Clinical Research

Does Body Mass Index Affect Seizures in Epilepsy Patients?

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ABSTRACT

Objective: Epilepsy, one of the common neurological disorders, is a disease characterized by chronically recurrent seizures. In our study, we aimed to investigate whether there is a relationship between body mass index (BMI) increase and seizure types and its relationship with antiepileptic drugs (AEDs).

Material and Method: This study was created by prospectively analyzing the data of epilepsy patients who applied to a university hospital emergency department. The height, weight, and values of the patients included in the study, the number of years they had epilepsy, the AEDs they used, seizure type, and seizure duration were noted.

Results: According to BMI, 4.1% of our patients were underweight, 47.9% were normal-weight, 31.2% were overweight and 16.5% were obese. Generalized tonic-clonic (GTC) was the most common seizure type with 79.2%. We did not observe any significant difference in seizures between normal weight and obese patients. However, it was observed that complex partial seizure and myoclonic seizure type patients were of normal weight, while GTC and focal seizure type patients were overweight. No significant difference was observed between AED types and BMI.

Conclusion: In our study, we could not conclude if BMI difference increases or decreases epileptic seizures. However, we saw that BMI varies across seizure types. Since it is not clear whether obesity triggers epileptic seizures or whether the presence of epilepsy increases obesity, more comprehensive studies are needed.

Keywords: *Epilepsy, Body Mass Index, Seizure, Antiepileptic Drug.*

ÖZ

Vücut Kitle İndeksi Epilepsi Hastalarında Nöbetleri Etkiler mi?

Amaç: Yaygın nörolojik hastalıklardan biri olan epilepsi, kronik tekrarlayan nöbetlerle karakterize bir hastalıktır. Çalışmamızda vücut kitle indeksi (VKİ) artışı ile nöbet tipleri arasında ilişki olup olmadığını ve bunun antiepileptik ilaçlar (AEİ) ile ilişkisini araştırmayı amaçladık.

Gereç ve Yöntem: Bu çalışma bir üniversite hastanesi acil servisine başvuran epilepsi hastalarının verilerinin prospektif olarak analiz edilmesiyle oluşturulmuştur. Çalışmaya dahil edilen hastaların boy, kilo, değerleri, epilepsi hastası oldukları yıl sayısı, kullandıkları AEİ'lar, nöbet tipi ve nöbet süreleri not edildi.

Bulgular: VKİ'ne göre hastalarımızın %4,1'i zayıf, %47,9'u normal kilolu, %31,2'si fazla kilolu ve %16,5'i obezdi. Jeneralize tonik-klonik (JTK) %79,2 ile en sık görülen nöbet tipiydi. Normal kilolu ve obez hastalar arasında nöbet açısından anlamlı bir fark gözlemlemedik. Ancak kompleks parsiyel nöbet ve miyoklonik nöbet tipi hastaların normal kilolu olduğu, JTK ve fokal nöbet tipi hastaların ise fazla kilolu olduğu görüldü. AEİ tipleri ile VKİ arasında anlamlı bir fark gözlenmedi.

Sonuç: Çalışmamızda VKİ farkının epileptik nöbetleri arttırdığı veya azalttığı sonucuna ulaşamadık. Ancak nöbet tiplerine göre VKİ'inin değiştiğini gördük. Obezitenin epileptik nöbetleri mi tetiklediği, yoksa epilepsi varlığının obeziteyi mi arttırdığı netlik kazanmadığından daha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: *Epilepsi, Vücut Kitle İndeksi, Nöbet, Antiepileptik İlaç.*

Bu makale atıfta nasıl kullanılır: Demir B, Şahin L. Vücut Kitle İndeksi Epilepsi Hastalarında Nöbetleri Etkiler mi?. Fırat Tıp Dergisi 2025; 30(4): 246-250.

How to cite this article: Demir B, Sahin L. Does Body Mass Index Affect Seizures in Epilepsy Patients?. Firat Med J 2025; 30(4): 246-250..

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Epilepsy, one of the most common neurological disorders, is a disease characterized by chronically recurrent seizures. Epileptic seizures are characterized by disorders in cognitive, behavioral, and movement functions that occur as a result of increased or synchronized neuronal activity in the brain (1).

Some changeable risk factors can negatively affect epilepsy. One of these is obesity, which is now considered a common public health problem all over the world. Obesity; is defined as "a chronic, multifactorial disease in which metabolic, psychological, genetic, physiological and behavioral reasons and excess body fat play a role" (2). Metabolic dysfunction, inflammation, and dyslipidemias caused by obesity can lead to some diseases such as alzheimer's and parkinson's diseases and are factors that cause the development of neurological disorders. Scientific evidence shows that these obesity-related changes cause nervous system damage and affect neurological structures (3).

The treatment process of epilepsy is long, and this causes some metabolic problems. Especially weight gain; It varies depending on gender, age, drug used,

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Geliş Tarihi/Received: 12.06.2024 Kabul Tarihi/Accepted: 07.11.2024

and dose. Stabilization of body mass index (BMI) and ketogenic diet are recommended mechanisms in the treatment of seizures (4, 5). It is not yet fully clear how and in what way the ketogenic diet, which is seen as an alternative treatment for epilepsy patients, works and its working principle. However, it is known that a high-fat, low-carbohydrate, and high-protein diet has been preferred for many years to treat epilepsy (6). Studies investigating the relationship between anti-epileptic drug (AED) use and BMI ratio often examined the effects of AEDs on weight gain (7). In our study, we aimed to investigate whether there is a relationship between BMI, seizure types, and preferred AEDs, which are not widely reported in the literature. We did not observe any significant difference in terms of seizures in normal or obese patients according to BMI. We believe that the data obtained as a result of our study will contribute to new studies.

MATERIAL AND METHOD

Study Design

This study was conducted prospectively over a one-month period with patients diagnosed with epilepsy who applied to the university hospital emergency department. The patients who formed the data of the study were composed of those who voluntarily agreed to participate in the study and met the criteria. Written consent was obtained from all patients who accepted the study.

Data Collection and Procedure

Inclusion criteria were as follows: having been diagnosed with epilepsy for at least one year, and being on monotherapy medication. Having started the medication he/she uses regularly at least one year ago and not having changed the medication even if the dose has been changed. Height and weight values must be measured accurately or the patient knows them.

Exclusion criteria were as follows: Being under 18 years of age, those with low education level or intellectual disability, those with a history of Diabetes Mellitus, atherosclerotic heart disease, thyroid disorder, chronic renal failure, cerebrovascular disease, or neurodegenerative disease. Those using rhythm regulators or antipsychotic drugs. Those whose seizure type cannot be classified, those who have active infections, those who use drugs and alcohol, and those who smoke.

BMI was calculated by measuring the height, weight, blood pressure values, and pulse rates of the patients included in the study. BMI: was defined as body weight (kg) divided by the square of height (m) and expressed in kg/m2. BMI: Underweight if BMI is less than 18.5 kg/m2, normal weight if BMI is between 18.5 and 25kg/m2, overweight if BMI is greater than or equal to 25 to 29.9 kg/m2, BMI 30 If it is equal to or greater than kg/m2, it is considered obesity (8). The duration of seizures in years was also noted. The epilepsy medications used by the patients were questioned in detail in their medical history. Seizures; they were classified as focal seizure, generalized tonic -clonic (GTC) and myoclonic subtypes of generalized seizure, and complex partial seizure. Other seizure types, which were very rare in number, were not included in the study in order not to disrupt the classification. No blood samples was taken, except for the determination of the clinical status of their disease. The patients were informed about the research protocol and all information was recorded after signing the informed consent form.

Statistical Analysis

Analyzes were evaluated in the SPSS 22 (Statistical Package for Social Sciences) program. In the study, descriptive data are shown as n and % values in categorical data, and as mean±standard deviation (Mean±SD) and median interquartile range (25-75 percentile values) values in continuous data. The suitability of continuous variables for normal distribution was evaluated with the Kolmogorov-Smirnov test. Kruskal Wallis test was used to compare more than two variables. Statistical significance was accepted as $p < 0.05$.

RESULTS

After all exclusion criteria, a total of 48 patients, 25 (52.1%) women and 23 (47.9%) men, were included in the study. A total of 40 patients who smoked, had chronic diseases, had missing data, did not use AEDs, had active infections, and consumed alcohol were excluded from the study. According to BMI, 4.1% of the patients were underweight, 47.9% were normal weight, 31.2% were overweight and the remaining 16.5% were obese (Figure 1).

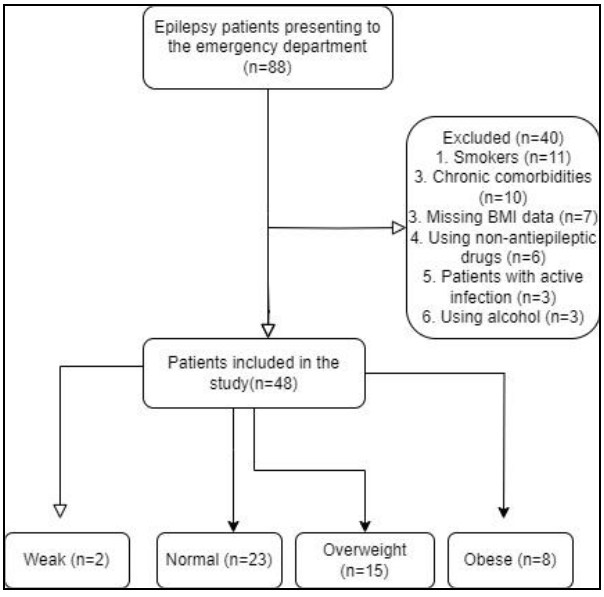

Figure 1. *Selection of the study population in flowchart.*

The average age of the patients is 34.4±13.2 (min =19-max =74) and the median age is 29.0 (IQR =23.5-44.0) years. When the blood pressure values were examined,

it was seen that there was no hypotensive or hypertensive patient. Although it is not exactly clear, the estimated data obtained showed that the average seizure duration was 120 seconds. When the seizure type of the patients is examined, 79.2% are GTC, 10.4% are focal motor, 6.3% are myoclonic seizures and 4.2% are complex partial, and the median seizure duration is 120 seconds. A total of 58.3% of the patients use Levatiracetam, 22.9% use Valproic acid (VPA), 8.3% use Carbamazepine, and 10.4% use Lamotrigine (Table 1).

Table 1. *Demographic and clinical characteristics of the patients.*

Variables		**Number**	**% / IQR**
Gender	Female	25	52,1
	Male	23	47,9
Age (year), Median (IQR)		29,0	(23,5-44,0)
Height (cm), Median (IQR)		167,0	(160,0-175,5)
Weight (kg), Median (IQR)		70,0	(62,0-84,0)
BMI, Median (IQR)		24,6	(22,5-27,6)
Systolic (mmHg), Median (IQR)		115,5	(110,0-120,0)
Diastolic (mmHg), Median (IQR)		75,0	(70,0-80,0)
Time to diagnosis (year), Median (IQR)		8,5	(3,0-17,5)
Seizure type	GTC	38	79,2
	Focal motor	5	10,4
	Myoclonic seizure	3	6,3
	Complex partial	2	4,2
Seizure duration (sec), Median (IQR)		120,0	(80,0-180,0)
Drugs	Levatiracetam	28	58,3
	Valproic acid	11	22,9
	Carbamazepine	4	8,3
	Lamotrigine	5	10,4
Monotherapy duration (months), Median (IQR)		36,0	(12,0-42,0)
Last seizure (month), Median (IQR)		12,0	(1,0-33,0)

Among the types of epilepsy, complex partial seizure and myoclonic seizure type patients were observed to be of normal weight, while GTC and focal seizure type patients were observed to be overweight. However, there was no significant difference in terms of epilepsy types, BMI (p =0.756) and gender (p =0.931) (Table 2).

Table 2. *Comparison of BMI value according to epilepsy types.*

Seizure type	**BMI**	**Female**	**Male**
	Median (IQR)	n (%)	n (%)
GTC	25,0 (22,7-27,7)	20 (80,0)	18 (78,3)
Focal motor	25,3 (24,6-27,2)	2 (8,0)	3 (13,0)
Myoclonic seizure	23,5 (21,7-27,8)	2 (8,0)	1 (4,3)
Complex partial	22,9 (21,6-24,2)	1 (4,0)	1 (4,3)
p	0,756*	0,931**	

**Kruskal Wallis analysis was applied.*

Levatiracetam was used in 60.5% of those with GTC-type seizures, VPA was used in 26.3%, carbamazepine was used in 2.6% and lamotrigine was used in 10.5%. Levatiracetam was used in 80% of those with focal motor-type seizures and carbamazepine was used in 20%. Levatiracetam was used in 33.3% of those with myoclonic seizure type, VPA was used in 33.3%, and lamotrigine was used in 33.3%. Carbamazepine was used in all patients with complex partial-type seizures. In addition, while the average BMI of the group using levatiracetam was overweight, patients in the other AED group were of normal weight according to BMI. There was no significant difference between drug types in terms of BMI (p =0.924) and gender (p =0.236) (Table 3).

Table 3. *Comparison of BMI value according to drug types.*

AED Groups	**BMI**	**Female**	**Male**
	Median (IQR)	n (%)	n (%)
Levatiracetam	25,5 (22,0-27,6)	16 (64,0)	12 (52,2)
VPA	24,2 (23,2-27,8)	3 (12,0)	8 (34,8)
Carbamazepine	24,4 (22,9-26,0)	2 (8,0)	2 (8,7)
Lamotrigine	23,5 (22,9-27,7)	4 (16,0)	1 (4,3)
p	0,924*	0,236**	

**Kruskal Wallis analysis, **Chisquare analysis was applied.*

DISCUSSION

Epilepsy, which can be seen at any age, has increasingly become a social problem in recent years. It is noteworthy that current research focuses on the causes and triggering factors of epileptic seizures (9). Even the fact that we determined the effect of BMI on AEDs in epilepsy patients distinguishes us from many studies in the literature. The epileptic seizure seen in most of the cases in this study was GTC, and when we evaluated according to BMI scoring, most of the patients were in the overweight class. Many studies show that epilepsy patients have a higher risk of developing overweight and obesity and have higher BMI values compared to the normal population (4, 10). In the Brazilian example, which is a cross-sectional study, the presence of abdominal obesity was detected in patients with epilepsy (10). Arya et al.'s (11) study showed that children with childhood absence epilepsy were overweight despite being fed a ketogenic diet. In our study, the presence of obesity did not differ for any age group. In addition among our cases, the most recent patient diagnosed with epilepsy was 3 years old, and the average age was recorded as 8.5 years. In terms of gender dist-

ribution, obesity was observed at a rate of 12% in women and 34% in men.

Obesity not only affects patients' physical condition and quality of life but also affects AED compliance and seizure control in patients. Metabolic disorders such as VPA-related insulin resistance, leptin deficiency, and endocrine dysfunction, especially lack of exercise, are also factors that can be addressed (12). Additionally, some neuroimaging studies have shown that excess weight is accompanied by focal structural changes in many regions of the brain (13, 14). There are studies reporting that AEDs VPA and carbamazepine cause metabolic disorders and an increase in serum lipids (15, 16). This situation causes unexpected weight gain. For example, VPA, which was also included in our study, is known for its highest rate of causing obesity among all AEDs (17). First of all, in our study, all our patients were on monotherapy according to AED intake. It was observed that there was no effective correlation between the patients' BMI status and the types of epilepsy and AEDs used. This result we obtained distinguishes our study from many studies. In our study, it was observed that complex partial seizure and myoclonic seizure type patients were of normal weight, while GTC and focal seizure type patients were overweight. However, no significant difference was observed between AED types and BMI ($p = 0.924$). In this respect, it will be important to consider the BMI index when choosing medication for patients in terms of both the pattern and control of the patient's seizures. In the study by Jaromir et al. (18), it was found that obesity was more common in patients treated with multiple therapies than in those treated with monotherapy. This study example supports the data of our study.

When we conducted a detailed literature search, we found that studies investigating the mechanism between obesity or BMI and epileptic seizures were mostly experimental animal studies (19). However, we noticed that the number of studies using humans as observational subjects is limited (20). Despite all the research, the effects of BMI on seizures in epilepsy patients and the contribution of the drugs used to the formation of obesity have not been determined with certainty. More evidence is needed through studies on volunteer patients. We think that our study will support providing this evidence. In the light of current data, it has been shown that there are positive developments between epilepsy and the ketogenic diet, which is a popular treatment for epileptic seizures, along with maintaining BMI (5). Epilepsy patients usually cannot know when they had a seizure and how long it lasted (21). However, they can tell us when they last had a seizure. This information can provide clinicians with information about the effectiveness of AED treatment. When we observed the patients in our study group, we found that they had a seizure at the earliest 1 month ago and at the latest 33 months ago. However, we could not find any relationship between the short or long duration of these periods and the AEDs they used.

There are some limitations in our study. The first and most important of these is that the patient sample was from a single center and the number of patients was small. In addition, the low variety of seizure types in the patients and the fact that it did not include all types of epilepsy can be considered as other limitations.

Conclusion

Appropriate and careful selection of AEDs should be implemented without abandoning therapeutic activities, supported by lifestyle counseling for exercise and diet, to prevent weight gain and potentially refractory epilepsy. It is not clear whether obesity triggers epileptic seizures or whether epilepsy increases obesity. Given that BMI influences seizure types, many more studies will be needed to clarify the interactions between BMI and all aspects of epilepsy.

Ethical Statement

Ethical approval was received from Malatya Turgut Özal University Non-Interventional Clinical Research Ethics Committee dated 22.04.2024 and numbered 42.

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