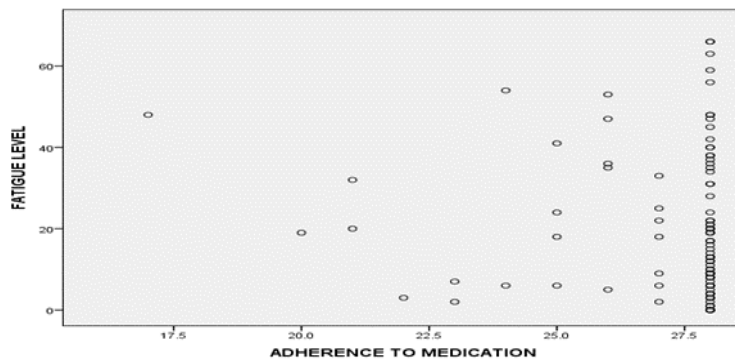


Figure 4 Relationship between fatigue and adherence to antiepileptic medications among patients with epilepsy

In the current study Figure 4 Shows a negative correlation of $r = -0.099$ ($p = 0.338$) is seen between the fatigue and the adherence to antiepileptic medications which is not significant. When fatigue increases the adherence to antiepileptic medications decreases.

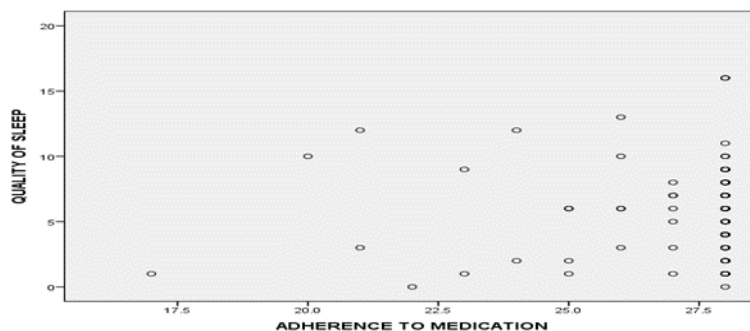


Figure 5 Relationship between the quality of sleep and the adherence to antiepileptic medication

Figure 5 Shows no correlation of $r = 0.0295$ ($p = 0.771$) between the quality of sleep and adherence to antiepileptic medications.

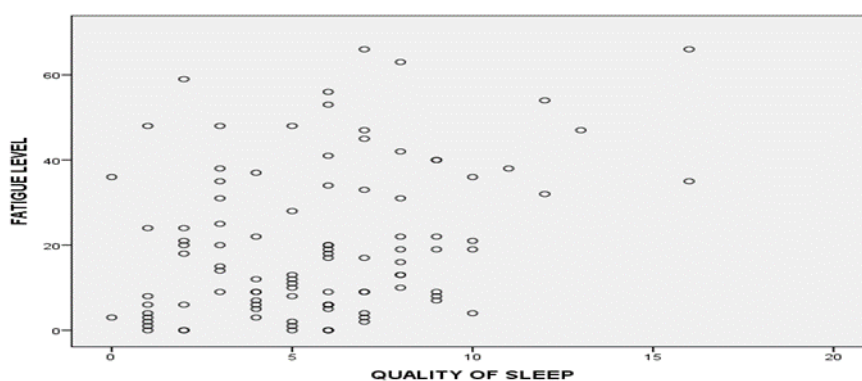


Figure 6 Relationship between the fatigue and quality of sleep

Figure 6 Shows a positive correlation of $r = 0.2831$ ($p = 0.004$) between fatigue and the quality of sleep, which is significant (as the value of fatigue increases the value of quality of sleep increases indicating poor sleep when the value is >5). So when fatigue increases the quality of sleep decreases. In the current study, a statistically significant association between quality of sleep and side effects of AED ($p < 0.05$), fatigue and provocative factor for seizures, type of AED ($p < 0.05$) was observed.

4. Discussion

The study revealed that many of the subjects belonged to age group ranging from 18-62 years (mean: 33.27 and SD of 10.648). More than half of them (57%) were males. An opposite was found in a study done in Iran to assess the quality of life among epilepsy patient, where females were 61.88% and males were 50.74% (5). This explains that the gender has no relation in developing the illness.

Many of them had secondary education (43%) which is similar to the study done among epilepsy patient in 2016 (5), where 57.7% have completed secondary education. Analysis of the study revealed that 46% were employed and 43% were unemployed. 40% of the subject had an income between Rs10,000- Rs20,000. Many studies have proved that patient's monthly income was significantly associated with medication adherence (8). As reported by the similar study done by Honnekeri, B et al (2016), the monthly cost of medication was found to influence medication non-adherence in our setting and that patients having higher income reported better adherence and patients with lower income may be compelled to stop the medication when it is not available free of cost in the public sector, cost of the drug being a burden.

More than half of them (79%) were from joint family. Majority (96%) of them had no history of any known co morbid conditions. But whereas in a cross-sectional study done in one of the largest hospital located in Ethiopia in 2019 had

reported that 114 (39%) out of 292 patients with epilepsy were found to have one or more co morbidities which was contradicting with result of the present study (14). The descriptive analysis of the clinical variables revealed that the age of onset of epilepsy was highest between 10-17 years (41%), as 70% of the diagnosis occur in late adolescence or adulthood (12). Most of the subjects (90%) suffered from the illness for more than five years. Many of them (74%) were diagnosed with generalized type of seizure and only 35% of the subjects were free from seizure among patients diagnosed between 6month to 1year, whereas 90% of the subjects were free from seizure for more than 1 year, in a study conducted by Staniszevska, A. et al (2017). Many (39%) reported that they had no reason to develop seizure episode in the present study ,but as reported by Staniszevska,A. et al (2017) , stress (36.4%) was the most common provocative factor associated with seizure attack and only 7.3% of them had no trigger.

Medication analysis revealed that Polypharmacy type of antiepileptic medications was the main mode of treatment (69%), but an opposite of this was found in the study done in 2017, where 53% of the subjects were on monotherapy. More than half quarter (83%) had no side effect of the drug and majorities (98%) of the subjects were regular in taking the medications in the present study (18).

The first objective of the study was to assess the quality of sleep, fatigue and adherence to antiepileptic medications among patients with epilepsy.

- Quality of sleep

It was found in the study that more than half (63.0%) of them had good sleep quality, severe difficulty in terms of sleep duration was 15.0% and habitual sleep efficiency was 68.0%. American co relational study found that lack of adequate sleep can cause a gradual decrease in the quality of life of patients with epilepsy particularly in areas of somatic health, social functioning and well-being (13).

- Fatigue

Majority (83%) was found to have no fatigue, 12% had mild fatigue and the remaining 5% had moderate fatigue. As many studies have proved that fatigue is highly prevalent in patients with epilepsy and has a major impact in the quality of life (20). A study done in an epilepsy community in 2016 which comprised of 3073 patients, of whom 50% of them had reported to have fatigue along with other problems when compared with present study (3).

- Adherence to antiepileptic medications

In the present study most (81%) of the subjects were adherent to antiepileptic medications, 18% were moderately adherent and only 1% of the total population were non-adherent. The result of the present study was the opposite to the study result done in Ethiopia among 292 PWE, where almost two-thirds (65.4%) of the patients were found to be non-adherent to their medication (14). Although there are many reasons there for non-adherence, many studies have reported that the most commonly identified factor was forgetfulness to take the medication followed by lack of time (7).

The second objective was to assess the relationship between quality of sleep, fatigue and adherence to antiepileptic medications

- I. There is was a negative correlation between fatigue and adherence to antiepileptic medications. In a cross-sectional observational study done in India (n=697) by Joshi, R. et al, have reported that PWE on AED were having both neurological and systemic adverse effect and fatigue was one of the adverse effect found under systemic type among 34.09% but whereas an opposite result was found in a recent study done by Çilliler, A. E., & Guven, B., (2020), it reports that there is no relation between fatigue and AED.
- II. On analyzing the correlation between quality of sleep and adherence to antiepileptic medications, there was no correlation found between the two variables, in the present study. Similar relation was found in a study done in 2018 (9). This study concluded that psychosocial factors of health status (p value=0.025) was found to influence adherence to medication. However other factors like quality of sleep, appetite qualities etc were all not associated to medication adherence.
- III. Analysis of the relationship of fatigue and the quality of sleep showed a positive correlation which is significant ($r = 0.2831, p = < .01$). This study result was similar to the study done among 75 consecutive PWE, where 32 (42.7%) patients had poor quality of sleep, (PSQI score >5) and 58.7% had fatigue (2). Similar results were found in another study in, 2016 where poor sleep quality in PSQI positively correlated with excessive day time

sleepiness. This clearly explains the fact that Poor sleep quality at night may lead to excessive day time sleepiness and day time dysfunction which is reported in many neurological disorders other than epilepsy (19).

The third objective was to assess the association between quality of sleep, fatigue and adherence to antiepileptic medication with selected socio demographic and clinical variables

There was no statistically significant association between quality of sleep and socio demographic variables. But in the study done by Turaga.S et al, (2016) reveals an opposite result, in which polytherapy, Partial seizure and poor seizure control were found to be playing a crucial role in contributing towards poor sleep quality and frequent seizure attack was also associated with decreased sleep quality. Similar result was found in a recent study done by Cilliler & Guven (2019).

- I. In the present study there is significant association found between quality of sleep and Side effects of AED ($p < 0.05$), but not with other variables like, age at onset of illness, duration of illness, frequency of seizure, type of seizure, duration of seizure free, provocative factor for seizures, type of AED, regularity of AED. This fact has been proved in many studies done among PWE, a study done in India (10) reported that the frequency of adverse effects of AEDs occurs always or frequently among PWE causing sleep deprivation which can trigger seizure and eventually lead to poorly controlled epilepsy which can profoundly diminish quality of sleep.
- II. Analysis was done to find out the association between Fatigue and socio demographic variables and clinical variables, and revealed no significant association. This study finding is supported by a cross-sectional research study done in a neurology clinic of a University-affiliated hospital in Tehran, Iran, to investigate the prevalence of fatigue and its related factor in PWE and psychogenic non-epileptic seizures (16).
- III. This finding is in stance with another similar study done among 105 epilepsy patients to identify the incidence and risk factors of fatigue (20).
- IV. There was no significant association found between adherence to antiepileptic medications and the socio demographic variables and clinical variables. This finding was controversial to a study conducted by Hasiso, T.Y. & Desse, T.A., (2016) where they found that there is significant association between adherence and marital status ($p < 0.001$), level of education ($p < 0.001$), monthly income ($p = 0.008$), occupation ($p < 0.001$), area of living and type of employment, but in line with the findings of the cross-sectional study done in 2017 conducted in India (6).

5. Conclusion

Recent research on epilepsy explains that a new classification of epilepsies helps us identify that when a single seizure can be considered as epilepsy on the basis of an abnormal EEG or imaging, it is also understood that sleep and epilepsy are closely related. However good compliance to sleep hygiene rules may help to have a preserved sleep quality. Attention related to sleep in patients with epilepsy has important implication for diagnosis, seizure control and a better quality of life.

It is accepted that fatigue is highly prevalent and is correlated with low sleep quality in patients with epilepsy, though majority did not report fatigue in the present study. Fatigue needs to be studied more in PWE, and need to control its risk factors, along with quality of sleep.

Studies have proved that majority of PWE on antiepileptic drugs were able to effectively control their illness but at the same time almost 30% of the people do not achieve full control over seizure with the best available treatment regimen. Since majority of them have better illness perception of the disease, adherence to AED were found to be high and have a better insight on non-adherence to antiepileptic medications which can lead to loss of seizure control.

Compliance with ethical standards

Acknowledgements

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Disclosure of Conflict of interest

There are no conflicts of interest.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors. The study was conducted only after obtaining the approval of Research committee of College of Nursing.

Statement of informed consent

Written and informed consent was obtained from the subject only after giving a full explanation. Privacy of the subject and confidentiality of the information was maintained throughout the study. The data was kept confidential with password protection accessible exclusively to the investigator. Anonymity and confidentiality of the subjects was maintained throughout the study. The study did not involve any interventions.

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