ASSESSMENT OF THE KNOWLEDGE ABOUT EPILEPSY AMONG EPILEPTIC PATIENTS, NONEPILEPTIC PATIENTS AND COMMUNITY PHARMACISTS AND THE PROVISION OF EDUCATION ON EPILEPSY

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To my precious mother and father...

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ABSTRACT

Macit C. Assessment of the Knowledge about Epilepsy among Epileptic Patients, Nonepileptic Patients and Community Pharmacists and The Provision of Education on Epilepsy. Yeditepe University Institute of Health Sciences Clinical Pharmacy Master Thesis. Istanbul, 2010.

Aim: Epilepsy is a chronic condition characterized by recurrent unprovoked epileptic seizures. Epilepsy has the greatest incidence in young children and the elderly. In treatment, a variety of antiepileptic drugs is used according to the seizure type. Epileptics meet lots of difficulties like misunderstanding, exclusion and limitation of social life due to having insufficient information about epilepsy. The aim of this study is to determine epilepsy knowledge of the epileptic patients', community pharmacists' and other patients' who come to these pharmacies and to assess effectiveness of clinical pharmacist.

Material and Method: This study was performed away thirteen community pharmacies in Istanbul Atasehir. To this study, epileptic patients and nonepileptic patients who come to these pharmacies participated, besides community pharmacists. The data of study was collected via questionnaire that was performed between 1 January - 1 July 2010 on community pharmacies. The questionnaire was carried out on two hundred and sixty (260) people but only two hundred nineteen (219) of them were accepted. Forty-seven (47) of the participants were epileptic patients and the remaining one hundred and seventy-two (172) were nonepileptic people. The questionnaire includes a total of twenty-three (23) questions. The questions asked in the survey are related to social life, nutrition, sleep patterns, drugs that are used and fertility of the epileptic patients. Answers of the many questions contain three choices in the form of "Yes, No, I have no information."

Results and Conclusion: Results of questionnaires were recorded as excel file and assessed via SPSS programme version 18. According to the results, community pharmacists, other (nonepileptic) patients and epileptic patients do not have enough knowledge about epilepsy. However, compared with other patients, epileptics have more knowledge, especially about their social problems so that they must live with the illness. Additionally, it is observed that female participants are more knowledgeable about personal issues. In conclusion; it was revealed that epileptic patients and community pharmacists who possess an important mission in providing health counselling to the public, must be educated about epilepsy disease.

Key Words: Epilepsy, Epileptic Patients, Community Pharmacies, Atasehir, Community Pharmacist, Seizure (Crisis).

ÖZET

Macit C. Epileptik Hastaların, Epileptik Olmayan Hastaların ve Eczane Eczacılarının Epilepsi Hakındaki Bilgilerinin Değerlendirilmesi ve Epilepsi ile ilgili Eğitimin Sağlanması. Yeditepe Üniversitesi Sağlık Bilimleri Enstitüsü Klinik Eczacılık Mastır Tezi. İstanbul, 2010.

Amaç: Epilepsi, sara nöbetlerin tekrarlaması sonucu oluşan kronik bir durumdur. En sık olarak küçük çocuklar ve yaşlılarda görülmektedir. Tedavisinde, nöbetin tipine göre çeşitli antiepileptik ilaçlar kullanılır. Epilepsi hastaları, insanların epilepsi hastalığı hakkında yetersiz bilgiye sahip olmasından ötürü, yanlış anlaşılma, dışlanmışlık ve kendilerinin sosyal yaşamlarının kısıtlanması gibi bir sürü zorlukla karşılaşırlar. Bu çalışmanın amacı; epileptik hastaların, eczane eczacılarının ve eczaneye gelen diğer hastaların epilepsi bilgi düzeylerini tespit etmek ve klinik eczacının etkinliğini değerlendirmektir.

Materyal ve Metot: Bu çalışma, İstanbul'un Ataşehir ilçesinde yer alan onüç serbest eczanede yapıldı. Çalışmaya, eczane eczacılarının yanı sıra bu eczanelere gelen epileptik hastalar ve epileptik olmayan hastalar da katıldı. Bu çalışmada yer alan veriler, 1 Ocak – 1 Temmuz 2010 tarihleri arasında serbest eczanelerde yapılan anketler sonucu toplandı. Anket toplam ikiyüzaltmış (260) kişiye uygulanmıştır fakat yanlızca ikiyüzondokuz (219) tanesi geçerli kabul edilmiştir. Bu katılımcıların kırkyedisi (47) epileptik hasta ve geri kalan yüzyetmişikisi (172) ise epileptik olmayan kişilerdir. Anket toplam yirmiüç (23) soru içermektedir. Ankette yer alan sorular epileptik hastaların sosyal hayatı, beslenmesi, uyku düzeni, kullandığı ilaçlar, epilepsi hastalarında doğurganlık ile alakalı sorulardır. Soruların çoğu "evet, hayır, bilgim yok'' formunda üç cevap seçeneği içermektedir.

Bulgular ve Sonuç: Anket verileri excel dosyası olarak kaydedildi ve SPSS programının 18. versiyonu kullanılarak değerlendirildi. Anket sonuçlarına göre, epilepsi hastalığı hakkında eczacıların, diğer insanların, ve epilepsi hastalarının yeterince bilgiye sahip olmadığı sonucu saptanmıştır. Fakat, diğer hastalarla karşılaştırıldığında epileptiklerin, hastalıkla yaşamak zorunda olduğu için özellikle sosyal sıkıntıları hakkında daha çok bilgili olduğu gözlemlenmiştir. Ayrıca, bayan katılımcıların kendilerini ilgilendiren sorularda daha bilgili oldukları gözlemlendi. Sonuç olarak, epilepsi hastalarının ve halka birinci derecede sağlık danışmanlığı yapma görevini elinde bulunduran eczacıların epilepsi hastalığı hakkında eğitilmesi gerektiği ortaya çıkmıştır.

Anahtar Kelimeler: Epilepsi, Epileptik Hastalar, Serbest Eczaneler, Ataşehir, Eczane Eczacısı, Nöbet (Kriz).

CONTENTS

SYMBOLS & ABBREVIATIONS

χ^2	Chi-square
AAN	American Academy of Neurology
AED	Antiepileptic Drug
AFP	Alfa-feto Protein
ASD	Atrial Septal Defect
BBB	Blood Brain Barrier
BC	Before Christ
Ca	Calcium
CBZ	Carbamazepine
CBZ-E	Carbamazepine-10, 11-epoxide
CHPS	Congenital Hypertrophic Pyloric Stenosis
CNS	Central Nervous System
CT	Computed Tomography
CVS	Cardiovascular System
DXA	Dual-energy X-ray Absorptiometry
EEG	Electroencephalogram
EPC	Epilepsia Partialis Continua
ETS	Ethosuximide
FBM	Felbamate
FDA	Food and Drug Administration
Fmri	functional Magnetic Resonance Imaging
FTA-ABS	Fluorescent Treponemal Antibody Absorbed
GABA	Gamma Aminobutyric Acid
$GABA_A$	Gamma Amino butyric Acid A subtype
GBP	Gabapentin
GIT	Gastrointestinal Tract
GUT	Gastrourinary Tract
H-OXC	10-Hydroxy-oxcarbazepine
HRT	Hormonal Replacement Therapy
ICEES	International Classification of the Epilepsies and Epileptic Syndromes

ICES	International Classification of Epileptic Seizures
ILAE	International League Against Epilepsy
IM	Intramuscular
IV	Intravenous
Kg	Kilogram
L	Liter
LEV	Levetiracetam
LTG	Lamotrigine
mcg	Microgram
MEG	Magnetoencephalogram
mg	Milligram
Ml	MilliLiter
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy
Na	Sodium
NCCP	Not Commonly Co prescribed
NE	None Expected
NICE	National Institute for Clinical Excellence
NIH	National Health Institute
NTD	Neural Tube Defect
OXC	Oxcarbazepine
PB	Phenobarbital
PC	Personal Computer
PDA	Patent Ductus Arteriosus
PET	Positron Emission Tomography
PHT	Phenytoin
PRM	Primidone
QOLIE-89	Quality of Life in Epilepsy-89
SIGN	Scottish Intercollegiate Guidelines Network
SMA	Supplementary Motor Area
SPECT	Single Photon Emission Computed Tomography
SPSS	Statistical Package for the Social Sciences
SV2A	Synaptic Vesicle 2A protein

TAFHCO	Turkish Armed Forces Health Capability Ordinance
TCA	Tricyclic Antidepressant
TGB	Tiagabin
TOF	Tetrology of Fallot
TPM	Topiramate
UK	United Kingdom
USA	United States of America
USG	Ultrasonography
VGB	Vigabatrin
VNS	Vagus Nerve Stimulation
VPA	Valproic Acid/Valproate
VSD	Ventricular Septal Defect
WHO	World Health Organization
WPSI	Washington Psychosocial Seizure Inventory
ZNS	Zonisamide

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1. INTRODUCTION

For hundred of years, humans have thought some disorders were associated with supernatural powers. This association has been made also for epilepsy and it has been explained as “Sacred Disease”. Thus, in the treatment of diseases, methods like magic, vow, offer, fortune and sacrifice have been used. However, according to the historical data obtained, humans in those ages have thought that mystic approaches were not sufficient and they represented realistic approaches. The use of plant derived and animal derived products by humans in order to treat any illness had been the evidence of the realistic approaches.

Within time, parallel to the development of positive medicine, treatment methods have been improved too. On the other hand, despite every improvement in the treatment methods, especially in central nervous system disorders like epilepsy and psychiatric illnesses, because of the insufficiency of medicine, mystic approaches have continued to be observed.

The word epilepsy, used today, was derived from Greek work “επιλαμβανειν” (epilambanein) that means attack. During history, in order to describe epileptic seizures, variety of words has been used by the several populations in different times. For instance, epilepsy was defined as “Bennu” in Babylon inscriptions more than 3000 years ago and according to the laws of Hammurabi if a person who had been bought as a slave was understood to be an epileptic, the epileptic person was returned to the supplier [1].

As mentioned above, epilepsy was defined with plenty of words in different populations. In Sumerians, “Antasubba” word was used, while ancient Hindu mentioned “Atreya” for epileptic seizures with convulsions and “Apasmara” for epileptic seizures without convulsions in Ayurveda which was the most important traditional medicine book of Indians. When looking to the Papyrus, we can show that

ancient Egyptians have also been aware about epilepsy and they supposed epilepsy was a disorder sent by a god. In traditional Chinese medicine, epilepsy has been named as “Dian” or “Xian” according to its type, and herbal products and acupuncture have been used in the treatment of epilepsy.

In Helens, the latin word “Lunatic” has been used to mention about epilepsy. Moreover, the “Sacred Disease” -the book about epilepsy- which has been written by Hippocrates, was the most valuable source of that age. In this book, written in 400 B.C., the early physician Hippocrates suggested that epilepsy was a disorder of the brain and we now know that he was right [1, 2]. Today, “Sar’a” word has still been used for explaining epilepsy and it has come from Arabic and it means to “fall down”. Additionally, epilepsy is explained as “falling sickness” in English.

Few experiences match the drama of a convulsive seizure. A person having a seizure may cry out, fall to the floor unconscious, twitch or move uncontrollably, drool, or even lose bladder control. Within minutes, the attack is over, and the person regains consciousness but is exhausted and dazed. This is the image most people have when they hear the word epilepsy. However, this type of seizure is only one kind of epilepsy. There are many kinds, each with a different set of symptoms.

Epilepsy was one of the first brain disorders to be described. The strange behaviour caused by some seizures has contributed through the ages to many superstitions and prejudices. People once thought that those with epilepsy were being visited by demons or gods.

Epilepsy is the tendency to have seizures on a chronic, recurrent basis. This implies that there is a permanent change in cortical function which renders neurons more likely to participate in a seizure discharge. This process is referred to as epileptogenesis, and the exact way in which it occurs is not known. A process thought to be similar to epileptogenesis in humans occurs after prolonged, intermittent electrical stimulation of animal brains and is known as kindling.

Epilepsy may develop days, months, or many years after an insult to the cortex. It may be that an originally small group of abnormal neurons causes adjacent or connected neurons to gradually become bombarded over time with frequent, repeated electrical impulses. When the network of abnormal neurons becomes sufficiently large, it becomes capable of sustaining an excessive firing pattern for at least several seconds: a seizure. This hyperexcitable network of neurons is then the seizure focus.

If the change to cortical electrical characteristics is permanent, why don't seizures occur all the time? This is probably because the occurrence of an individual seizure depends upon the interplay of environmental and internal brain factors which from time to time result in loss of normal mechanisms that contain and control abnormal neuronal firing. Some common factors are sleep loss and fatigue, but it is impossible to determine what sets off a particular seizure in most patients.

In some patients, epilepsy worsens over time, with the seizures becoming more frequent as patients grow older. This does not occur in most patients with epilepsy. In those so affected, it is possible that the seizures themselves may cause some damage to the cortex; loss of neurons, especially inhibitory neurons, has been demonstrated in tissue from seizure foci. Other changes occur in brain areas affected by seizures: reorganization of connections between groups of neurons may strengthen excitatory connections and weaken inhibitory connections, making the occurrence of future seizures more likely. For this reason, an argument can be made for controlling epileptic seizures with medications as early as possible. This may reduce the possibility of permanent changes in brain function [3].

2. THEORETICAL PART

2.1. EPIDEMIOLOGY

According to World Health Organization (WHO), approximately 450 million people are affected with mental and neurological disorders worldwide and around 50 million of this population have epilepsy [4].

In most countries worldwide, the estimated proportion of the general population with active epilepsy (i.e. continuing seizures or the need for treatment) is between 4 to 10 per 1,000 people. For instance, approximately 5.5 million people in India, 300,000 people in United Kingdom (UK) and 2 million people in the United States of America (USA) have epilepsy [2, 5, 6, 7].

In most developed countries, the incidence of epilepsy cases is between 40 to 70 per 100,000 people in the general population. In developing countries, this figure is often close to twice- from 100 to 190 per 100,000 people- as high due to the higher risk of experiencing conditions that can lead to permanent brain damage. Close to 90% of epilepsy cases worldwide are found in developing regions [5, 8] (see Figure 1).

Author, year of study	Country	Rate (per 100,000)	Remarks
Pond, 1960	UK	70	All seizures
Krohn, 1961	Norway	11	All seizures
Sato, 1964	Japan	17	All seizures
Zielinski, 1974	Poland	26	Excluding SS, FS
Juul-Jensen, 1983	Denmark	39 (men)	
		28 (women)	Excluding FS
Granieri, 1983	Italy	31	Excluding SS, FS, PS
Placencia, 1992	Ecuador	190	Excluding FS
Hauser, 1993	USA	44	Excluding SS, FS, PS
Mani, 1997	India	49,3	Excluding HWE

FS: Febrile Seizures; SS: Single Seizure; PS: Provoked Seizure;
HWE: Hot Water Epilepsy

Figure 1. Incidence of Epilepsy

Unfortunately, there is no research into epilepsy incidence in Turkey [9].

Prevalence is an estimate of number of people with epilepsy in a given population at a specific time or during a defined time interval. Prevalence represents a complex interaction between several factors such as incidence, death or remission of illness. The prevalence rates from some of the studies from different parts of the world are given in Figure 2 [5].

Author, year of study	**Country**	**Prevalence (per 1000)**	**Remarks**
Pond, 1960	UK	6,2	Active epilepsy
Krohn, 1961	Norway	2,3	Active epilepsy
Bird, 1962	South Africa	3,7	
Sato, 1964	Japan	1,5	Active epilepsy
Rose, 1973	USA	18,6	Lifetime prevalence, children only
Juul-Jensen, 1983	Denmark	12,7	Lifetime prevalence
Granieri, 1983	Italy	6,2	Active epilepsy
Li, 1985	China	4,4	Age adjusted
Sridharan, 1986	Libya	1,9	Age adjusted, age> 15 years only
Haerer, 1986	USA	6,7	Active epilepsy
Haerer, 1986	USA	10,4	Lifetime prevalence
Osuntokun, 1987	Nigeria	5,3	Active epilepsy
Hauser, 1991	USA	6,8	Active epilepsy
Hauser, 1991	USA	8,2	Lifetime
Aziz, 1997	Pakistan	9,98	Crude rates
Aziz, 1997	Turkey	7,0	Crude rates
Sridharan, 1999	India	5,59	Meta-analysis active epilepsy
Radhakrishnan, 2000	India	4,7	Age adjusted, active epilepsy

Figure 2. Prevalence of epilepsy- data from some countries

Some prevalence studies performed at the different regions of Turkey are available. In these studies, some methodological and terminological differences are observed and because of these, comparison of these studies is very difficult.

Prevalence studies that were mostly performed with limited population were conducted in Istanbul, Sivas, Ankara, Izmir and Bursa [10, 11, 12, 13, 14, 15, 16, 17]. Data obtained from these studies are given below in Table 1 [9].

Table 1. Epilepsy prevalence studies performed in Turkey and their results (prevalence values; according to 1000 people)

Region	Population (#)	Population Area	Age Range	Researchers & Year	Prevalence (Act. Epilepsy)
Ankara	11497	Urban-Rural	Every age	Aziz H, et al. 1997	7
Sivas	5294	Urban	Every age	Topalkara K, et al. 1999	6,1
Istanbul	4803	Rural	Except Newborn	Karaagac N, et al. 1999	10,2
Istanbul	2187	Rural	Every age	Onal E, et al. 2002	5,9
Izmir	4216	Schools	7-17	Aydin A, et al. 2002	5,6
Turkey	46813	Urban-Rural	0-16	Serdaroglu A, et al. 2004	8
Sivas	14253	Rural	Every age	Sahin A, et al. 2004	8,8
Bursa	2116	Urban	Except Newborn	Calisir N, et al. 2006	8,5

2.2. ETIOLOGY

Epilepsy is a disorder with many possible causes. Anything that disturbs the normal neuronal activity can lead to seizures. Epilepsy may develop because of an abnormality in brain wiring, an imbalance of nerve signalling chemicals called neurotransmitters, or some combination of these factors. Researchers believe that some people with epilepsy have high levels of excitatory neurotransmitters that increase neuronal activity, while others have an abnormally low level of inhibitory neurotransmitters that decrease neuronal activity in the brain. Both conditions can cause increased neuronal activity and result in epilepsy.

One of the most studied neurotransmitter is GABA (gamma-amino butyric acid), which is an inhibitory neurotransmitter. Research on GABA has led to drugs that alter

the amount of this neurotransmitter in the brain or change how the brain responds to it. Researchers are studying excitatory neurotransmitters such as glutamate, too.

Research has shown that cell membrane that surrounds each neuron has a very important role in epilepsy. Cell membranes are crucial for neuron to generate electrical impulses. For this reason, researchers are studying details of the membrane structure, how molecules move in and out of the membranes. A defect in any of these processes may cause epilepsy [2].

Approximately 60 % of all epilepsies are idiopathic or cryptogenic [5]. The most common aetiology for epilepsy in all countries is cerebrovascular disease especially ischemic stroke among adults, while perinatal insults seem to be most common among children. Neoplasm, trauma and congenital disorders are other common causes [5, 18, 19] (Figure 3).

	Country				
	Iceland [a]	Sweden [b]	UK [c]	Estonia [d]	Range
Vascular	14	21	15	20	14-21
Ischemia		18		16	16-18
Haemorrhage		3		4	3-4
Trauma	0	2	3	16	2-16
Neoplasm	7	7	6	10	6-10
Infection	2	0	2	1	0-2
Degenerative	2	5		1	1-5
Congenital	5	7		4	4-7
Other	0	4	13	4	0-13
Remote or progressive symptomatic [e]	31	46	39	56	31-56
Unknown	69	54	61	44	44-69

a Olafsson , et al., (1996).
b Forsgren , et al., (1996) and Sidenvall , et al. (1993). Studies include single seizures.
c Sander , et al., (1990). Include single seizures and 15% with acute symptomatic seizures.
d Ŏun , et al., (2003b).
e Summary of all aetiologies mentioned above.

Figure 3. Estimated proportions (%) of presumed causes of epilepsy in population-based incidence studies.

2.2.1. Risk factors:

There are factors such as head injury and infection for which a clear and substantial risk for epilepsy has been established and a direct causal relationship can be assumed.

About 5 % of persons with head trauma, cerebrovascular disease and CNS (Central Nervous System) infections have acute symptomatic seizures of which the occurrence is associated with an additional increase in risk for epilepsy.

Individuals with cerebrovascular disease have a 20-fold increase in risk of developing epilepsy. Survivors of an infection of CNS have a 3-fold higher risk of epilepsy. The risk is 5-fold elevated for bacterial meningitis and 10-fold for viral encephalitis.

About 30 % of patients with brain tumours present with seizures as an initial symptom and epidemiological studies show that brain tumours account only few ratios in all epilepsy cases, even in elderly.

Some neurological diseases like Alzheimer's disease and Parkinson disease are thought to be related to epilepsy. Alzheimer's disease is associated with a 10-fold increase in risk for epilepsy. On the other hand, Parkinson disease is considered to be protective against seizures and may be associated with improvement in seizure control in people with epilepsy [20].

Additionally, alcohol consumption increases the risk of having epilepsy. For those who drink 300 g or more of alcohol daily, the risk is increased more than 20-fold. Moreover, factors such as cigarette smoking that affects acetylcholine in the brain that increases the neuronal firing, drug abuse, asthma, and hypertension have been found to have a higher risk for epilepsy. Epilepsy also can result from intolerance to wheat gluten (also known as celiac disease), or from a parasitic infection of the brain called neurocysticerosis.

With regard to family history, siblings of patients with epilepsy have 2, 5 times elevated risk for epilepsy and the risk may be somewhat higher in offspring. Furthermore, neurological handicaps at birth such as cerebral palsy and mental retardation are associated with an elevated risk for epilepsy [5].

2.2.2. Genetic factors:

Researches suggest that genetic abnormalities might be some of the most important factors contributing to epilepsy. Some types of epilepsy have been traced to an abnormality in a specific gene. Many other types of epilepsy tend to run in families. Some researchers estimate that more than 500 genes play a role in this illness.

Today, several kinds of epilepsy have been linked to defective genes for ion channels, the “gates” that control the flow of ions in and out of cells and regulate neuron signalling. Another gene, which is missing in people with progressive myoclonus epilepsy, codes for a protein cystatin B. This protein regulates enzymes that break down other proteins. Another gene, altered in LaFora’s disease has been linked to a gene that helps to break down of carbohydrates.

They also may influence the disorder in hidden and different ways. For example, one study showed that many people with epilepsy have an active but abnormal version of gene that increases the resistance to drugs. This may help to explain why anticonvulsant drugs are not useful in some epileptic people. In addition, genes control the individual’s seizures and seizures threshold.

In some cases, genes may contribute to development of epilepsy even in people with no family history of the disorder. These people may have a newly developed abnormality, or mutation, in an epilepsy-related gene [2].

2.2.3. Prenatal Injury and Developmental Problems:

The developing brain is susceptible to many kinds of injury. Maternal infections, poor nutrition, and oxygen deficiencies are just some of the conditions may lead to cerebral palsy, which often is associated with epilepsy, or they may cause epilepsy that is unrelated to any other disorders. With advanced brain imaging techniques, some cases of epilepsy that occur with no obvious cause may be associated with areas of dysplasia in the brain that develop before birth, have been revealed [2].

2.2.4. Poisoning:

Seizures can result from exposure to lead, carbon monoxide, and many other poisons. They also can result from exposure to street drugs and from overdoses of antidepressant and other medications. Sleep deprivation is a powerful trigger of seizures. Because of this, people with epilepsy should take care of their sleep schedule as much as possible [2].

2.3. CLASSIFICATION OF EPILEPSIES

The Commission on Classification and Terminology of International League Against Epilepsy (ILAE) created a comprehensive classification for epilepsies and epileptic syndromes approximately 30 years ago. Despite subsequent revisions, the classification remains too complicated to be of utility in clinical practice and epidemiological research [21].

First, in 1964, international epilepsy experts met and classification studies started. As a result of the long time work of the ILAE classification commission, in 1981 the Epileptic Seizures Clinical and Electroencephalographic Classification (Figure 4) and in 1989, the Epilepsies and Epileptic Syndromes Classification were prepared and they have been still used and accepted by the whole world and have provided common

terminology in the explanation of seizures and epileptic syndromes [22, 23]. With time, imaging techniques and developments in molecular biology and genetic area provided new perspectives to our information and so these classifications became inadequate [24].

1. Partial (focal, partial) seizures
    1.1. Simple partial seizures (consciousness not impaired)
        1.1.1. With motor signs
        1.1.2. With somatosensory or special sensory symptoms
        1.1.3. With autonomic symptom or signs
        1.1.4. With psychic symptoms
    1.2. Complex partial seizures
        1.2.1. Simple partial onset followed by impairment of consciousness
        1.2.2. With impairment of consciousness at onset
    1.3. Partial seizures evolving to secondarily generalized seizures (tonic-clonic, tonic or clonic)
        1.3.1. Simple partial seizures evolving to generalized seizures
        1.3.2. Complex partial seizures evolving to generalized seizures
        1.3.3. Simple partial seizures evolving to complex partial, evolving to generalized seizures

2. Generalized seizures (convulsive or non-convulsive)
    2.1. Absence seizures
        2.1.1. Typical absence seizures
        2.1.2. Atypical absence seizures
    2.2. Myoclonic seizures
    2.3. Clonic seizures
    2.4. Tonic seizures
    2.5. Tonic-clonic seizures
    2.6. Atonic (astatic) seizures

3. Unclassified epileptic seizures

Figure 4. 1981 International Classification of Epileptic Seizures (ICES) simplified version [22].

On behalf of ILAE Classification Commission, Dr. Engel's final classification suggestion published in 2001, was opened to criticism via web page of ILAE (www.epilepsy.org/ctf) and according to the comments, commission declared that 1989 Epilepsies and Epileptic Syndromes Classification of ILAE was decided to use [25, 26] (see Figure 5).

1. Localisation-related epilepsies and syndromes
    1.1. Idiopathic (with age-related onset)
        Benign childhood epilepsy with centrotemporal spikes
        Childhood epilepsy with occipital paroxysms
        Primary reading epilepsy
    1.2. Symptomatic
        Chronic progressive epilepsia partialis continua of childhood
        Syndromes characterized by seizures with specific modes of precipitation
        Temporal, frontal, parietal and occipital lobe epilepsies
    1.3. Cryptogenic
        Temporal, frontal, parietal, and occipital lobe epilepsies

2. Generalized epilepsies and syndromes
    2.1. Idiopathic (with age-related onset)
        Benign myoclonic epilepsy in infancy
        Childhood absence epilepsy / juvenile absence epilepsy
        Juvenile myoclonic epilepsy (impulsive petit mal)
        Epilepsy with generalized tonic-clonic seizures on awakening
        Syndromes characterized by seizures with specific modes of precipitation
        Other idiopathic generalized epilepsies
    2.2. Cryptogenic or symptomatic (in order of age)
        West syndrome (infantile spasms)
        Lennox-Gas taut syndrome
        Epilepsy with myoclonic-astatic seizures
        Epilepsy with myoclonic absences
    2.3. Symptomatic
        2.3.1. Non-specific aetiology
            Early myoclonic encephalopathy
            Early infantile epileptic encephalopathy with suppression burst
            Other symptomatic generalized epilepsies
        2.3.2. Epilepsies due to specific neurological diseases

3. Epilepsies undetermined whether focal or generalized
    3.1. With both generalized and focal seizures
        Neonatal seizures
        Severe myoclonic epilepsy in infancy
        Epilepsy with continuous spike waves during slow-wave sleep
        Acquired epileptic aphasia (Landau-Kleffner syndrome)
        Other undetermined epilepsies
    3.2. Without unequivocal focal or generalized features

4. Special syndromes
    4.1. Situation-related epilepsies
        Febrile convulsions
        Isolated seizures or status epilepticus
        Seizures due to an acute toxic or metabolic event

Figure 5. The 1989 International Classification of the Epilepsies and Epileptic Syndromes (ICEES) [23].

A while later, in the 2006 report, this classification was updated by ILAE Classification core group [27] (Figure 6).

Then, commission decided to prepare a new clear and forthcoming classification. In trying to do this, they found that the word “classification” has been used to refer to at least three different although related concepts: A. The list of entities that are recognized as distinct forms of epilepsy; B. The concepts and structure underlying the organization and presentation of that list. C. The methods and process that determine which entities are recognized and those features by which those entities are organized.

As a result, of a large number of studies and the proceedings of the Montreale workshop (Capovilla et. al. 2009), the classification was revised and updated by ILAE Commission and the report was published on 28 July 2009 on the website of ILAE [28].

Self-limited epileptic seizures
Generalized onset
- Seizures with tonic and/or clonic manifestations
  - Tonic-clonic seizures
  - Clonic seizures
  - Tonic seizures
- Absences
  - Typical absences
  - Atypical absences
  - Myoclonic absences
- Myoclonic seizure types
  - Myoclonic seizures
  - Myoclonic astatic seizures
  - Eyelid myodonia
- Epileptic spasms
- Atonic seizures

Focal onset/partially
- Local
  - Neocortical
    - Without local spread
      - Focal clonic seizures
      - Focal myoclonic seizures
      - Inhibitory motor seizures
      - Focal sensory seizures with elementary symptoms
      - Aphasic seizures
    - With local spread
      - Jacksonian march seizures
      - Focal (asymmetrical) tonic seizures
      - Focal sensory seizures with experimental symptoms
  - Hippocampal and parahippocampal
    - With ipslateral propagation to
      - Neocortical areas (includes hemiclonic seizures)
      - Limbic areas (including gelastic seizures)
    - With contralateral spread to
      - Neocortical areas (hyperkinetic seizures)
      - Limbic areas [(dyscognitive seizures with or without automatisms (psychomotor)]
- Secondarily generalized
  - Tonic-clonic seizures
  - Absence seizures
  - Epileptic spasms (unverified)

Neonatal seizures

Status epilepticus
Epilepsia partialis continua (EPC)
- As occurs with Rasmussen's syndrome
- As occurs with focal lesions
- As a component of inborn errors of metabolism

Supplementary motor area (SMA) status epilepticus
Aura continua
Dyscognitive focal (psychomotor, complex partial) status epilepticus
- Mesial temporal
- Neocortical

Tonic-clonic status epilepticus
Absence status epilepticus
- Typical and atypical absence status epilepticus
- Myoclonic absence status epilepticus

Myoclonic status epilepticus
Tonic status epilepticus
Subtle status epilepticus

Figure 6. The International League Against Epilepsy (ILAE) classification of seizure type (2006 report of ILAE Classification core group) [29].

2.4. DIAGNOSIS

Doctors have developed a number of different tests to determine whether a person has epilepsy or not and what kind of seizures the person has. In some cases, people might have symptoms like a seizure but in fact are nonepileptic events caused by other disorders [2]. In order to understand if a person has epilepsy or not, a standard diagnostic evaluation of patients with recent onset of seizures is shown in Table 2 [30].

Table 2. Evaluation of a new seizure disorder in a stable patient.

History (including medications or drug exposure)
General physical examination
Complete neurological examination
Blood tests
Fasting blood glucose
Serum calcium
Serum FTA-ABS
Serum electrolytes
Complete blood count
Renal function studies
Hepatic function studies
EEG (positive in 20-59% of first EEGs; 59-92% with repeated EEGs)
Brain MRI (especially with abnormal examination, progressive disorder, or onset of seizures after 25 years of age)

EEG: Electroencephalogram
MRI: Magnetic Resonance Imaging
FTA-ABS: Fluorescent Treponemal Antibody Absorbed

2.4.1. Medical History

Taking a detailed medical history, including symptoms and duration of the seizures, is still one of the best ways available to determine if an individual has an epilepsy or not and if he or she is an epileptic, what kind of seizures he/she has. The physicians ask about the seizures and any illnesses or conditions that person may have had in the past.

Usually, patients do not remember what happened at that time due to the seizure and loss of consciousness. Thus, caregiver's info and observations while seizure was happening have a key role for the evaluation [2].

2.4.2. EEG Monitoring

The diagnosis of epilepsy is based on clinical recognition of the seizure types. In order to diagnose epilepsy, the EEG can be a helpful confirmatory test in distinguishing seizures from other causes [30]. The first application of EEG was performed by Hans Berger in 1929 through use of electrodes that were put on hairy skin via recording of human brain electrical activity and today, EEG still has been conserved its validity in the examination of cerebral bioelectrical activity [31]. This is the most common diagnostic test for epilepsy. People with epilepsy frequently have changes in their normal pattern of brain waves, even when they are not experiencing a seizure. While EEG can be very useful in order to diagnose epilepsy, it is not foolproof because some patients can show normal brain wave patterns even after they have experienced a seizure.

Whenever possible, an EEG should be performed within 24 hours of a patient's first seizure. Due to the differences in brain activity during sleep and daytime, it is preferred to perform while the patient is sleeping (see Figure 7 and 8) [32, 33].

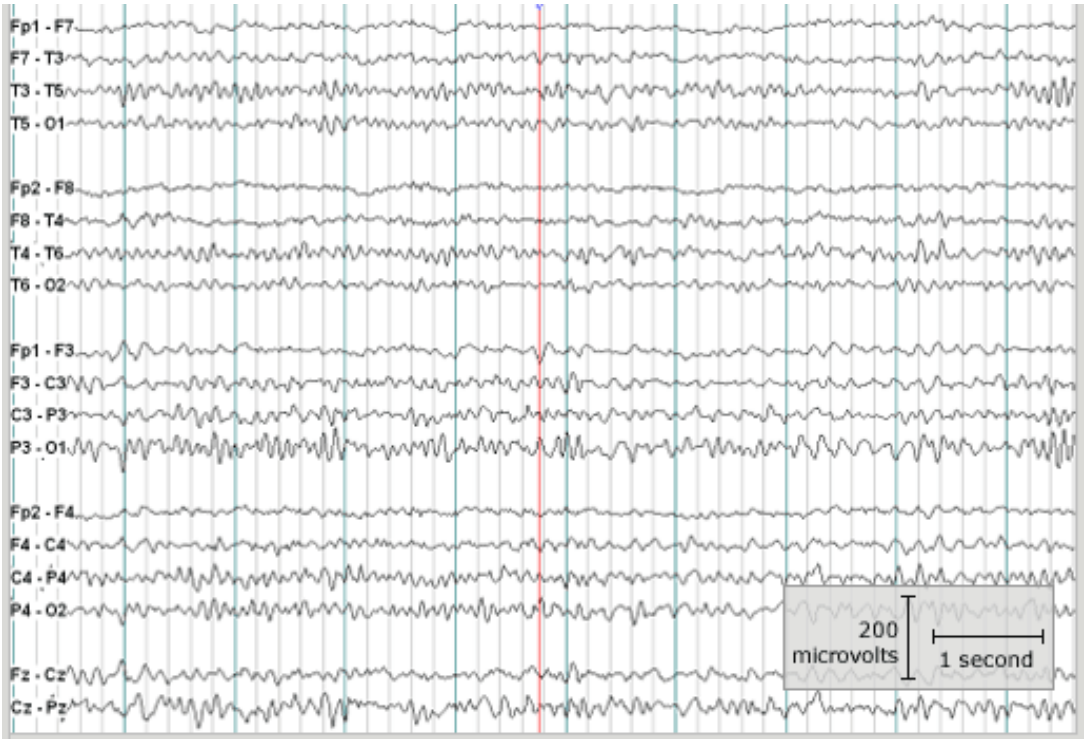


Figure 7. EEG displays the activity of an awake state showing normal amplitudes, frequencies, waveforms; similar features between hemispheres; and no epileptiform activity (Normal EEG pattern).

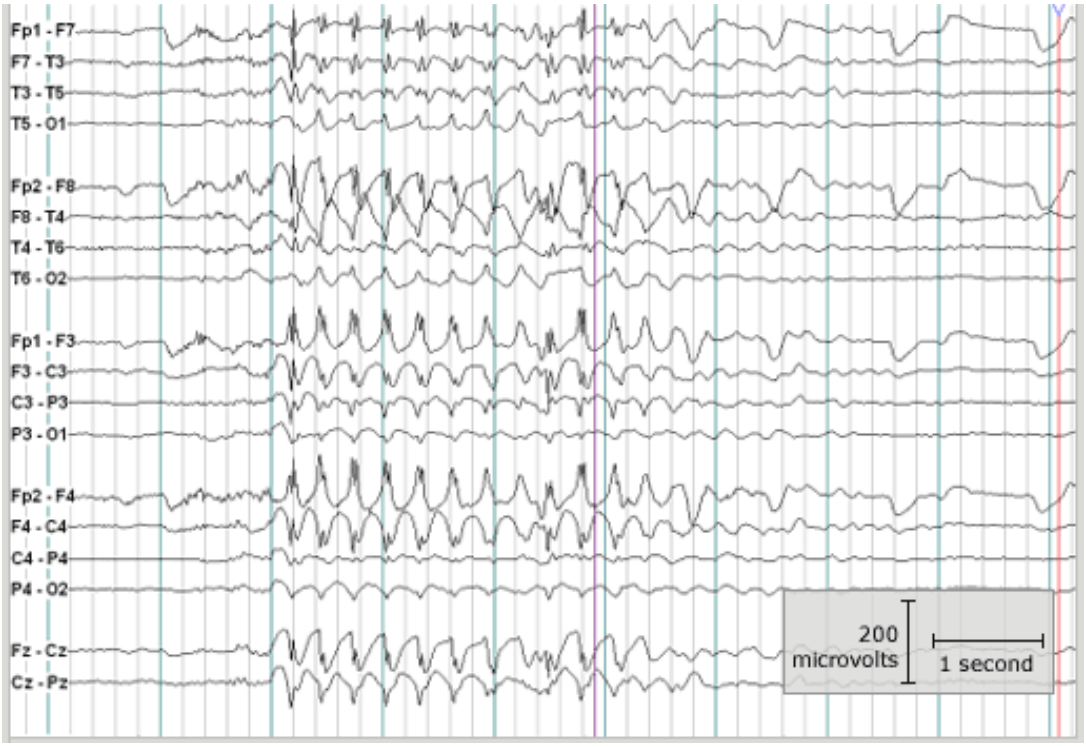


Figure 8. EEG displays an abnormal discharge called a generalized spike and wave. Typical EEG pattern for absence seizures.

Consequently, video monitoring is also used in combination with EEG to explain the nature of patient's seizures [2].

2.4.3. Brain Scans

One of the most important ways of diagnosing epilepsy is radiological imaging. The main role of radiological imaging in epilepsy is to determine the any possible structural abnormality or pathology and to help patient's treatment protocol. Radiological data play important role especially in patients who are considered to have a surgery, in determination of prognosis and follow-up of illness. During past 10-15 years, imaging methods have been developed importantly [34].

The most commonly used brain scans include CT (Computed Tomography), PET (Positron Emission Tomography), and MRI (Magnetic Resonance Imaging). CT and MRI scans reveal the structure of the brain, which can be beneficial for identifying brain tumours, cysts, and adapted kind of MRI called functional MRI (fMRI) can be used to monitor the brain's activity and detect abnormalities in how it works. SPECT (Single Photon Emission Computed Tomography) is a relatively new kind of brain scan that is sometimes used to locate seizure foci in the brain.

In some cases, physicians may use an experimental type of brain scan called MEG (Magnetoencephalogram). MEG detects the magnetic signals generated by the neurons to allow doctors to monitor brain activity at different points in the brain over time, showing diverse brain functions. While MEG is similar in concept to EEG, it does not need electrodes and it can detect signals from deeper in the brain than an EEG does.

Doctors also are experimenting with brain scans called Magnetic Resonance Spectroscopy (MRS) that can detect abnormalities in the brain's biochemical processes, and with near-infrared spectroscopy, a technique that can detect oxygen levels in brain tissue.

2.4.4. Blood tests

Physicians sometimes want to show laboratory studies from a serum sample while diagnosing epilepsy in order to determine the origin of illness whether epilepsy has a metabolic or genetic sources. They also are used to identify problems such as infections, poisoning, diabetes and anaemia which may trigger the seizures.

Some researchers recommend routine determination of some serum parameters, such as glucose, calcium, magnesium and urea in the evaluation of seizure aetiology and to diagnose if there is epilepsy [35]. However, according to some studies, blood tests are not a useful diagnostic key in order to determine whether patient's seizure raised from

epilepsy or not. In addition to this, some authors believe that these tests do not contribute to the seizure therapy and are costly and time-consuming [36].

Consequently, Akhavan Karbasi S. and his colleagues showed in their study that routine serum chemistry laboratory work-ups in paediatric patients presenting with seizures are unnecessary unless careful history and/or physical examination suggest otherwise [37].

2.4.5. Neurological, developmental and behavioural tests

In order to diagnose epilepsy, physicians can perform tests to their patients to consider their motor ability, intellectual capacity and behaviour. These tests also give clues and idea to doctor about type of epilepsy the patient has.

2.5. TREATMENT

Treatment approaches for epilepsy that have been known from ancient period of human kind, has been reached from first age to now. The aim of epilepsy treatment for any patients is eradication of seizures without any adverse effects or with minimal side effects.

An efficient and suitable treatment provides patient to continue his/her normal lifestyle. For children and teens, the treatment enables to perform well in school, to communicate effectively with family and friends. Additionally, for young and adult people, treatment provides to drive, to hold a reasonable job and to have good relationship with other people in community.

Consequently, in order to treat seizures and epilepsy some approaches are found such as nonpharmacological like ketogenic diet and vagus nerve stimulation (VNS), pharmacological treatment like antiepileptic drugs and surgery.

2.5.1. Nonpharmacological Treatment of Epilepsy

2.5.1.1. Ketogenic Diet

The ketogenic diet is a valuable therapeutic approach for epilepsy, especially in children. Although the mechanism by which the diet protects against seizures is unknown, the ketone body acetone has anticonvulsant activity and could play a role in the seizure control.

Since 1920s, ketogenic diet has been used successfully to treat patients with intractable epilepsy. The diet is high in fat and low in carbohydrate and protein, providing sufficient protein for growth but not enough amounts of carbohydrates for all the metabolic needs of the body [38]. In this case, energy is derived from fatty acid oxidation in mitochondria.

All we know that, glucose is most significant energy source of human brain and also know that fatty acids can not be used because they do not across the blood brain barrier (BBB). On the other hand, during the ketogenic diet, ketone bodies partly replace with glucose as fuel for the brain. Basically, the ketone bodies are converted to acetyl-CoA and then enter the brain in order to produce energy [39].

Although the ketogenic diet has been applied clinically in the treatment of epilepsy for more than 85 years and provided disease modifying actions in epilepsy, the actual mechanism of diet how it provides seizure protection is still poorly identified [40, 41].

2.5.1.2. Vagus Nerve Stimulation (VNS)

In 1938, Bailey and Bremmer performed vagal nerve electric stimulation in cats. With these studies, decreasing of the interictal epileptiform decharges via VNS was shown. Human studies have followed these animal studies, then [42].

VNS was approved by US Food and Drug Administration (FDA) as an adjunctive therapy in the treatment of medically intractable partial epilepsy in people aged 12 years old and older [43, 44] who are no chance for resective epilepsy surgery [45, 46]. In the process of time, VNS usage was shown to be useful in adults and in children under 12 years of age and in patients with generalized epilepsy [47, 48, 49].

The mechanism of action of VNS is still unclear, however, it is well-known that VNS inhibits neuronal activity of hypersynchronisation in partial and generalized seizures. Additionally, VNS increases the excretion of inhibitory neurotransmitter GABA in cerebro spinal fluid (CSF) [50].

VNS is not generally related with the common central nervous system side effects like ataxia, insomnia, weight gain, dizziness or cognitive impairment [51]. Most common side effects of VNS are shown in Table 3 [52].

Table 3. Side Effects of Vagal Nerve Stimulation

Pachynsis (hoarseness of voice)
Local infection
Feeling of stimulus when stimulation terms
Coughing
Cynanche (throat ache)
Paresthesia in throat
Vocal cord paralysis

Finally, studies have shown that in one third of patients treated with VNS, frequency of seizures decreases more than 50 %, in other one third of patients decreases less than 50 %, and in last one third of cases VNS provides complete recovery [53].

2.5.2. Pharmacological Treatment of Epilepsy

The most common approach to treat epilepsy is antiepileptic drugs. However, waiting must have been required to the mid of the XIX century for the discovery of first effective chemical active ingredient; Potassium bromide. On 11 May 1857, Sir Charles Locock declared that beneficial results in seizure control had observed in 14 epilepsy patients except one. As a result, first effective antiepileptic drug was explained to whole world.

From that time to now, plenty of antiepileptic drugs –more than 20– have been developed, especially in recent 50 years. On the other hand, any of these drugs used are not ideal if they are considered as their side effects and treatment efficacy that we want [54].

However, there is a basic treatment algorithm which is accepted and applied by most of the doctors for management of seizure disorders and epilepsy (see Figure 9) [3, 55].

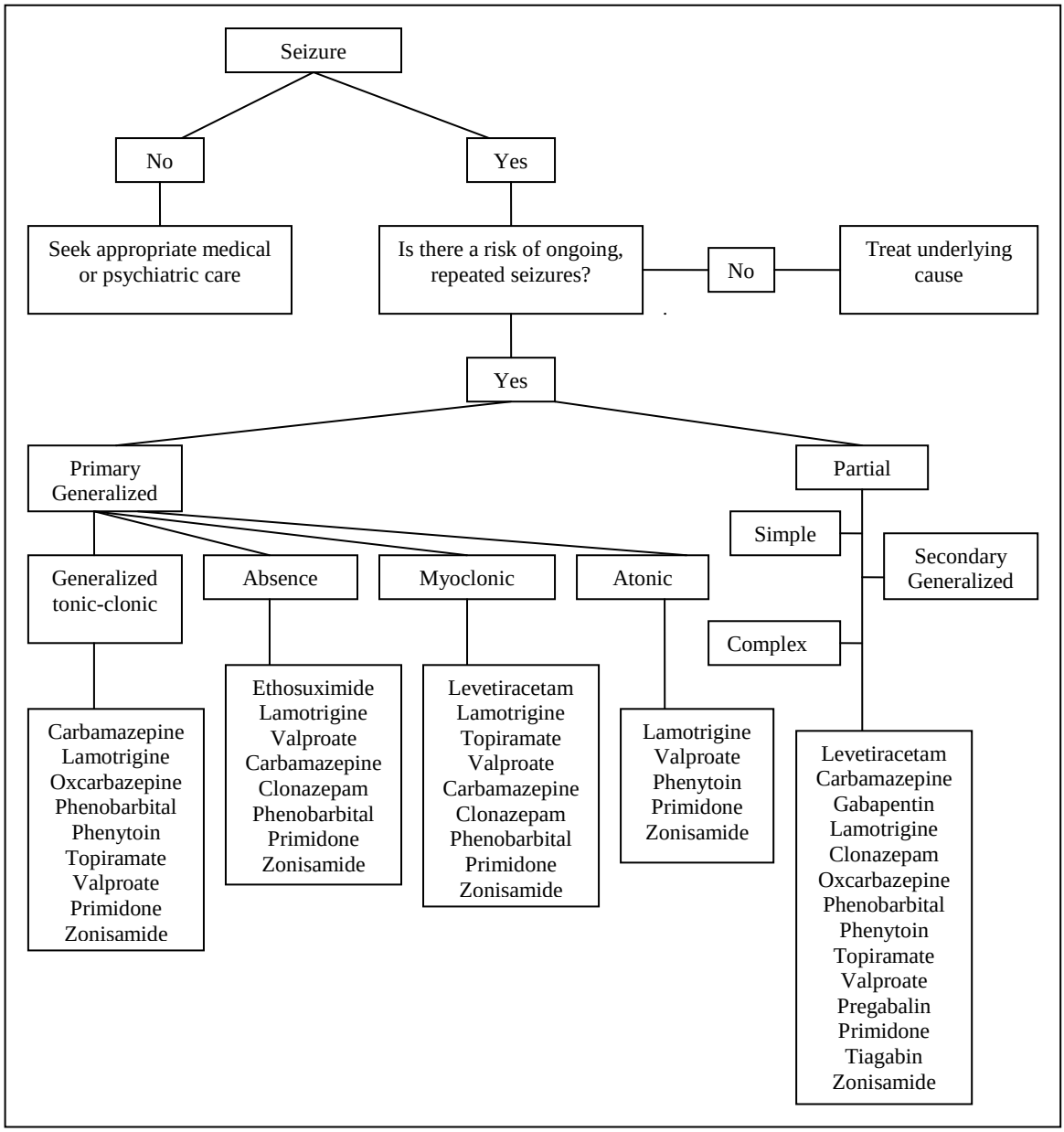


Figure 9. Treatment algorithm for management of seizure disorders and epilepsy.

Not all of the antiepileptic drugs are suggested in all guidelines, in the same way. Several consensus treatment guidelines from the Scottish Intercollegiate Guidelines Network (SIGN), the National Institute for Clinical Excellence in the United Kingdom (NICE), and the American Academy of Neurology (AAN) all use determination of seizure type as the basis for selection of pharmacotherapy.

In many cases, a recommendation is not made, because there are no published data on which to make an evidence-based decision. Therefore, a drug may not currently be suggested for only one seizure type. For instance; according to the AAN, in absence seizures, first-line treatment recommendation is Lamotrigine in especially children, but on the other hand, Ethosuximide, Lamotrigine and Vaproate in SIGN and NICE guidelines and also second-line treatment suggestion of NICE is Clobazam, Clonazepam and Topiramate. There are a lot of different treatment recommendations like these.

All these drugs are used as monotherapy or in combination as polytherapy according to some crucial factors including the type, duration and frequency of seizures, patients' lifestyle and age, psychology, whether the seizures are under control or not and side effects of drugs on patients and especially for women that she will become pregnant.

Moreover, pharmacokinetic properties, metabolism of drugs and mechanism of action of these drugs play very important role in drug selection (Table 4) [3, 30, 54, 56, 57, 58].

In polytherapy, inhibitory, additive and synergistic properties and interactions of antiepileptic drugs have more importance. Because, in the case of any wrong drug combinations inefficient responses are observed and unwanted effects can be observed.

Furthermore, drug-drug interaction, drug-nutrient interaction also affect the regimen. For instance, cytochrome P 450 system plays the most important role for the metabolism of AEDs. Cytochrome P 450 enzyme system is found nearly in all tissues but mostly in liver. Among all enzymes of system, CYP 1, CYP 2 and CYP 3 are responsible from the metabolism of xenobiotic drugs, forms over the 70 % of CYP enzymes in human liver. CYP 3A4, CYP 2D6, CYP 2C9, CYP 1A2 are the subtypes of CYP 1, CYP 2 and CYP 3 enzymes and these are responsible for metabolism of 95 % of all drugs, including antiepileptic ones. Carbamazepine, phenytoin, phenobarbital and

primidone are old type and classic drugs. They stimulates the activation of different subtypes of cytochrome P 450 system. Levetiracetam, gabapetin and vigabatrin are new generation drugs and they do not have ant inductory or inhibitory effects so they do not show much interactions. Inhibitory and synergistic interactions of antiepileptic drugs are shown below in Table 5 [59] and Table 6 [60].

Table 4. Characteristics of Common Antiepileptic Drugs

Drug	Mechanism of Action	Dose	Pharmacokinetic Parameters	Usual Serum Concentration Ranges	Dose-related Adverse Effects	Idiosyncratic Adverse Effects
Carbamazepine	Modulate Sodium (Na) channels	*Loading dose: Not recommended due to excessive dose-related toxicity *Maintenance dose: Titrate dosage to target over 3-4 weeks Adults: 10-20 mg/kg per day as a divided dose Children: 20-30 mg/kg per day as a divided dose	*Half-life: 10-25 hours with chronic dosing *Apparent volume of distribution: 0,8-1,9L/kg *Protein binding: 67-81% *Primary elimination route: Hepatic	4-12 mcg/mL	Diplopia, nausea, sedation, drowsiness	Aplastic anaemia, leucopoenia, osteoporosis, rash, hyponatremia
Clonazepam	Enhance GABA activity	*Loading dose: Not recommended due to increased adverse effects *Maintenance dose: Initiate at 0,5 mg one to three times daily, titrate dose to effectiveness usually 3-5 mg daily in 2-3 divided doses	*Half-life: 30-40 hours *Apparent volume of distribution: 3,2L/kg *Protein binding: 47-80% *Preliminary elimination route: Hepatic	0,02-0,1 mcg/mL	Ataxia, memory impairment, sedation, slowed thinking	

Ethosuximide	Modulate calcium (Ca) channels	*Loading dose: Not recommended due to increased adverse effects *Maintenance dose: Initiate at 250 mg twice a day and titrate 500-1000 mg twice daily	*Half-life: 60 hours *Apparent volume of distribution: 0,6-0,7 L/kg *Protein binding: none *Preliminary elimination route: Hepatic	40-100 mcg/mL	Ataxia, sedation	Hepatotoxicity, rash, neutropenia
Lamotrigine	Modulate Na channels	*Loading dose: Not recommended due to increased risk of rash *Maintenance dose: 150-800 mg/day in2-3 divided doses. Doses should be initiated and titrated according to the manufacturer's advices to reduce the risk of rash.	*Half-life: In monotherapy: 24 hours In concurrent enzyme inducers: 12-15 hours In concurrent enzyme inhibitors: 55-60 hours *Apparent volume of distribution: 1,1 kg/L *Protein binding: 55% *Preliminary elimination route: Hepatic	5-15 mcg/mL (provisional)	Ataxia, drowsiness, headache, insomnia, sedation	Rash

Gabapentin	Modulate Ca channels and enhance GABA activity	*Loading dose: Not recommended due to short half-life *Maintenance dose: 900-3600 mg/day in 3-4 divided doses (doses up to 10,000 mg/day have been tolerated)	*Half-life: 5-7 hours (proportional to Cl_{Cr}) *Apparent volume of distribution: 0,6-0,8 L/kg *Protein binding: less than 10% *Primary elimination route: Renal	4-16 mcg/mL (provisional)	Drowsiness, sedation	Peripheral oedema, weight gain
Phenobarbital	Modulate Na channels	*Loading dose: 10-20 mg/kg as a single or divided IV infusions or orally in divided doses over 24-48 hours *Maintenance dose: Adults: 1-4 mg/kg per day, as a single or divided dose Children: 3-6 mg/kg per day, as a divided dose Neonates: 1-3 mg/kg per day as divided dose	*Half-life: Adults: 49-120 hours Children: 37-73 hours Neonates: ~115 hours *Apparent volume of distribution: 0,7-1,0 L/kg *Protein binding: ~50% *Primary elimination route: Hepatic	15-40 mcg/mL	Ataxia, drowsiness, sedation	Attention deficit, cognitive impairment, osteoporosis, hyperactivity, passive-aggressive behaviour

Oxcarbazepine	Modulate Na channels	*Loading dose: Not recommended due to excessive adverse effects *Maintenance dose: 600-1200 mg/day start at 300 mg twice daily and titrate upward as indicated by response.	*Half-life: Parent drug ~2 hours ; 10 monohydroxy metabolite ~ 9 hours *Apparent volume of distribution: 0,5-0,7 L/kg *Protein binding: 40% *Primary elimination route: Hepatic	12-30 mcg/mL	Diplopia, dizziness, somnolence	Hyponatremia, 25-30% cross sensitivity in patients with hypersensitivity to carbamazepine
Felbamate	Inhibit glutamate activity	*Loading dose: Not recommended due to increased adverse effects *Maintenance dose: 1200-3600 mg/day in 3-4 divided doses	*Half-life: In monotherapy: 20 hours In concurrent enzyme inducers: 11-16 hours *Apparent volume of distribution: 0,7-0,8 L/kg *Protein binding: 25-38% *Primary elimination route: Hepatic	40-65 mcg/mL	Anxiety, insomnia, nausea	Anorexia, aplastic anaemia, headache, weight loss, hepatotoxicity

Levetiracetam	Binding to the synaptic vesicle protein SV2A.	*Loading dose: Not recommended due to excessive adverse effects *Maintenance dose: 1000-3000mg/day. Start at 1000 mg/day and titrate upward as indicated by response	*Half-life: 6-8 hours *Apparent volume of distribution: 0,5-0,7 L/kg *Protein binding: less than 10% *Preliminary elimination route: 70% Renal 30% Hepatic	10-40 mcg/mL (provisional)	Somnolence, dizziness	Depression
Topiramate	Modulate Na channels; enhance GABA activity; inhibit glutamate activity	*Loading dose: Not recommended due to excessive adverse effects *Maintenance dose: 100-400 mg/day in 2-3 divided doses. Doses should be started at 25-50 mg/day and gradually titrated upward over 3-6 weeks to avoid excessive adverse effects	*Half-life: In monotherapy: 21 hours In concurrent enzyme inducers: 11-16 hours *Apparent volume of distribution: 0,55-0,8 L/kg *Protein binding: 13-17% *Primary elimination route: 60% Renal 40% Hepatic	4-12 mg/mL (provisional)	Ataxia, dizziness, drowsiness, slowed thinking	Acute glaucoma, metabolic acidosis, oligohidrosis, parasthesisas, renal calculi, weight loss

Tiagabine	Enhance GABA activity	*Loading dose: Not recommended due to excessive adverse effects *Maintenance dose: 32-56 mg/day in four divided doses. Doses should be titrated upward over 6 weeks, starting at 4 mg/day	*Half-life: In monotherapy: 7-9 hours In concurrent enzyme inducers: 2,5-4,5 hours *Apparent volume of distribution: 0,6-0,8 L/kg *Protein binding: 96% *Primary elimination route: Hepatic	100-300mcg/mL (provisional)	Dizziness, somnolence, irritability, slowed thinking	
Primidone	Modulate Na channels	*Loading dose: Not recommended due to excessive adverse effects *Maintenance dose: Started with lower doses than gradually increased Adults: 250-750 mg Children: 15-30 mg/kg	*Half-life: 10-25 hours *Apparent volume of distribution: 0,6 L/kg *Protein binding: 20% *Primary elimination route: Hepatic	4-12 mcg/mL	Sedation, dizziness	Attention deficit, cognitive impairment, osteoporosis, hyperactivity, passive-aggressive behaviour

Valproic acid / Divalproex Na	Modulate Na channels	*Loading dose: 20-40 mg/kg *Maintenance dose: Adults: 15-45 mg/kg per day in 2-4 divided doses Children: 5-60 mg/day per day in 2-4 divided doses.	*Half-life: Adults: 8-15 hours Children: 4-15 hours Infants less than 2 months: 65 hours *Apparent volume of distribution: 0,1-0,5 L/kg *Protein binding: 90% (decreases with increasing serum concentrations) *Primary elimination route: Hepatic	50-100 mcg/mL Children may need concentrations up to 150 mcg/mL	Drowsiness, nausea, sedation, tremor	Hepatotoxicity, osteoporosis, pancreatitis, weight gain
Zonisamide	Modulate Na and Ca channels	*Loading dose: Not recommended due to excessive adverse effects *Maintenance dose: 100-600 mg/day; start at 100 mg/day and titrate upward as indicated by response.	*Half-life: ~ 63 hours *Apparent volume of distribution: 1,45 L/kg *Protein binding: 40% *Primary elimination route: Hepatic	10-40 mcg/mL (provisional)	Dizziness, somnolence	Oligohidrosis, parasthesia, renal calculi, metabolic acidosis

Pregabalin	Modulate Ca channels	*Loading dose: Not recommended due to increased adverse effects *Maintenance dose: Initiate at 150 mg/day in 2-3 divided doses and titrate to a maximum dose of 600 mg/day	*Half-life: 6,3 hours, proportional to Cl_{Cr} *Apparent volume of distribution: 0,5L/kg *Protein binding: Negligible *Primary elimination route: Renal	Not established	Ataxia, dry mouth, dizziness, somnolence, blurred vision	Oedema, weight gain
Phenytoin	Modulate Na channels	*Loading dose: Adults: 15-20 mg/kg single IV dose or divided oral dose Infants less than 3 months: 10-15 mg/kg single IV dose Neonates: 15-20 mg/kg single IV dose *Maintenance dose: Adults: 5-7 mg/kg per day as a single or divided dose	*Half-life: Follows capacity-limited or Michaelis-Menten pharmacokinetics. Half-life increases as the dose and serum concentration increases. *Apparent volume of distribution: Adults: 0,7L/kg Children: 0,8 L/kg Neonates: 1,2 L/kg *Protein binding: Adults and children: 88-92% Neonates: 65%	Total concentration: 10-20 mcg/mL Unbound concentration: 1-2 mcg/mL	Ataxia, diplopia, drowsiness, sedation	Anaemia, gingival hyperplasia, hirsutism, rash, osteoporosis, lymphadenopathy

		Children: 6-15 mg/kg per day as divided dose Neonates: 3-8 mg/kg per day as divided dose	*Primary elimination route: Hepatic			

Table 5. Expected changes in plasma concentrations when an AED is added to a pre-existing regimen

	Pre-existing AED														
AED added	**PB**	**PHT**	**PRM**	**ETS**	**CBZ**	**VPA**	**OXC**	**LTG**	**GBP**	**TPM**	**TGB**	**LEV**	**ZNS**	**VGB**	**FBM**
PB	.....	PHT ↑↓	NCCP	ETS ↓	CBZ ↓	VPA ↓	H-OXC↓	LTG ↓	↔	TPM ↓	TGB ↓	↔	ZNS ↓	↔	FBM ↓
PHT	PB↑	.....	PRM↓ PB↑	ETS ↓	CBZ ↓	VPA ↓	H-OXC↓	LTG ↓	↔	TPM ↓	TGB ↓	↔	ZNS ↓	↔	FBM ↓
PRM	NCCP	PHT ↑↓	.....	ETS ↓	CBZ ↓	VPA ↓	?	LTG ↓	↔	TPM ↓	TGB ↓	↔	ZNS ↓	↔	FBM ↓
ETS	↔	↔	NE	.....	↔	VPA ↓	NE	NE	NE	NE	NE	NE	NE	NE	NE
CBZ	↔	PHT ↑↓	PRM↓ PB↑	ETS ↓	.....	VPA ↓	H-OXC↓	LTG ↓	↔	TPM ↓	TGB ↓	↔	ZNS ↓	NE	FBM ↓
VPA	PB ↑	PHT ↓*	PB ↑	ETS↑ ↓	CBZ-E↑	.....	↔	LTG ↑		TPM↓	↔	↔	↔	NE	↔
OXC	PB↑	PHT ↑	?	?	CBZ↓	↔	.....	LTG↓	NE	?	?	NE	?	NE	?
LTG	↔	↔	NE	NE	↔	↔	NE	.....	NE	NE	NE	↔	↔	NE	NE
GBP	↔	↔	NE	NE	↔	↔	NE	NE	.....	NE	NE	↔	NE	NE	NE
TPM	↔	PHT ↑	↔	NE	↔	VPA ↓	?	?	NE	.....	?	NE	?	NE	?

TGB	↔	↔	↔	NE	↔	↔	NE	NE	NE	NE	.....	NE	NE	NE	NE
LEV	↔	↔	↔	NE	↔	↔	NE	↔	↔	NE	NE	.....	NE	NE	NE
ZNS	↔	↔	NE	NE	CBZ↑↓	↔	?	↔	NE	NE	NE	NE	.....	NE	?
VGB	PB↓	PHT ↓	PRM↓ PB↓	NE	CBZ↑	↔	NE	NE	NE	NE	NE	NE	NE	.....	FBM
FBM	PB ↑	PHT ↑	?	?	CBZ↓ CBZ-E↑	VPA ↑	↔	↔	NE	?	?	NE	?	↔	……

PB: Phenobarbital; PHT: Phenytoin; PRM: Primidone; ETS: Ethosuximide; CBZ: Carbamazepine; VPA: Valproic acid; TGB: Tiagabine; LTG: Lamotrigine; GBP: Gabapentin; TPM: Topiramate; LEV: Levetiracetam; ZNS: Zonisamide; VGB: Vigabatrine; FBM: Felbamate; OXC: Oxcarbazepine; H-OXC: 10-Hydroxy-oxcarbazepine (active metabolite of OXC); CBZ-E: Carbamazepine-10,11-epoxide; NE: None Expected; * : free (pharmacologically active) concentration may increase; NCCP: Not Commonly Co prescribed; ↔: No change; ↓: a minor (or inconsistent) decrease in plasma concentration; ↓ : a clinically significant decrease in plasma concentration; ↑: a minor (or inconsistent) increase in plasma concentration; ↑ : a clinically significant increase in plasma concentration

Table 6. Interactions between Antiepileptics and Nonantiepileptics

Non-AED	AED	Pharmacologic outcome of drug interaction	Potentially clinically relevant outcome of the drug interaction
Oral contraceptive pill	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB, FBM, OXC and TPM)	Increased metabolism of the contraceptive pill and reduced hormone levels.	Pregnancy
Theophylline	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	Increased metabolism of theophylline	Reduced efficacy against asthma and chronic bronchitis
Dicoumarol/warfarin	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	Increased metabolism of dicoumarol/warfarin and reduced anticoagulant activity	Decreased anticoagulant activity could be life threatening. If AED is subsequently removed there is the risk of dicoumarol/warfarin toxicity (e.g., haemorrhage)
Digoxin	PHT and TPM	Decreased plasma concentration of digoxin	Reduced efficacy in cardiac failure
Corticosteroids	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	Increased metabolism of corticosteroid	Reduced therapeutic effects. May need to increase the dose of the corticosteroid
Antacids	CBZ, PHT, PB and GBP	Reduced gut absoption of the AEDs	Reduced efficacy of the AEDs and seizure exacerbation
Omeprazole	PHT	Inhibition of phenytion metabolism	If the patient experiences phenytion toxicity, phenytoin dose reduction will be necessary
Cimetidine	PHT	Inhibition of phenytion metabolism	If the patient experiences phenytion toxicity, phenytoin dose reduction will be necessary
Tricyclic antidepressants (TCAs)	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	Bidirectional interaction with TCA concentrations reducing and AED concentrations increasing	Reduced efficacy of TCA and possible toxicity of AEDs

Fluoxetine	CBZ and PHT	Inhibition of AED metabolism and increased plasma concentrations of CBZ and PHT	Initiate at or lower dose of CBZ/PHT to the lower end of the therapeutic dose range. Look for signs of CBZ/PHT toxicity (e.g. dizziness)
Sertraline	LTG	Inhibition of AED metabolism and increased plasma concentrations of LTG	Look for the signs of LTG toxicity and reduce the dose of LTG if necessary
Benzodiazepines	CBZ, PHT and PB	Increases metabolism and derceases plasma concentration of benzodiazepines	Adjust doses if necessary
Haloperidol	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	Increased metabolism of haloperidol with a subsequent decrease in plasma concentration	It may be useful to monitor the plasma concentrations of haloperidol and adjust the dose if necessary
Fluconazole	PHT	Inhibition of PHT metabolism with a possible increase in PHT plasma concentration	If the patient experiences phenytion toxicity, phenytoin dose reduction may be necessary
Griseofulvin	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	Increased metabolism of Griseofulvin and reduced plasma concentrations	Reduced antifungal activity
Erythromycin	CBZ	Inhibition of metabolism of AEDs and increased plasma concentrations	Observe the patient carefully for signs of AED toxicity and, if necessary, reduce the dose
Clarithromycin	CBZ	Inhibition of AED metabolism and increased plasma concentrations of CBZ	If coadministered, the patients must be carefully monitored for signs of CBZ toxicity. Reduce the dose if necessary.

Antiviral agents that are metabolised by CYP 3A4	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	AEDs can increase the metabolism of and reduce the plasma concentrations of antiviral agents	Reduced efficacy, increased viral replication, and the development of resistance
Cyclosporine	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	AEDs can increase the metabolism of and reduce the plasma concentrations of cyclosporine	Reduced immunosuppressant activity. It will be necessary to increase the dose of cyclosporine
Anticancer agents	Enzyme-inducing AEDs (e.g., CBZ, PHT, PB)	AEDs can increase the metabolism of anticancer agents and reduce therapeutic efficacy	Reduced efficacy of of the anticancer agnet and the potential for a poorer outcome for the patient
St. John's wort	CBZ and PHT	The metabolism of CBZ and PHT may be increased by St. John's wort	AED efficacy reduced with possible loss of seizure control

2.6. SOCIAL PROBLEMS AND EPILEPSY

Community surveys have indicated that people with epilepsy experience difficulties with education, work, recreational activities and social situations, particularly if they have frequent seizures [61, 62, 63, 64, 65, 66]. In France, England, Canada and the United States, at least 80 % of epileptics must make their way in the world with the handicap of a syndrome poorly understood by the public [67]. Thus, in epileptic patients, the possibility of development of depression, social isolation and situation of not being able to marry is common and they potentially, are unemployed and recorded as permanently ill. In conclusion, we can say "Being an epileptic can be more miserable than having a seizure" [55].

The problems of the epileptic child at school age are of critical importance to his/her future. Experience shows that under the right conditions 80% of epileptic children can be educated in any ordinary school and there is no need for special educational facilities. The most important thing is that the parents' aim in the early years of an epileptic child's life should be to allow the child to lead as normal a life as possible. Parents must encourage their child to participate in a variety of social activities and should support child in making friends with his/her peers. Additionally, we can see a lot of and brilliant epileptics who were famous: Martin Luther, Caesar, Napoleon, Isaac Newton, Beethoven, Alfred Nobel and Neyzen Tevfik. These are evidence of that not all epileptics have educational or creativity insufficiency [68, 1].

After their education process, epileptic patients have greater difficulty in finding jobs. Employment concerns for people with epilepsy may involve the complex issues of prejudice, safety and the law [69]. Inadequacies in academic education, cognitive disorders, mood disorders, problems in driving and unhealthy social relationships are the basic causes of the unemployment [70]. However, the beneficial effects of a suitable occupation cannot be over-emphasized [68]. They prefer job areas that positively affect their quality of life. Employment provides financial security, self confidence and self-worth to the patient. The Epilepsy Foundation of America estimates that 80% of people

with epilepsy are able to work [71]. As a result, epileptic patients can work in a suitable jobs according to their abilities and concerns regardless of the fact of having seizures.

A person with epilepsy has a greater possibility of developing depression or related problems. Connected to this, quality of life of an epileptic person is worse than that of a normal person. Studies confirmed this thesis. In our country, a few studies were found about the association of quality of life and epilepsy. Study of Mollaoglu , et al. by the use of Quality of Life in Epilepsy-89 (QOLIE-89) test which showed that quality of life level of Turkish epilepsy patients is worse than those of American and Norwegian epileptic patients [72]. Additionally, in the study of Ozkara , et al. via Washington Psychosocial Seizure Inventory (WPSI), dense psychosocial disorders were identified in epileptic patients and quality of life of Turkish epileptic patients detected as less than those of developed countries [73]. These results about Turkey may be dependant on cultural and social reasons [70].

The general wellbeing of epileptic patients is a very complex subject. There are plenty of studies about this. Chaplin and colleagues [74] performed a study and according to the results few patients were found socially restricted and in bad condition with feeling of stigmatised. Additionally, in the study of the Medical Research Council, the extent of reported problems was related to the timing of the last seizure [75]. Similar findings were also reported in the studies of Trostle , et al. [76] and Collings , et al. [77].

Among the questions most frequently asked in regard to epilepsy is the suitability of the epileptic for marriage and the risk to the offspring. In many countries including Turkey, epilepsy is a restrictive factor for marriage on the grounds of hereditary, possible mental retardation, economic doubts a rising from possible unemployment etc. Thus, the marriage ratio in epileptics is less than those of normal people. In a report of 8 marriages of epileptics, six were successful, two ended in divorce because the spouse was not told before marriage [78]. Furthermore, according to the results of a study that was performed on 12,119 parents and siblings, there were 39 chances in 40 of an

epileptic married to a normal spouse having a normal child [67]. Another study also shows that the chances a nonepileptic parents having an epileptic child are about 1 in 200, whereas if one parent is epileptic the risk increases to 1 in 40 [68].

Another important point is participation of epileptics in the physical exercises and/or other sports. Many epileptics do not know well which activity they can do. Actually, it is very easy to answer this question. For a person with a history of seizures, the decision to participate in a sport should be evaluated on an individual basis. People with epilepsy have been encouraged to participate in sports to improve self-esteem, well-being, and fitness. Reports on epileptics involved with a regular physical activity were generally favourable and cited a moderate seizure-prevention effect about 30 % to 40%. Table 7 shows the relative risk of different sporting activities for epileptic patients [79].

Table 7. Relative Risk of Various Sporting Activities for People with Epilepsy*

Low Risk
Track
Cross-country skiing
Golf
Bowling
Table tennis
Baseball
Weight training (machines)
Moderately Risk
Football
Hockey
Biking
Soccer
Gymnastics
Horseback riding
Basketball
Boating/Sailing
High Risk
Scuba diving
Hang gliding
Motor sports
Boxing
Downhill skiing/Ski flying
Long distance swimming

* Adapted with permission from Mesad SM, Devinski O. Epilepsy and the athlete. In: Jordan BD, Tsairis P, Warren RF (Eds). Sports Neurology. (2nd. Ed.) Lippincott-Raven Publishers, Philadelphia, pp 275-287, 1998.

In conclusion, there is a great necessity to educate the general public regarding this disease and tell them exactly what epilepsy is, what epileptics can do and are doing, and how best their problems can be dealt with in the best interest of society as a whole and the epileptic in particular.

2.7. EPILEPSY AND WOMEN

Epilepsy and antiepileptic drugs substantially affect women's health in the areas of menstruation, contraception, fertility, sexual function, pregnancy, menopause and bone health. Also, family planning is affected by seizures and antiepileptic drugs [80]. The marriage rate of epileptic patients, especially women, is lower than the general population due to their fear of drug related teratogenicity and the increased risk of giving birth to an epileptic baby [78].

To sum up, via improved education and surveillance of women, enhanced knowledge and better management for young girls and women with epilepsy will be achieved.

2.7.1. Menstruation

The increase in seizures near the time of menses, *catamenial epilepsy*, was first documented more than 100 years ago. Seizures are possibly related to menses because sex hormones change the neuronal excitability. For example, oestrogen inhibits the γ-amino butyric acid channel and increases the glutamate transmission. In addition to these, oestrogen leads to decrease of $GABA_A$ receptor subunits' numbers in long term. As a consequence, excitation heightens, inhibition decreases. On the other hand, progesterone has the opposite effect; its metabolite potentiates the barbiturate-like ligands at the γ-amino butyric acid channel, resulting in increased inhibition with fewer seizures [81].

2.7.2. Contraception

Contraception is the issue frequently asked about by the women with epilepsy. It is exactly a so important subject so that if oral contraceptive drug is not taken at enough doses, and if the drugs used for epilepsy have hepatic enzyme inducing properties, pregnancy can be observed unexpectedly [82].

Drugs like phenobarbital, phenytoin, tiagabine (according to its dose), carbamazepine, oxcarbazepine, topiramate and felbamate induce hepatic enzyme metabolism [83, 84, 85, 86]. This leads to acceleration in the catabolism of steroid hormones present in oral contraceptives, resulting in 50% or may be much lower blood concentration of these hormonal drugs [87, 60]. Consequently, effectiveness of oral contraceptives decreases. So, if oral contraceptives are used with these antiepileptic drugs, dose of contraceptive pills should be increased in order to provide benefit. On the other hand, sodium valproate, lamotrigine, gabapentin, pregabalin, clonazepam, levetiracetam and vigabatrin have not shown any interaction with oral contraceptives and they can be used safely [88, 89].

In conclusion, women with epilepsy must know whether their AED interacts with oral contraceptive pills which they use or not. Additionally, epileptic women should be informed about other protection methods like condom, cap and diaphragm [60]. If suitable and required, the morning-after contraceptive pills can be used in epileptic women after unprotected sexual intercourse [83, 90]. Despite all of these, the protectiveness of hormonal protection is nearly same as that of intra uterine device and better than the barrier methods [81].

2.7.3. Fertility

There are some epidemiologic studies indicating that women with epilepsy have fewer numbers of babies compare to the normal women. According to general accepted idea, fertility of the women with epilepsy is two third of the normal population [81, 91].

The causes are multifactorial, including not marrying due to her illness, fear of giving birth to an epileptic baby or having a problematic pregnancy, unwanted effect of antiepileptic drugs, lowered libido, social and genetic factors. Sexual function problems also affect and are related to the fertility [92].

2.7.4. Sexual function

When compared to the other neurological disorders, in epileptic patients, the risk of having sexual problems is higher and it was reported as 14-50 % in women with epilepsy [93]. Epileptic women complain about vaginismus, anorgasmia, arousal insufficiency and sexual anxiety [80].

Once sexual dysfunction is determined, it is essential to find its duration and its aetiology. In order to solve this problem, the patient's history should be questioned and physical examinations should be performed. If needed, laboratory screening and ultrasound examination must be performed. Despite all these, if no organic cause is found, patient must be assessed psychologically [80].

To sum up, sexual problems have negative effects on all all aspects of the patients' quality of life. So, sexual problems of epileptic women are very important point in their life and not neglected [94].

2.7.5. Pregnancy

In the management of epilepsy for a pregnant woman, the aim is to remain seizure free throughout pregnancy. Most women reported no increases in their seizure frequency, but nearly 25% women were observed as increased frequency of seizure in their pregnancy term. The reasons for increased seizure frequency may be poor medication compliance, lowered AED concentration, sleep deprivation, and stress [95].

In duration of pregnancy, drug adjustment for epilepsy treatment is very important. If the seizures of pregnant women with epilepsy are under control with monotherapy, AED mustn't be given up because this may cause teratogenic side effects [94]. Additionally, if the seizures of a pregnant woman are under control with polytherapy, monotherapy may be tried but in this case, patient must be monitored often and carefully. Table 8 shows the suggestions for management of epilepsy [3].

Table 8. Management of Antiepileptic Drug during Pregnancy

* Give supplemental folic acid, 1-4 mg daily, to all women of child-bearing potential
* Use monotherapy whenever possible
* Use the lowest doses that control seizures
* Continue pharmacotherapy that best controls seizures prior to pregnancy
* Monitor antiepileptic drug serum concentrations at the start of the pregnancy and monthly thereafter
* Adjust antiepileptic drug doses to maintain baseline serum concentrations
* Administer supplemental vitamin K during the eight month of pregnancy to women receiving enzyme-inducing antiepileptic drugs
* Monitor postpartum antiepileptic drug serum concentrations to guide adjustments of drug doses

In some studies, in the common complications of pregnancy, 2 to 3 fold increases have been shown in Table 9. In order to prevent any complications during pregnancy, when she is aware of her pregnancy, AED blood concentration should be measured to identify the baseline, and drug level measurements should be repeated regularly. In addition to this folic acid levels must be controlled. Moreover, alfa-feto protein (AFP) and Ultrasonography (USG) scans should be performed.

With anatomic USG and α-FP detection in maternal serum, major malformations are revealed as well as heart anomalies. If pregnant women with epilepsy use a hepatic enzyme inducing AED, in their babies, haemorrhages can be observed associated with vitamin K deficiency (Factor II, VII, IX, X). Thus, keeping every possibility in mind,

pregnant women with epilepsy use a hepatic enzyme-inducing AED are recommended vitamin K 10-20 mg/day in last month of their pregnancy [83]. After the labour of baby, he/she is recommended 1 mg administration of vitamin K intramuscularly (IM), too. Finally, in order to reduce the risk of neural tube defect (NTD) which can be developed due to the inadequate absorption or increased metabolism of folate, pregnant women are suggested to take supplementary folic acid 1-4 mg daily.

Table 9. Common Complications of Pregnancy that Occur at an Increased Rate in Women with Epilepsy

Pregnancy	**Labour and Delivery**
*Hyperemesis *Vaginal Haemorrhage *Preeclampsia *Eclampsia *Vitamin D Deficiency *Vitamin K Deficiency *Megaloblastic Anaemia (Decreased Folate)	*Premature Labour *Caesarean Section *Postpartum Haemorrhage

2.7.6. Menopause

Menopause and its effects on epileptic women can not be explained clearly and still under-researched. According to some studies menopause occurs 3 to 4 years earlier in women with epilepsy compare to healthy women [96]. Additionally, according to the study in which perimenopausal and menopausal seizures were assessed, it was shown that hormonal replacement therapy (HRT) had no significant effect on seizures. On the other hand, it was shown that catamenial seizure pattern may be associated with seizure decrease during menopause but an increase during perimenopause [96, 97].

As a result, in order to prevent frequency of seizures in perimenopause and menopause, women with epilepsy should be informed about this subject. For example, in perimenopausal and menopausal term hot flushes and sleep disturbances can increase

and as is well known sleep disturbances and long-term awakeness trigger the seizures. Thus, the patient must give more attention to her sleep and may need psychological support [80].

2.7.7. Bone health

Antiepileptic drugs cause hypocalcaemia, hypokalemia, decrease in vitamin D levels in serum and so in bone, secondary hyperparathyroidism and osteoporosis.

Especially, women with epilepsy have increased risk of these illnesses. Risks increase in the case of using hepatic enzyme-inducing antiepileptic drug like phenytoin, valproic acid, phenobarbital and carbamazepine. In these patients, bone mineral density can be measured via Dual-energy X-ray absorptiometry (DXA) to identify whether there is a problem in bone or not [96].

Consequently, The National Institute of Health (NIH) recommend that not only epileptic women but also all healthy people between the ages of 25 and 65 years consume at least 1,000 mg of calcium/day.

2.7.8. Teratogenicity of AEDs

Compared to healthy women, epileptic women have higher risk of having babies with anomalies because of the teratogenic effects of antiepileptic drugs. This ratio is 2% to 3% for healthy women in US and doubles for women with epilepsy [81, 94].

The formation of teratogenic effects is multifactorial. Common reasons are production of AED toxic intermediate metabolites, folic acid deficiency, hypoxia, some genetic problems and neuronal suppression. According to the studies performed and to

recent databases, valproic acid is more teratogenic than carbamazepine and the combination of valproate and lamotrigine also shows teratogenicity [98].

The AEDs may show their teratogenic effects on cardiovascular, gastrointestinal, skeletal and connective tissues and central nervous systems. These are summarized in Table 10 [99].

Table 10. Incidence of Malformations Among the 3228 Children Born Alive of Mothers Treated with Antiepileptic Drugs.

System	**Malformations**	**Number**	**%**
CVS	TOF, ASD, VSD, PDA, Pulmonary Atresia, Single Ventricle	66	2,0
Craniofacial	Cleft lip, Cleft palate	59	1,8
Skeletal	Club foot, Hip dislocation	29	0,9
CNS	Neural Tube Defects	23	0,7
GIT	Oesophageal Atresia, Omphalocele, Hernia (diaphragm, inguinal, umbilical), CHPS	10	0,3
GUT	Renal agenesis, Hydronephrosis, Hypospadias, Undescended testes	11	0,3
Others		45	1,4
TOTAL		**243**	**7,5**

*ASD: Atrial Septal Defect; PDA: Patent Ductus Arteriosus; CHPS: Congenital Hypertrophic Pyloric Stenosis; TOF: Tetrology of Fallot; VSD: Ventricular Septal Defect.

3. RESEARCH DESIGN & METHODOLOGY

3.1. RESEARCH DESIGN

Survey research, also known as descriptive, is using a questionnaire to gather data in order to determine and describe the attitudes and opinions of certain people regarding specific issues. The most popular form of survey design is the “cross-sectional” design to collect data about current altitudes, opinions, or beliefs at one point in time and the most popular application method is “face to face” or “interview” research method [100].

In this study, interview survey type questionnaire form was used in the design. In the interview survey, different from a questionnaire, it is the important point that the researcher/interviewer records answers given by the participants.

After the identification of aim, population and location of the research, the design of a survey should be done. Additionally, how the data collected and assessment of these data are planned before design process. Design of the questionnaire has three important parts. First is determination of questions. Second is selection of the question type for each of them in the survey like “Yes/No”, “open ended”, “close ended” “single/multiple responses”, “ranking” and “rating” question types. Third and final one is design and sequence of the questions overall questionnaire layout [101].

In this interview survey, twenty-three questions are identified and a lot of question types are combined. Most of the questions are “Yes/No” type, some are “single/multiple response” type and remaining are open ended questions. Beside theses questions, demographic data is also collected by this survey.

3.2. RESEARCH OBJECTIVES

The aim of this study is assessment of the knowledge about epilepsy among epileptic patients, nonepileptic patients and community pharmacists.

Secondly, this study aims to compare whether education level affects the information about the epilepsy or not. Additionally, whether there is a difference between genders of patients having epilepsy.

Thirdly, the questions asked in the survey are related to the social and psychological life of epileptic patients, nutrition, sleep patterns, drug used and fertility of the epileptic patients. Finally, the research aims to throwlight on these aspects of the lifestyle of epileptic patients.

3.3. STUDY POPULATION & STUDY AREA

This study was performed in community pharmacies found in Atasehir/Istanbul between 1 January 2010 and 1 July 2010. Survey population includes 13 community pharmacists, epileptic and nonepileptic patients who came to these pharmacies. 219 questionnaires were applied to the participants. A total of 172 of them were nonepileptic patients and the other remaining 47 were epileptic patients.

3.3.1. Eligibility Criteria

3.3.1.1. Inclusion Criteria

- Pharmacies must be located in Atasehir.
- Patients age must be ≥ 15

3.3.1.2. Exclusion Criteria

- Pharmacies which are not located in Atasehir.
- Patients whose age < 15

3.4. DATA COLLECTION METHOD

Data collection method has two important processes. One of them is application of survey in the pharmacies and the other process is conversion of the collected data to numerical outcomes.

Surveys were first carried out with the community pharmacists face to face then to the patients who came to these pharmacies. Application of surveys was conducted by the author and a voluntary student of Yeditepe University School of Pharmacy.

The second part of the study is related to the numerical outcomes of the collected data. It is based on the participants' responses recorded via surveys and converting of these responses to numerical data on computerized media.

3.5. QUESTIONNAIRE DESIGN

The questionnaire was developed after a through literature review. In this process, the questionnaires were examined in terms of benefit, some instructors and physicians were asked for advice.

Before final form of questionnaire was conducted, it was applied to thirty students of Yeditepe University Faculty of Pharmacy several times and according to their

comments, some changes were made. Some of questions were removed and some of them changed.

The final form of the survey was prepared as twenty-three questioned. All together, 260 questionnaires were applied, however, 219 of these were found to be usable. It took 2 to 3 minutes to complete all twenty-three questions found in the inquiry.

The first part of the questionnaire was about the demographics of the participants. These were gender, what educational background they have such as elementary grade, high school grade, university grade or master/doctorate degree educational profile. Besides these, ages of respondents and their professions were also requested.

In the second part, there were questions that queried the knowledge level of participants about the epilepsy. In this part, most of the questions were “Yes/No” questions and also multiple response type questions were used. In total, there were twenty-three questions in this part.

The first question was to identify whether participants had epilepsy or not. If they said “Yes”, participants were invited to write which drugs they used and to give answer the second question. However, if they said “No”, they invited to by-pass the second one and give an answer to the third question, directly.

The second question asked whether the seizures of the epileptic patients were kept under control or not.

The third question asked whether there were any restrictions for an epileptic person drinking fizzy beverages like coke or not.

The forth question asked whether there were any restrictions for an epileptic person on taking a driving licence and/or driving a car or not.

The fifth question aimed to identify how well informes people were about the military status of an epileptic men.

The sixth question of the questionnaire asked if alcohol was hazardous to epileptic patients or not.

The seventh question asked whether cigarette smoking was hazardous to epileptic patients.

The eighth question asked about the importance of drug timing in patient with epilepsy.

The ninth question asked whether epilepsy can affect social life and can cause psychological problems.

The tenth question of survey asked whether epilepsy was a contagious disease or not.

The eleventh question of the inquiry asked "Can epilepsy be treated completely?"

The twelfth question asked whether there were any restrictions for an epileptic woman on being pregnant.

In the thirteenth question, it was asked if an epileptic woman could bear normally.

The fourteenth question asked whether there can be any problem in the baby or not in the situation of being pregnancy of an epileptic woman.

The fifteenth question asked “Can epilepsy be seen in the child of an epileptic person?”

The sixteenth question was about the effect of tea and coffee like stimulant drinks to the epilepsy.

The seventeenth question asked “Do you use any drugs in an influenza infection?” If the participants said “Yes”, they were asked to note drugs they used.

In the eighteenth question, “Can epileptic patients do sport?” was asked and if “Yes” “Which sports can they do?” was wanted to point by respondents among the choices.

The nineteenth question asked whether there is an association between epilepsy and mental retardation or not.

The twentieth question asked whether there is a relation with epilepsy and sleep pattern.

In question twenty-one, participants were asked whether they have any information or not about which drugs increase the epileptic seizures and if they said “Yes”, they wanted to provide their names of those drugs.

Question twenty-two of the survey asked “Can epilepsy be seen at any age?”

Finally, question twenty-three was related to the information sources of the people about epilepsy.

3.6. DATA ANALYSIS TECHNIQUE

The findings were transferred to the electronic media and analyzed by descriptive statistics and chi-square (χ^2) tests by using Statistical Package for the Social Sciences (SPSS) PC software. This data collection aims to find relationship between demographics and other parameters and also the relationship between parameters.

4. RESULTS

In this section, the results of cross tabulation and χ^2 tests analyses were tabulated and summarized. This section is composed of two sections. First part mainly includes demographic and descriptive info and the second part contains the cross tabulations and assessment of them.

Totally, 260 questionnaires were applied but 219 of them were used because of their suitability and reliability.

4.1. FREQUENCY DISTRIBUTION

4.1.1. Demographic Characteristics

General frequencies were used in order to show distribution of the variables and combining variables to produce useful data for the cross tabulation.

Table 11. Gender distribution

SEX DISTRIBUTION		Frequency	Percent	Valid Percent	Cumulative Percent
GENDER	MALE	122	55,7	55,7	55,7
	FEMALE	97	44,3	44,3	100,0
	Total	219	100,0	100,0	

Totally, 219 people were assessed. Of these 97 were female and 122 were male participants. 55, 7 % of the respondents were male and 44, 3 % were female as shown figure 10 below.

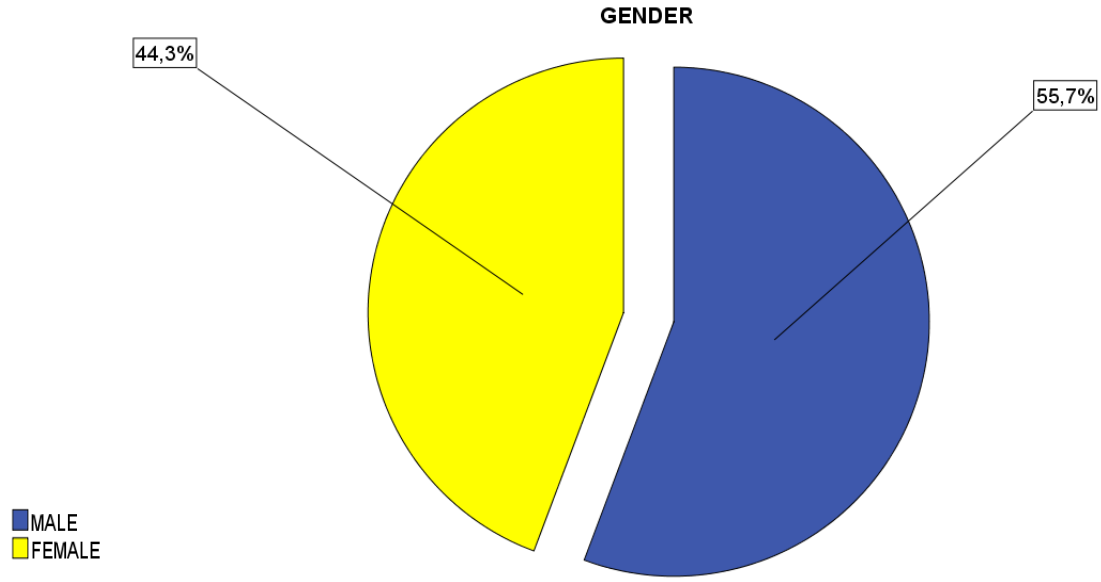


Figure 10. Gender distribution of participants

According to the data obtained from questionnaires, 12,8 % of participants are between age of 10-24; 38,4 % of them are between age of 25-39; 28,3 % respondents are in the 40-54 age range; 16,4 % of participants are between the age of 55-69 and finally remaining 4,10 % of are in the 70-84 age range. Distributions of the age ranges of participants are shown in the figure 11 below.

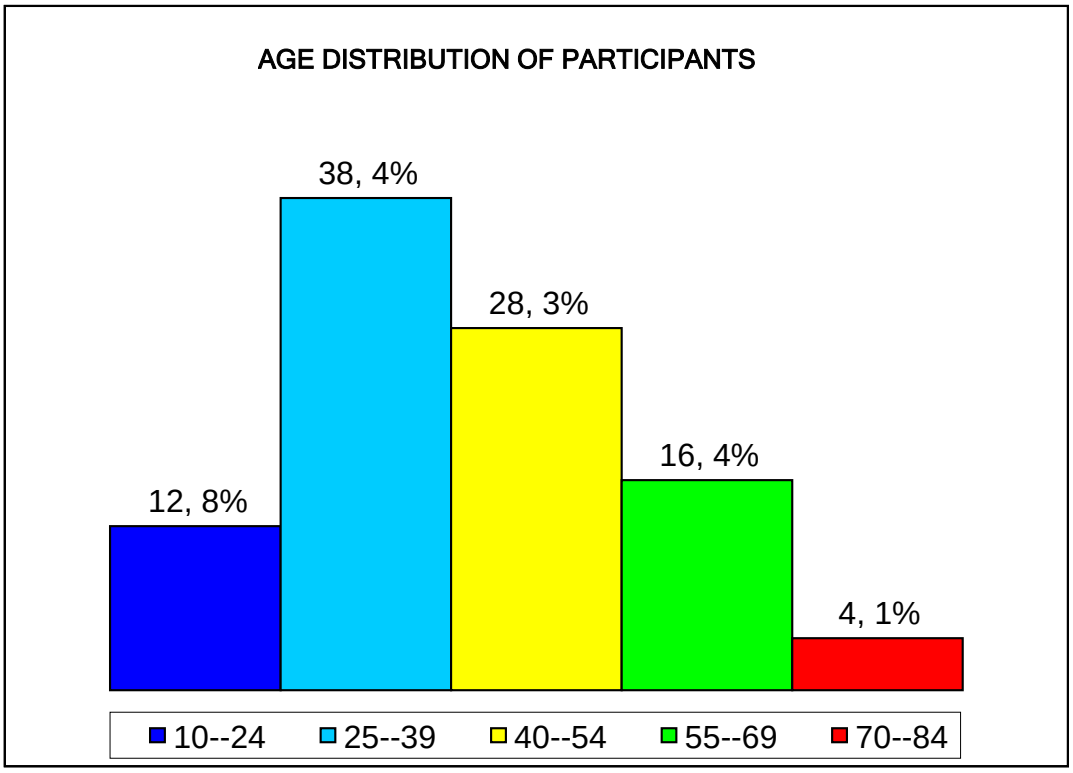


Figure 11. Age distribution of participants

Additionally, data of educational level was assessed. According to the results, 5 % of participants (n: 11) have primary; 31, 1 % of participants (n: 68) have intermediate; 60, 7 % of people (n: 133) have university and finally 3, 2 % of participants (n: 7) have master/doctorate degree educational level. It is shown in table 12 and figure 12 below.

Table 12. Education level of participants

EDUCATION LEVEL	Frequency	Percent	Valid Percent	Cumulative Percent
PRIMARY	11	5,0	5,0	5,0
INTERMEDIATE	68	31,1	31,1	36,1
UNIVERSITY	133	60,7	60,7	96,8
MASTER/DOCTORATE	7	3,2	3,2	100,0
Total	219	100,0	100,0	

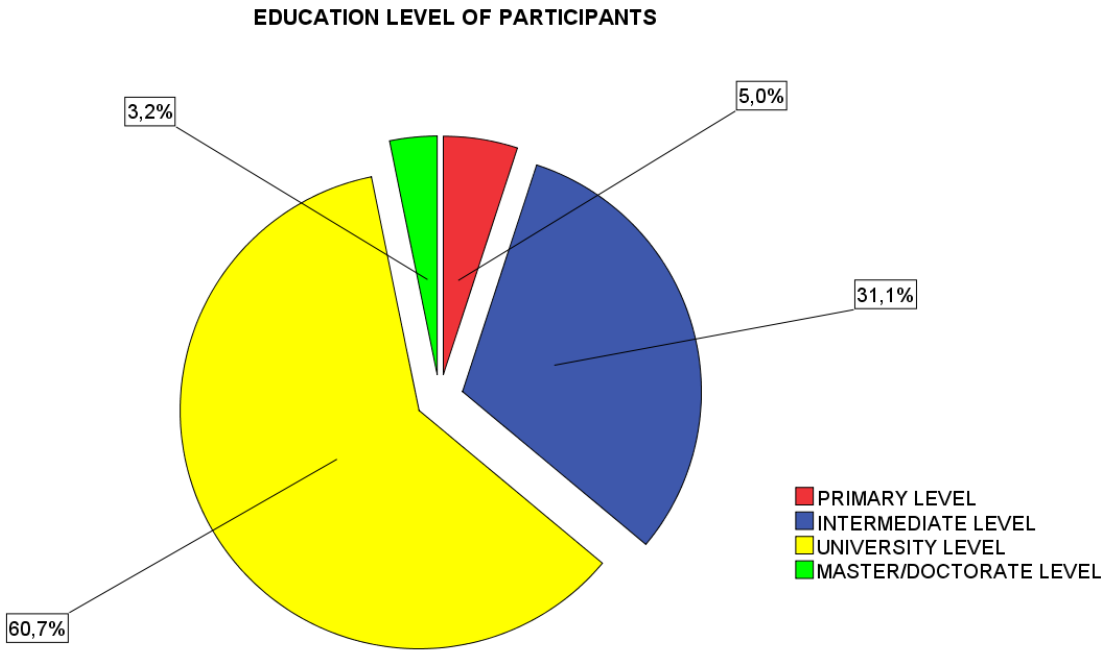


Figure 12. Education level of participants

4.1.2. Descriptive Statistics and Cross tabulations

In this part, the responses of the participants were assessed and statistically significant results were shown as frequency tables and graphics or as both. Some essential comparisons were done like how much effect the education level and the profession of the participants has on the knowledge about epilepsy.

Not all results obtained were significant. However, all criteria which were compared, without any exception, were commented on and discussed briefly. Moreover, if a participant was not an epileptic, he/she was told “there is no need to answer the second question and response directly third one. Thus, in some questionnaires second question was not answered.

In conclusion, all data obtained from questionnaires from 219 participants were assessed in detail and supported with cross tabulations and frequencies.

According to the results of first question, 78, 5 % of participants (n: 172) are nonepileptic people and the remaining 21, 5 % are epileptics. This result is shown in table 13 and figure 13.

Table 13. Frequency of epileptics & nonepileptics

PARTICIPANTS	Frequency	Percent	Valid Percent	Cumulative Percent
EPILEPTICS	47	21,5	21,5	21,5
NONEPILEPTICS	172	78,5	78,5	100,0
Total	219	100,0	100,0	

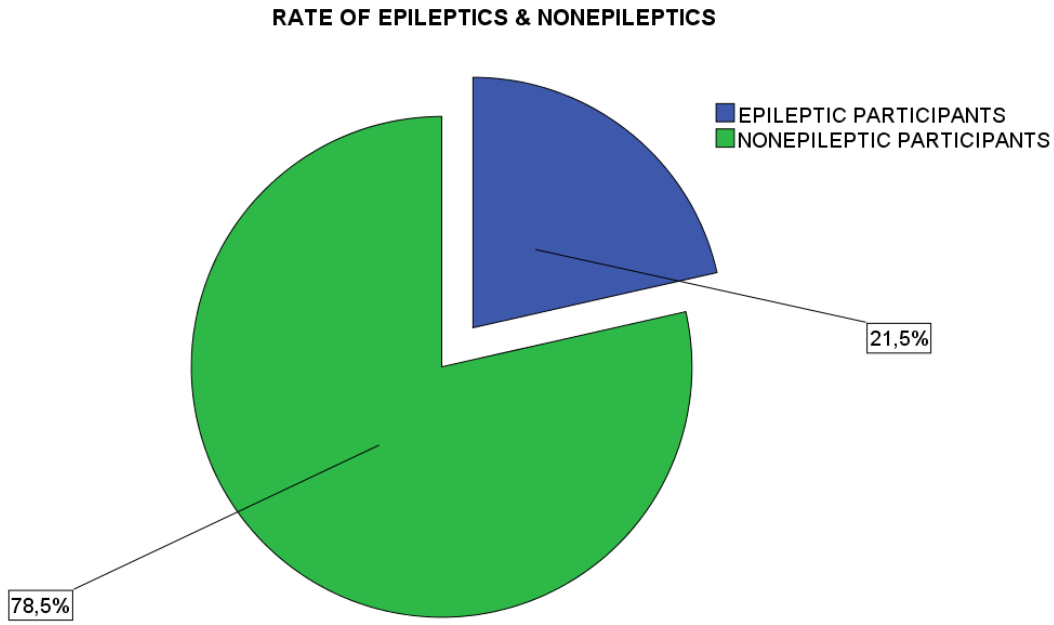


Figure. 13. Rate of epileptic and nonepileptic participants

The second question asked for epileptic respondents to define whether their seizures under control or not and after assessments, the results showed that 72,3 % of the respondents noted that their seizures are under control and remaining 27,7 % said that their seizures were not controlled. It is shown below in detail table 14.

Table 14. Situation of seizure control

SEIZURES	Frequency	Percent	Valid Percent	Cumulative Percent
UNDER CONTROL	34	72,3	72,3	72,3
UNCONTROLLED	13	27,7	27,7	100,0
Total	47	100,0	100,0	

When looking to the table 15, cross tabulation of question 1 & 3, it is shown that 42, 6 % of epileptics and 14 % of nonepileptics have no idea about whether epileptic people can drink fizzy drinks or not. 34, 0 % (n: 16) of all epileptic participants (n: 47) know the right answer and only 17, 4 % of all 92 people who gave right answer “NO”, are epileptics (n: 16).

Although fizzy drinks should be consumed by epileptics safely, it must be known that if they drink fizzy beverages with their antiepileptic drugs, these can affect the efficacy and bioavailability of drugs.

Table 15. Epilepsy and fizzy drinks

CROSSTABULATION OF Q1 & Q3			QUESTION 3			
			YES	NO	NO IDEA	Total
QUESTION 1	EPILEPTICS	Count	11	16	20	47
		Expected Count	17,8	19,7	9,4	47,0
		% within Q1	23,4%	34,0%	42,6%	100,0%
		% within Q3	13,3%	17,4%	45,5%	21,5%
	NONEPILEPTICS	Count	72	76	24	172
		Expected Count	65,2	72,3	34,6	172,0
		% within Q1	41,9%	44,2%	14,0%	100,0%
		% within Q3	86,7%	82,6%	54,5%	78,5%
Total		Count	83	92	44	219
		Expected Count	83,0	92,0	44,0	219,0
		% within Q1	37,9%	42,0%	20,1%	100,0%
		% within Q3	100,0%	100,0%	100,0%	100,0%

In the fourth question, whether there is a limitation for epileptic person to be given a driving licence or not was asked to the participants. Most of the participants 54, 3 % (n: 119) responded as “YES” there is a limitation while 36, 5 % saying “NO” and 9, 1 % saying “I have NO IDEA”. This is shown in table 16 below.

Table 16. Driving licence and Epilepsy

	Frequency	Percent	Valid Percent	Cumulative Percent
YES	119	54,3	54,3	54,3
NO	80	36,5	36,5	90,9
NO IDEA	20	9,1	9,1	100,0
Total	219	100,0	100,0	

There is a variety of applications and laws in the different countries in world. For example, in UK, the only exception to the rule is occurring seizure during sleep, with this pattern established for three years. But this pattern needs to be established for two years in Belgium and only one year in the Netherlands. As a conclusion, regulations on commercial driving and supportive laboratory criteria differ widely [102]. Finally, in Turkey, epileptics can have H class driving licence and can use automobile that has special equipments [103].

5th question is "Is it possible for an epileptic male to do military service?" To this question, most of the participants 70, 3 % (n: 154) said "NO" shown as in table 17.

Table 17. Military service and epileptic males

	Frequency	Percent	Valid Percent	Cumulative Percent
YES	41	18,7	18,7	18,7
NO	154	70,3	70,3	89,0
NO IDEA	24	11,0	11,0	100,0
Total	219	100,0	100,0	

There are some different rules and regulations about this subject in different parts of the world. In Turkey, whether an epileptic male is convenient for military service or not, is determined according to the 12th article of Turkish Armed Forces Health Capability Ordinance (TAFHCO) [104].

That is to say, if an epileptic male is assessed as suitable for military service after the variety of examinations, especially neurological, he can do his military service. So, participants gave wrong answer. This result may rises from prejudices to the epileptic patients.

Next, the effect of alcohol was searched in the questionnaire. Result of this question is obtained as expected. 191 of 219 respondents gave right “YES” answer, 4 respondents said “NO” and remaining 24 people said “NO IDEA” as shown in figure 14.

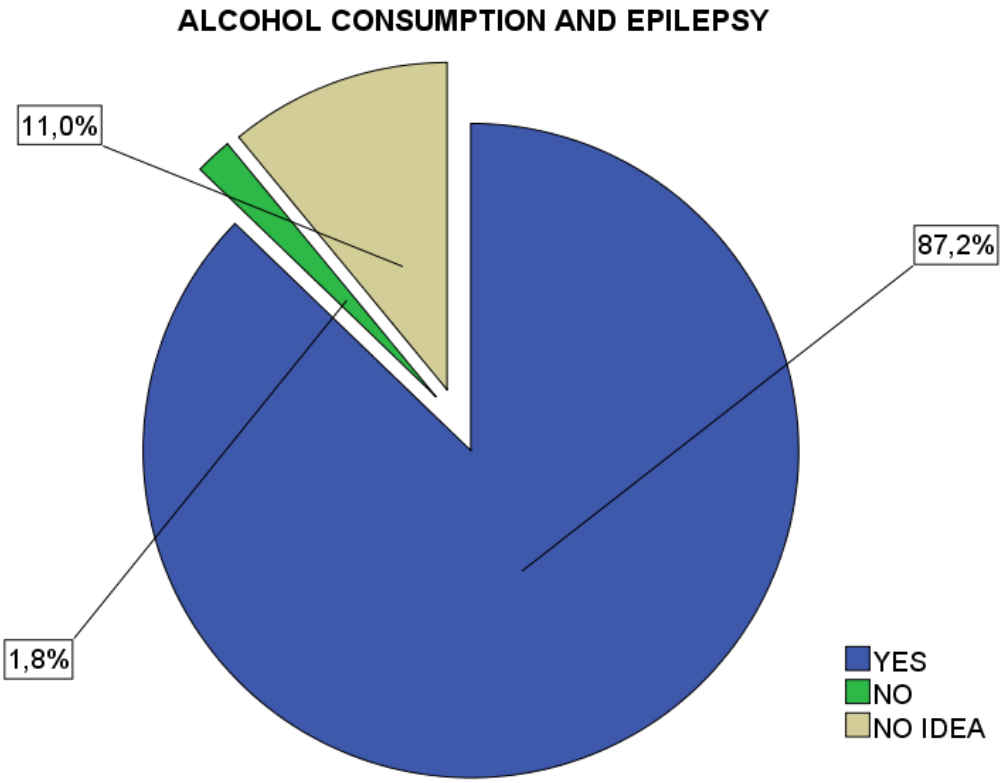


Figure 14. Knowledge of alcohol consumption and epilepsy

Similar question was asked participants about smoking and results are very interesting. As a result of statistical assessments, it is shown that ratio of right answer among epileptic people is very much lower (38, 3 %) from expected count. However, opposite data is observed among nonepileptic participants (69, 2 %). As a general, most of the participants (62, 6 %) gave right answer. Additionally, among participants who gave right answer (n: 137), the ratios of epileptics and nonepileptics are 13, 1 % and 86, 9 %, respectively.

In the questionnaire, there is a question related to the importance of drug timing in antiepileptic drugs. The result is not found statistically significant. To sum up, 84, 9 % of all participants said “YES”, 4, 1 % said “NO” and remaining 11% said “NO IDEA”.

The 9th question is one of the most important questions in this survey. It interrogated the social life and knowledge about psychological problems of epileptics. Results are obtained as expected and statistically significant. It is shown with cross tabulation of Q1 and Q9 in table 18.

Table 18. Knowledge comparison on social life and psychological problems

CROSSTABULATION OF Q1 & Q9			QUESTION 9			
			YES	NO	NO IDEA	Total
QUESTION 1	EPILEPTICS	Count	35	9	3	47
		Expected Count	25,3	13,9	7,7	47,0
		% within Q1	74,5%	19,1%	6,4%	100,0%
		% within Q9	29,7%	13,8%	8,3%	21,5%
	NONEPILEPTICS	Count	83	56	33	172
		Expected Count	92,7	51,1	28,3	172,0
		% within Q1	48,3%	32,6%	19,2%	100,0%
		% within Q9	70,3%	86,2%	91,7%	78,5%
Total		Count	118	65	36	219
		Expected Count	118,0	65,0	36,0	219,0
		% within Q1	53,9%	29,7%	16,4%	100,0%
		% within Q9	100,0%	100,0%	100,0%	100,0%

$\chi 2$: 10,624 p: 0,005

According to the results shown above, 74,5 % (n:35) of all epileptic participants (n:47) and 48,3 % of nonepileptic participants gave “YES” answer and said that epilepsy can affect the social life and can cause psychological problems.

One another question is that whether epilepsy is a contagious disease or not. Result of this question is not statistically significant. Most of the participants (94, 1 %) know that epilepsy is not a contagious illness.

In the questionnaire, participants were asked whether epilepsy has a treatment or not. According to the given responses, result is not significant statistically. It can only be commented most of the participants (58, 9 %) explained that epilepsy has not got any treatment just now.

In the 12^{th}, 13^{th}, 14^{th} and 15^{th} questions, two comparisons were performed. One of them is to compare knowledge of epileptics and nonepileptics and the second one is male and female comparison regardless having epilepsy disorder.

In the 12^{th} question, results are statistically significant in both comparisons. These are shown in the table 19 and 20, respectively.

Table 19. Sex and knowledge on pregnancy of an epileptic female

CROSSTABULATION OF SEX & Q12			QUESTION 12			Total
			YES	NO	NO IDEA	
SEX	MALE	Count	17	59	46	122
		Expected Count	22,8	64,1	35,1	122,0
		% within SEX	13,9%	48,4%	37,7%	100,0%
		% within Q12	41,5%	51,3%	73,0%	55,7%
	FEMALE	Count	24	56	17	97
		Expected Count	18,2	50,9	27,9	97,0
		% within SEX	24,7%	57,7%	17,5%	100,0%
		% within Q12	58,5%	48,7%	27,0%	44,3%
Total		Count	41	115	63	219
		Expected Count	41,0	115,0	63,0	219,0
		% within SEX	18,7%	52,5%	28,8%	100,0%
		% within Q12	100,0%	100,0%	100,0%	100,0%

$\chi 2$: 11,924 p: 0,003

According to the results, female participants have higher knowledge than male about pregnancy. 56 (57, 7 %) of 97 females noted that there is no restrictions for epileptic females to become pregnant. It is observed that male participants have lower knowledge on this subject.

When looking to the result of second comparison, 46, 8 % of epileptic participants have no idea on this subject and most of the nonepileptic respondents (57, 6 %) have higher knowledge level about this question, interestingly. While participants are assessed as general, 52, 5 % of all participants gave right answer.

Table 20. Knowledge of all participants on pregnancy

CROSSTABULATION OF Q1 & Q12			QUESTION 12			
			YES	NO	NO IDEA	Total
QUESTION 1	EPILEPTICS	Count	9	16	22	47
		Expected Count	8,8	24,7	13,5	47,0
		% within Q1	19,1%	34,0%	46,8%	100,0%
		% within Q12	22,0%	13,9%	34,9%	21,5%
	NONEPILEPTICS	Count	32	99	41	172
		Expected Count	32,2	90,3	49,5	172,0
		% within Q1	18,6%	57,6%	23,8%	100,0%
		% within Q12	78,0%	86,1%	65,1%	78,5%
Total		Count	41	115	63	219
		Expected Count	41,0	115,0	63,0	219,0
		% within Q1	18,7%	52,5%	28,8%	100,0%
		% within Q12	100,0%	100,0%	100,0%	100,0%

$\chi 2$: 10,664 p: 0,005

In question 13, whether an epileptic female can bear normally or not was asked to participants. To this question, more than half of epileptic people (51, 1 %) explained that they had no idea and 31, 9 % of epileptics gave right answer. Right answer ratio was observed higher in nonepileptics (40, 1 %) and in general assessment, counts of wrong answer and lack of knowledge are high. The result of this question is shown in table 21.

It may be due to the participation of males (55, 7 %) and nonepileptics (78, 5 %) in higher ratio when compare to others.

Table 21. Knowledge about normally bearing of an epileptic female

CROSSTABULATION OF Q1 & Q13			QUESTION 13			
			YES	NO	NO IDEA	Total
QUESTION 1	EPILEPTICS	Count	15	8	24	47
		Expected Count	18,0	13,3	15,7	47,0
		% within Q1	31,9%	17,0%	51,1%	100,0%
		% within Q13	17,9%	12,9%	32,9%	21,5%
	NONEPILEPTICS	Count	69	54	49	172
		Expected Count	66,0	48,7	57,3	172,0
		% within Q1	40,1%	31,4%	28,5%	100,0%
		% within Q13	82,1%	87,1%	67,1%	78,5%
Total		Count	84	62	73	219
		Expected Count	84,0	62,0	73,0	219,0
		% within Q1	38,4%	28,3%	33,3%	100,0%
		% within Q13	100,0%	100,0%	100,0%	100,0%

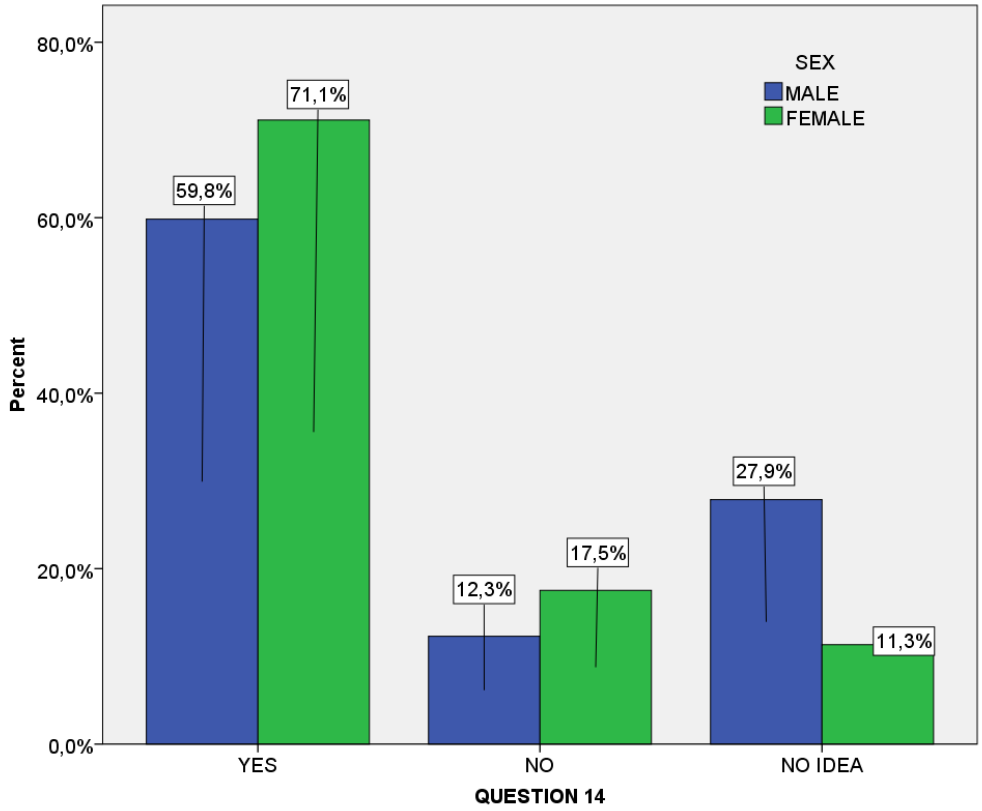
According to the cross tabulation of sex and question thirteen, 47, 4 % of females gave “YES” answer while 31, 1 % of males said “YES”. Totally, 84 participants gave right answer and when they are compared, it is shown in table 22 that female have higher knowledge than males.

Table 22. Knowledge comparison of males and females in normally bearing of an epileptic woman

CROSSTABULATION OF SEX & Q13			QUESTION 13			
			YES	NO	NO IDEA	Total
SEX	MALE	Count	38	32	52	122
		Expected Count	46,8	34,5	40,7	122,0
		% within SEX	31,1%	26,2%	42,6%	100,0%
		% within Q13	45,2%	51,6%	71,2%	55,7%
	FEMALE	Count	46	30	21	97
		Expected Count	37,2	27,5	32,3	97,0
		% within SEX	47,4%	30,9%	21,6%	100,0%
		% within Q13	54,8%	48,4%	28,8%	44,3%
	Total	Count	84	62	73	219
		Expected Count	84,0	62,0	73,0	219,0
		% within SEX	38,4%	28,3%	33,3%	100,0%
		% within Q13	100,0%	100,0%	100,0%	100,0%

An other important question asked that whether there can be a problem in the baby of an epileptic woman. When it is considered as genetically, it is possible to have a baby with some problems. The result of this question is also observed as statistically significant. It is shown in the figure 15.

To this question, 142 people gave right “YES” answer. 73 of them are male (59, 8 % of all males) and 69 of them are female (71, 1 % of all females). It is statistically significant *(p: 0, 01)*. When looking to the participants, totally 64, 8 % of 219 people (n: 142) gave right answer and ratio of epileptics and nonepileptics who gave right answer are 11, 3 % and 88, 7 %, respectively. Finally, 44, 7 % of epileptics have no idea on this subject.



$\chi 2$: 9,260 p: 0,01

Figure 15. Knowledge comparison of males and females on possibility of problematic baby

15th question is also related with genetic structure of epileptic patients, without exception of gender. The result is not statistically significant. Respondents would say "YES". Amazingly, 89, 6 % of participants who gave right answer are nonepileptics and other interesting data is that not having idea of most epileptic participants about this subject (42, 6 %).

As it is known, if there is an epileptic situation in father or in mother, there is a possibility to have an epileptic baby for that family. For example according to the results of scientific studies, if a member of the family has epilepsy, the ratio of possibility to have an epileptic baby increase [66, 67].

In this questionnaire, incidence of epilepsy in males and females is compared. For this comparison, cross tabulation is performed with question one and sex and if the participant is epileptic he/she noted that “YES”. The result was obtained as statistically insignificant. As it is shown in the figure 16, there is no more difference between male and female.

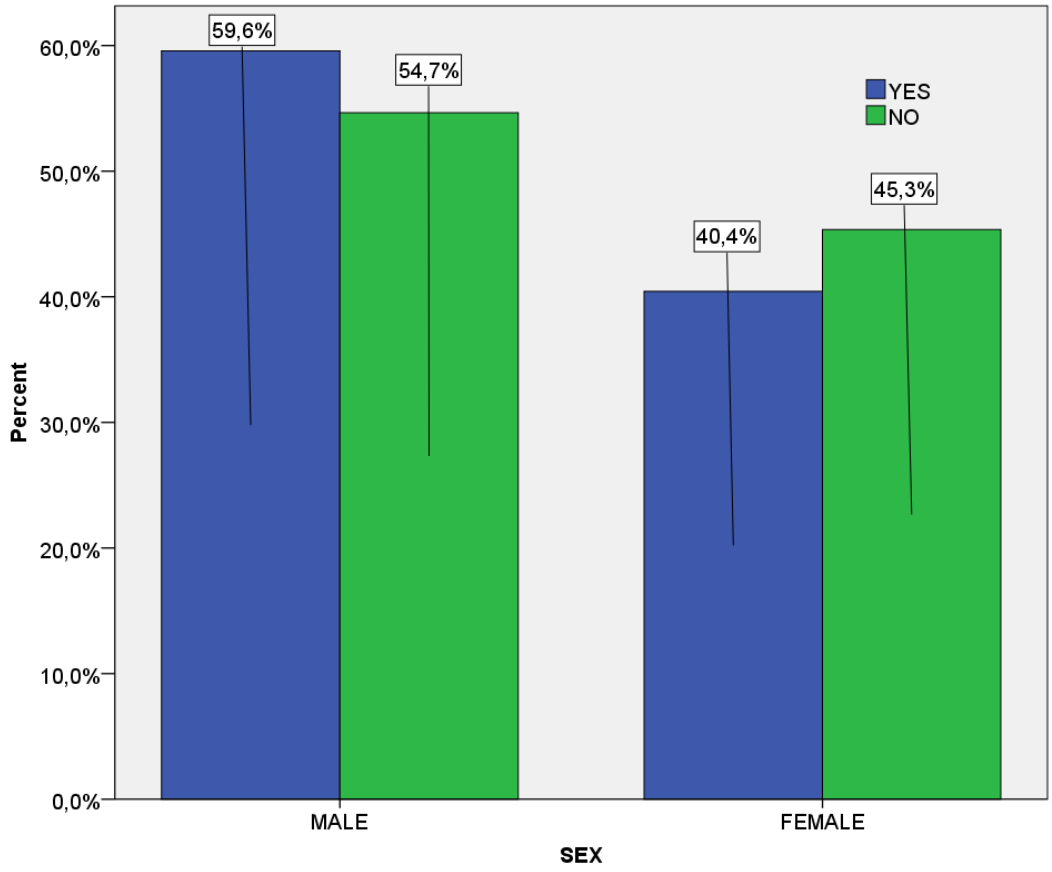


Figure 16. Incidence of epilepsy between male and female

16th question is nearly same with the question three. Tea and coffee include theine and caffeine, respectively and these ingredients have stimulant effects on human body. On the other hand, it can be said that these drinks are not hazardous for epileptic people and they can be consumed safely.

However, there are some important points in the consumption. First of all, these drinks can not be consumed with the antiepileptic drugs or before and after antiepileptic drugs. Second point is that much more consumption of tea and coffee are harmful as like as other beverages, basically like water. It can be summarized in figure 17.

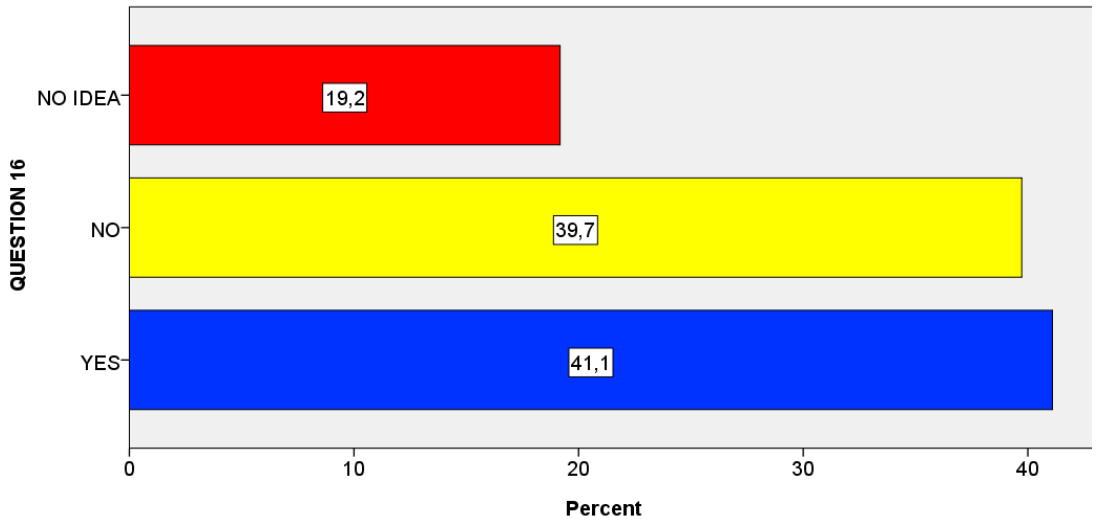


Figure 17. Participants' opinions about harmfulness of tea and coffee on epilepsy

It must be well known especially by the epileptic individuals, some drugs are harmful for epilepsy and increase the frequency of seizures. Among these drugs, most important ones are the drugs used in the situation of influenza. 17th question was asked in order to learn whether epileptic patients use any drug for influenza. According to the results, 35 (74, 4 %) of the 47 epileptic people use kinds of drugs to treat influenza. When looking to the drug distribution among these patients, it can be exactly shown that every epileptic patient uses pastilles (100 %). Then, with ratio of 91, 4 % antigribal drugs come. Antigribal drug class covers the analgesics, antipyretics, decongestants, antihistaminics and antitussives due to the combination preparates. 60 % of epileptic patients, who use drug for influenza, are using also variety of antibiotics and finally 22, 9 % of 35 epileptic participants prefer to use vitamins. Secondly, all nonepileptic participants use any drug. These ratios change in the nonepileptics compare to

epileptics. Pastilles, vitamins, antigribals and antibiotics are used by the ratios of 30, 3 %; 67, 4 %; 83, 1 %; 50, 6 %, respectively. These data is shown in the figure 18 below.

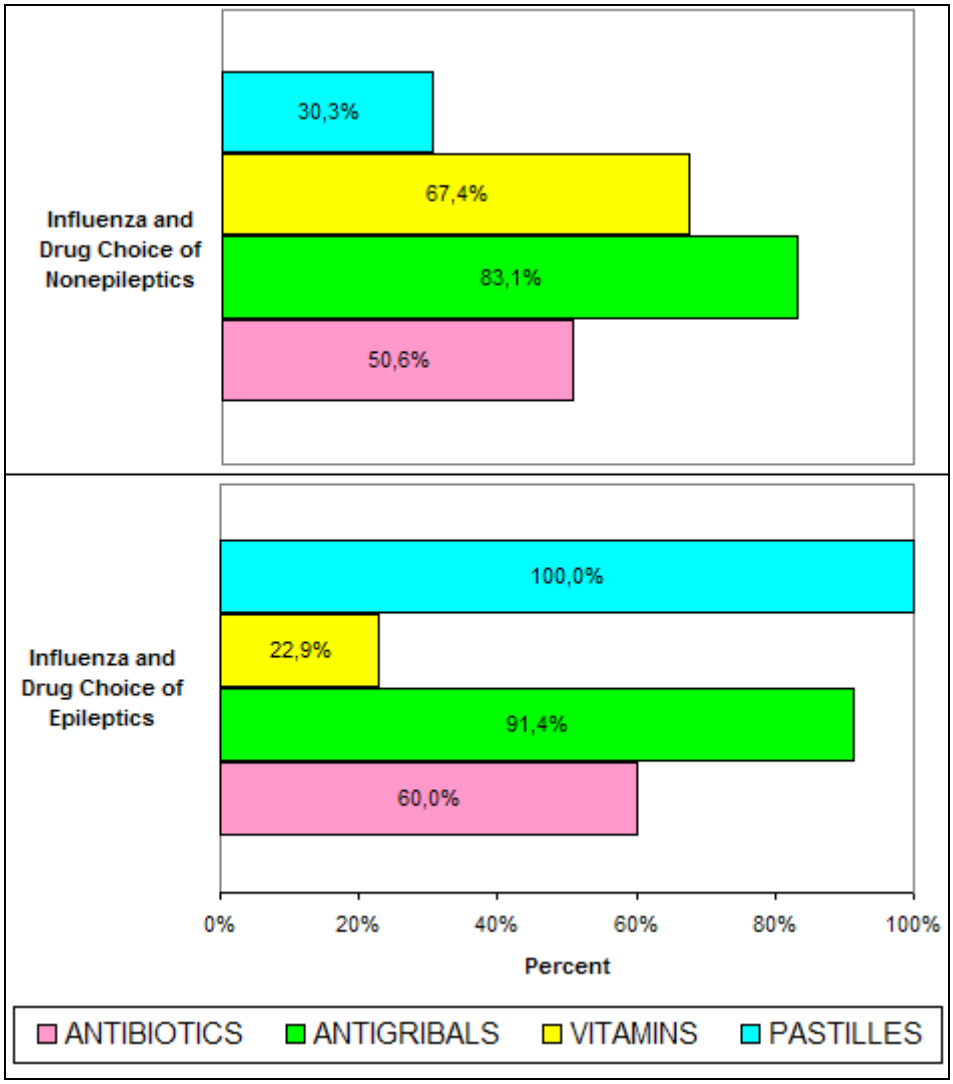


Figure 18. Drug choice of participants when they have influenza

The 18th question asks to participants whether epileptics can do any of the sports or exercises or not.

A lot of different idea and responses were given by the participants. According to the scientific researches, there is no limitation for epileptics to do a sporting activity, except extreme sports.

In some sports, they should be more careful and must protect themselves. For instance, when they are swimming, they can swim with someone, or when they are cycling they must use helmet. Some sports may be dangerous for epileptics like bungee jumping, parachute because they are classified as extreme sports.

As a conclusion, in their social life epileptic people do not have any restrictions for their sportive activity unless they want to do extreme sports and if they provide required protection.

90, 4 % of all participants noted that epileptic patients can do sportive activity (n: 198). The figure was prepared according to 198 participants. As it is shown in the figure 19 below, epileptics and nonepileptics gave nearly the same answer for tracking, 100 % and 98, 1 %, respectively. Then, jogging comes secondly among the responses, 55, 2 % by epileptics and 89, 4 % by nonepileptics. 80, 8 % of epileptic said there is no limitation to do sportive activity.

Finally, 13, 2 % of these epileptic participants explained that water sports can be done while nonepileptics explain as 43, 8 %.

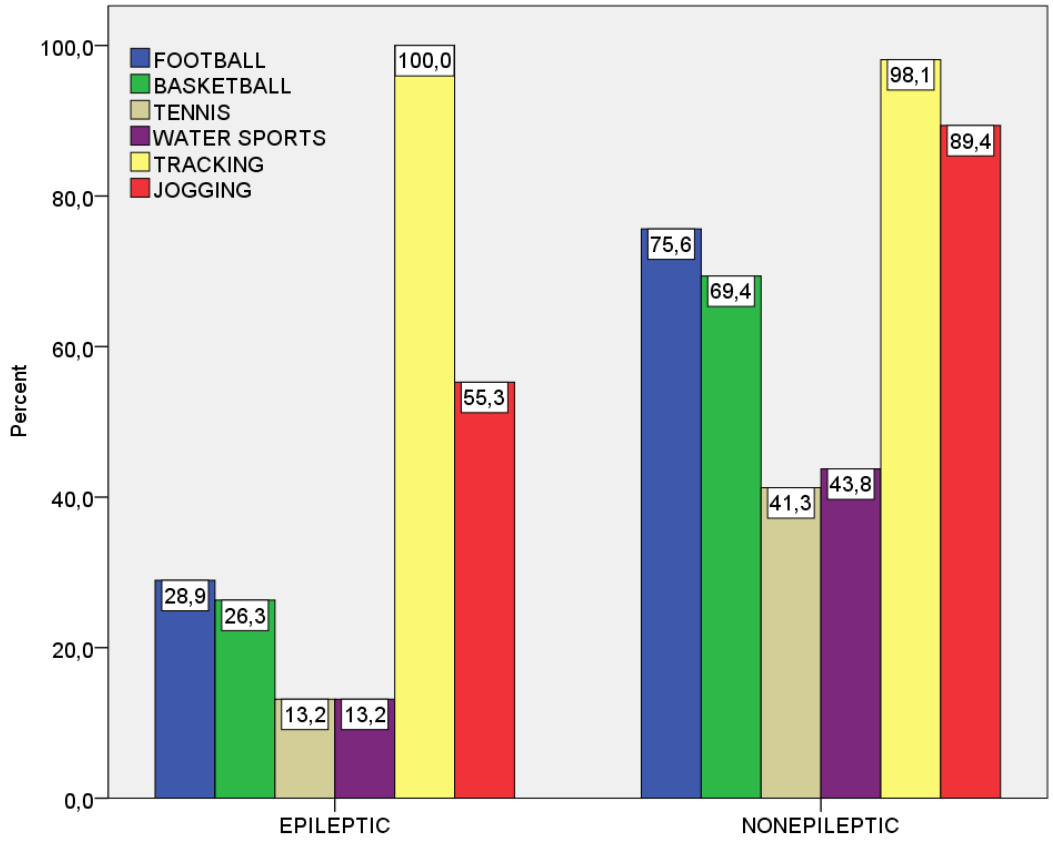


Figure 19. Comments of epileptic and nonepileptic participants on sportive activities

Among people, there is a prejudgement that epileptic patients exactly have mental retardation. This behaviour of other people to epileptic people can lead to them to have depressive mood. As a result, epileptics feel themselves lonely and isolated.

In the researches, there is no association between mental retardation and epilepsy. Insomuch that, according to the some beliefs and examples from the life, epileptics have superior abilities. For instance, Napoleon, Julius Cesar, Neyzen Tevfik, Beethoven were brilliant epileptics of their ages.

According to the result of the questionnaire, 68, 1 % of epileptic participants said “NO” and gave right answer while 77, 9 % of nonepileptics noted as “NO”. It is shown in the table 23 below, cross tabulation of question 1 and 19.

Table 23. Comments of participants on epilepsy and mental retardation association

CROSSTABULATION OF Q1 & Q19			MENTAL RETARDATION			
			YES	NO	NO IDEA	Total
PARTICIPANTS	EPILEPTIC	Count	3	32	12	47
		% within Q1	6,4%	68,1%	25,5%	100,0%
	NONEPILEPTIC	Count	2	134	36	172
		% within Q1	1,2%	77,9%	20,9%	100,0%
Total		Count	5	166	48	219
		% within Q1	2,3%	75,8%	21,9%	100,0%

As it is understood, knowledge about this subject is not very well because when it is looked to the total population of participants, 21, 9 % of them also noted that they had no idea for this question. So, people should be informed and told that there is no association between epilepsy and mental retardation.

One of the most important things for epileptics is sleeping. Epileptic patients must have enough sleep and sleep at same time possibly because insufficient sleep time can increase the frequency of seizures. So, it can be said that epilepsy is related with sleep pattern of the patients.

According to the answers of the respondents, 60, 7 % of all participants are aware of relationship between sleep pattern and epilepsy. 49 of all respondents said “NO IDEA” (22, 4 %) and finally, 16, 9 % of participants noted that there is not an

association between epilepsy and sleeping. When it is examined well, it is obviously seen that last two percentages are not low to regard as too little. The results are shown below, in the figure 20.

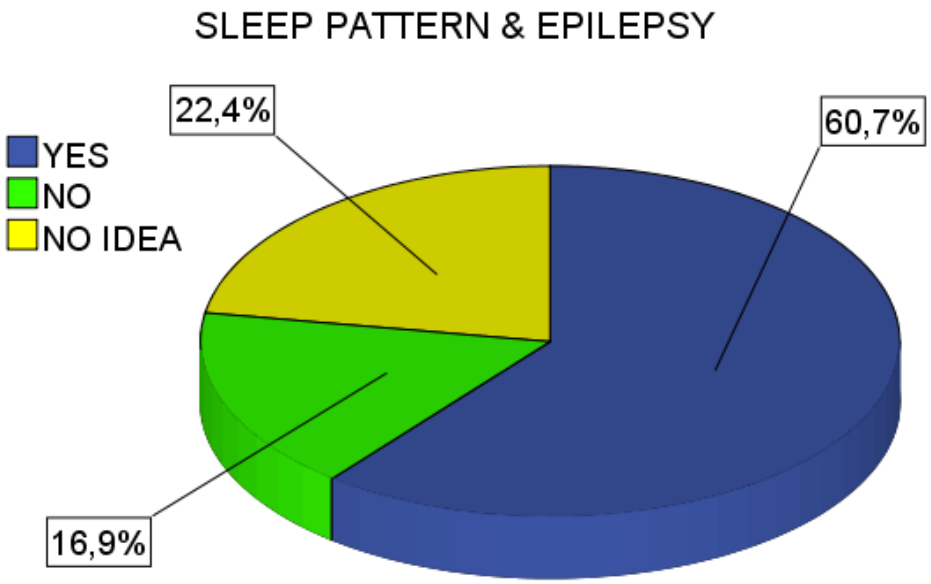


Figure 20. Relationship between epilepsy and sleep pattern

In the 21st question, which drugs effect the seizures are asked to the participants and assessment of this question was done in two parts.

First, health employees are compared such as doctors and pharmacists. According to the results, shown in the table 24, both doctors and pharmacists have knowledge on drugs which affect the seizures.

Table 24. Knowledge comparison of health employees about drugs that affect epileptic seizures

			DRUG INFO	
			YES	Total
JOB	DOCTOR	Count	5	5
		Expected Count	5,0	5,0
		% within JOB	100,0%	100,0%
	PHARMACIST	Count	13	13
		Expected Count	13,0	13,0
		% within JOB	100,0%	100,0%
Total		Count	18	18
		Expected Count	18,0	18,0
		% within JOB	100,0%	100,0%

Secondly, knowledge difference between health employees and other profession employees is compared. According to the result, all 18 health employees know that which drugs affect the seizures while 18, 9 % (n: 38) of remaining 201 people who are the members of variety of occupations know the drugs that affect negatively.

Table 25. Knowledge comparison of health employees and other sectors employees about drugs that affect frequency of seizures

			DRUG INFO		
			YES	NO	Total
JOB	HEALTH	Count	18	0	18
		% within JOB	100,0%	,0%	100,0%
	OTHERS	Count	38	163	201
		% within JOB	18,9%	81,1%	100,0%
Total		Count	56	163	219
		% within JOB	25,6%	74,4%	100,0%

When looking to the total knowledge distribution of the participants, it is obviously seen in table 25 above that 74, 4 % of all respondents gave “NO” answer and explained that they did not know any drug that affect the seizures.

22nd question asked whether epilepsy is shown at any age in the lifetime. The result of the question is observed as expected. According to the results, 90, 0 % of all participants said “YES” while remaining 8, 2 % and 1, 8 % said “NO IDEA” and “NO”, respectively. When looking to the ratios shown in the figure 21, result is not significant statistically.

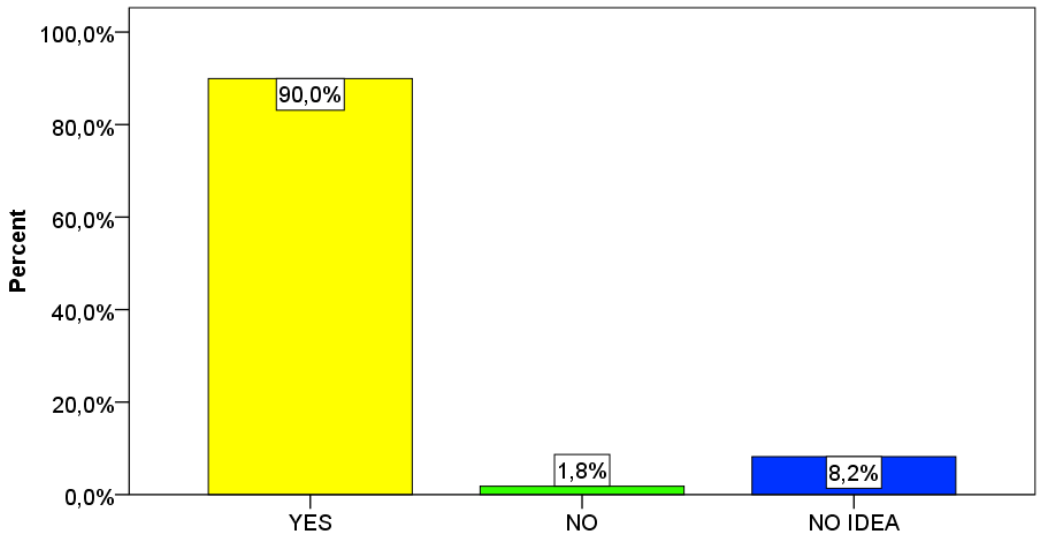


Figure 21. Can epilepsy be observed at any age?

Finally, the last question of the questionnaire was about source of knowledge on epilepsy disease, asked to the respondents. This question compares the educational levels and information sources of the participants. For example, 71,4% of master / doctorate degree participants take information from their neighbours. Additionally, neighbour ratio is high in participants with university education (55, 6 %). Again,

internet use among participants with primary education degree is very high as a source for obtaining epilepsy.

When considering the doctors and pharmacists as information source of epilepsy, both of them have same ratios in primary and master/doctorate education grade participants, 45, 5 %, 42, 9 %, respectively.

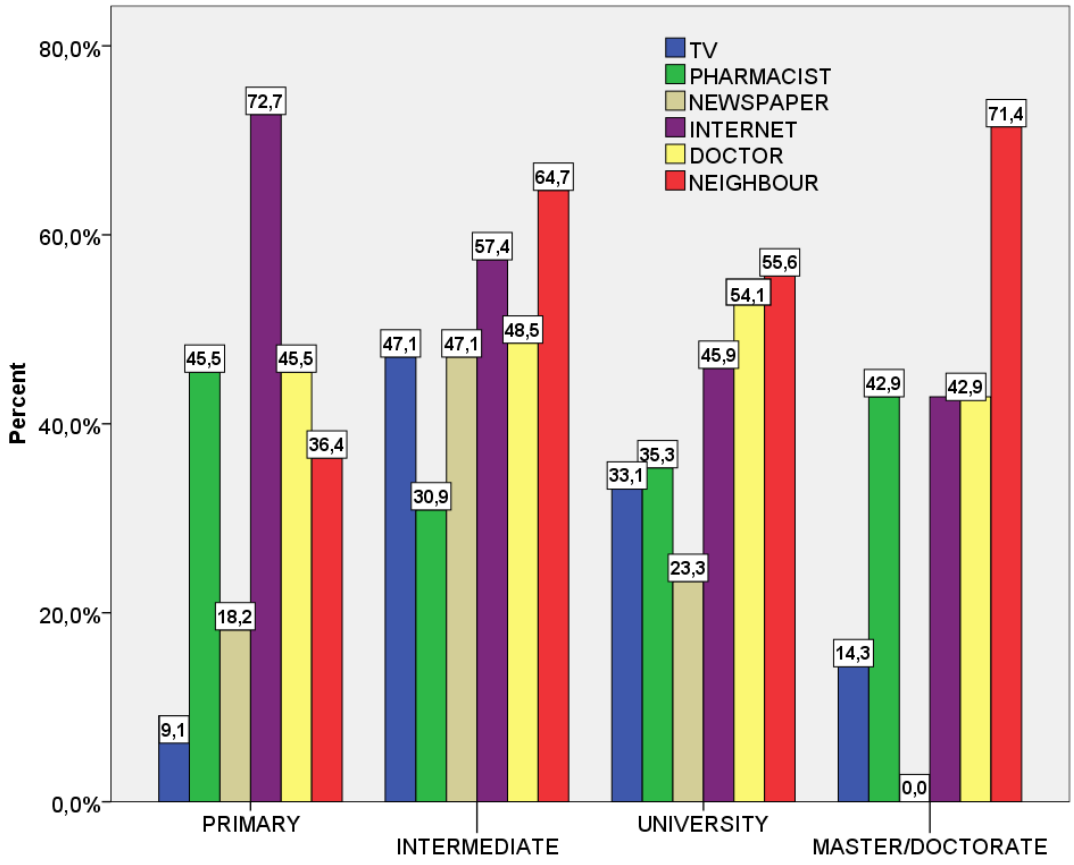


Figure 22. Education levels and information source

5. DISCUSSION

This study has a so important property that this is the first scientific research which aims to measure the epilepsy knowledge of the public in Turkey. With this study, wrong information known as right by the public are revealed and tried to correct.

When the overall findings are assessed, it can be said that gender has no statistically significant effect to become or being epileptic. So, epilepsy incidences in females and males are 59, 6 % and 40, 4 %, respectively.

The result shows that seizures of 72, 3 % epileptic people are under controlled. It could be commented in this way that new antiepileptic drugs are more effective and successful in order to control seizures. With the improvement of technology, science and medicine, perhaps epilepsy will be completely cured in future.

When the findings are examined, it can be seen that people do not know that coffee, tea and fizzy drinks like coke are not hazardous if they are not consumed in high quantities and at the same time with drug. On the other hand, although most of the participants said alcohol and smoking is banned to consume, especially for epileptics, remaining few of them explained there is no limitation to consume. Thus, people are informed about these points.

Most of the participants (n: 119) do not have enough detailed info about driving licence for epileptics. Driving licence regulations for epileptics show differences from country to country. According to the regulations in Turkey, epileptics can have H class driving licence and can use their automobiles that have special equipment. When an epileptic person applies for a driving licence, first he/she go to a neurologist and must take a health report that shows her/his suitability to drive a car with contain special kits and equipments. As a conclusion, they are educated, informed and if there is a need, they are directed.

It is obviously seen that there is a prejudice against epileptic people. Statements of most participants about military service of the epileptic male are the evidence of this. All epileptic males are not free of military service. There are some regulations for the assessment of this. In Turkey, whether an epileptic male is suitable for military service or not, is determined according to the 12th article of Turkish Armed Forces Health Capability Ordinance. So, public and especially epileptic males are also educated and informed about military service subject.

Nearly, all participants have enough knowledge about drug timing (n: 84, 9). It is not only important for antiepileptic drugs but also for other drugs. However, against any possibility, patients are informed, warned and recommended about drug timing.

In the questionnaire, one question is the most identical for social life problems of epileptic people and to this question epileptic participants (74, 5 %) gave much more accurate answer than nonepileptic participants (48, 3 %). It can obviously be understood from the results that epileptic people are aware of their social problems and they are exposed to social forces mostly by other people. Thus, they can be informed and educated about their social possibilities. If these efforts are insufficient in order to solve the problem, they should be directed to the psychologist. Because unless it is treated, these problems can lead to depressive condition.

About treatment and cure of epilepsy there are very different and inconsistent answers from respondents. Possibly, they do not know the difference between treatment and cure. So, people should be told that there is no cure but it can be treated and under controlled with drugs. Besides these, all epileptic patients, their families and neurologists hope for the discovery of a mysterious drug or brilliant surgical procedure to get rid of epilepsy completely, in the future.

Some questions like 12th, 13th, 14th and 15th were used to compare knowledge of men and women. It was expected that women know well and parallel to the expectation, results show that women have more info about these questions related to

themselves. Especially, in the question about pregnancy restriction that is 12th question, 57, 7 % of females gave right answer explain that there was no restriction for epileptic females to become pregnant.

Secondly, in the 13th question, 46 of 97 female participants said epileptic women can bear normally, there is no need caesareans and gave right answer.

Also, to the 14th question related to connection of epilepsy and genetic structure of an epileptic woman, 142 participants gave right answer. 71, 1 % of females and 59, 8 % of males are the distribution ratios of these 142 respondents. Also, 44, 7 % of all epileptics explain that they had no idea on this subject. This condition is very thought-provoking so public, especially epileptic people must be informed by the pharmacists on this subject.

Finally, in the 15th question, it may be possible to have epileptic baby if a member of parent has epilepsy so most of the respondents (89, 6 %) said that it is possible to see epilepsy in baby.

To sum up, although women participants have more knowledge than men, public should be informed about these subjects. Because these events can effect health of the baby, mother or father or of all family in their future life. In addition, they should be recommended required tests before conception process.

One of the most essential subjects is drug usage in epileptics. If a person has epilepsy disease, he/she must be more careful at drug preference. Whenever epileptic person has any illness, he/she should define that he/she is an epileptic to the doctor. Because, if the doctor does not know the condition of patient, people with epilepsy may be recommended hazardous drug, accidentally and seizures may increase unfortunately.

In this questionnaire, drug use and preference in the most common disease, influenza, was examined among epileptics and nonepileptics and then both group were compared. The results show that epileptic patients use drugs, unconsciously. The most obvious example of this is antibiotic ratio that 60 % of epileptic who use drug when they have influenza, use antibiotic. All of the epileptics use pastille to relieve their throat and when compare with the nonepileptic patients, epileptic patients use more antibiotics than nonepileptics. When considering the result, it is understood that epileptics do not have sufficient information about antibiotic usage.

To sum up, it is understood obviously from the findings that, epileptic patients should ask for advice from their doctor or pharmacist in order to treat any of their disease in order to prevent any possible side effect raised from wrong drugs choice. Additionally, not only doctors or pharmacists should inform their patients but also epileptic patients improve themselves. If there is a problem in the prescription of the epileptic person, pharmacist should connect with patient's doctor and warn the patient, considering the patient, possibility of not to explain his/her epileptic condition to the doctor.

Moreover, both epileptic and nonepileptic respondents explained that all epileptic patients can do sportive activity. This is partially right but some of them especially extreme sports like fencing are very hazardous and they are not recommended by the doctors. Tracking and jogging sports are the most popular answers given by the respondents. Additionally, some sports like cycling and swimming can also be done if they are accompanied by a person.

There is no evidence and accuracy that epilepsy causes mental retardation. However in our public, there is a common prejudgement that epileptics lack mentally. This is a wrong opinion causes epileptic patients depressive, shy in the public and isolated from the life. In order to prevent this prejudice, people must be informed by pharmacist, doctors. If needed medical television programmes and advertisements should be organized. Furthermore, brochures, handbooks and pocketbooks should be published

and distributed to the people in order to inform them about epilepsy by Ministry of Health. Thus, prejudice of the public against epileptic patients can be prevented.

Yet another important knowledge measurement is about relationship between sleep pattern and epilepsy. As it is known that from scientific researches, sleep regularity is important complementary part of the epilepsy treatment. Epileptic patients pay attention their sleeping time. They must sleep at same time everyday, possibly. Patients with epilepsy and their families should be informed about regularity of sleep pattern and epileptic patients have to be in the habit of sleeping at same time.

Among participants, there are 5 doctors and 13 pharmacists and when they are compared regarding on drugs that increase frequency of seizure, findings shows that both professions have good info about these drugs. On the other hand, when looking to the members of the other occupations, most of the respondents have no knowledge about these drugs. Considering that the most of the participants learn information epilepsy from their neighbours, it can be very dangerous. Because in our country, if a drug treat disease of someone's' neighbour, he/she use that drug easily. In this case, if there is a drug interaction between two drugs, because they are not aware of this, unwanted event can be seen. As conclusion, all people must be informed by the health authorities and consumer reports as in USA.

Another comparison is the effect of education level on epilepsy knowledge. There are few important statistically significant results. However, in general the education level does not affect the knowledge about epilepsy.

This result can be interpreted in this way, that most of the participants including university and master/doctorate graduates, obtain their knowledge from their neighbours. Secondly, internet is the most common info resource of the participants. As is well-known whole of the internet info is not reliable and correct.

To sum up, people must be informed scientifically by the authorities and public is directed to the reliable and correct sources. Besides these applications, people get information from their pharmacists and doctors.

6. CONCLUSION

In order to break prejudgements of public and to prevent the isolation of epileptic people due to misunderstood by community, some future works may be organized.

For example, consumer leaflets or reports may be prepared and distributed to the public in order to improve their knowledge about epilepsy, as in USA. Moreover, seminars should be organized by Society of Clinical Pharmacy to increase the knowledge capacity of pharmacists. Thus, with this educational seminars, they can help and give more and more accurate information to their both epileptic and nonepileptic patients.

Additionally, articles about epilepsy should be published by the authorities in order to inform public. If needed extra brochures may be distributed to the patients in community pharmacies.

As a conclusion, by the help of these informative activities, people with epilepsy are treated and understood well by nonepileptic people and they do not suffer from feeling of isolation.

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APPENDIX 1

EPİLEPSİ BİLGİLENDİRME FORMU

Ad - Soyad : **Eğitim durumu:** İlköğretim □

Cinsiyet: Ortaöğretim □

Yaş: Üniversite □

Meslek: Üniversite üzeri □

S-1) Epilepsi (Sara) hastalığına sahip misiniz?

Evet □ Hayır □

Evet ise: Hastalığınız için hangi ilaçları kullanıyor sunuz?

.....

.....

.....

.....

1. soruya HAYIR cevabını verdiyseniz 2. soruyu cevaplamadan 3. soruya geçiniz.

S-2) Hastalığınız (nöbetleriniz) kontrol altında mı?

Evet □ Hayır □

S-3) Epileptik bir kişinin kola ve benzeri gazlı ürünlerden içmesinde sakınca var mıdır?

Evet □ Hayır □ Bilgim yok □

S-4) Epileptik bir kişinin sürücü belgesi almasına ve araç kullanmasına engel var mıdır?

Evet □ Hayır □ Bilgim yok □

S-5) Epilepsi hastalığı olan bir erkek askerlik yapabilir mi?

Evet □ Hayır □ Bilgim yok □

S-6) Alkol alınmasının epileptik hastalara bir zararı var mıdır?

Evet □ Hayır □ Bilgim yok □

S-7) Epileptik bir kişinin sigara içmesinin hastalığa bir etkisi var mıdır?

Evet □ Hayır □ Bilgim yok □

S-8) Antiepileptik ilaçların kullanım zamanları önemli midir?

Evet □ Hayır □ Bilgim yok □

S-9) Epilepsi sosyal yaşamı etkileyebilir ve psikiyatrik sorunlara yol açabilir mı?

Evet □ Hayır □ Bilgim yok □

S-10) Epilepsi hastalığı bulaşıcı mıdır?

Evet □ Hayır □ Bilgim yok □

S-11) Epilepsi tamamen tedavi edilebilir mi?

Evet □ Hayır □ Bilgim yok □

S-12) Epileptik bir bayanın hamile kalmasında bir engel var mıdır?

Evet □ Hayır □ Bilgim yok □

S-13) Epileptik bir bayan normal doğum yapabilir mi?

Evet □ Hayır □ Bilgim yok □

S-14) Epileptik bir bayanın hamile kalması durumunda doğacak bebekde bir sorun olabilir mi?

Evet □ Hayır □ Bilgim yok □

S-15) Epilepsi hastalığına sahip bir kişinin çocuğunda da epilepsi görülebilir mi?

Evet □ Hayır □ Bilgim yok □

S-16) Çay, kahve gibi içeceklerin hastalığa etkisi var mıdır?

Evet □ Hayır □ Bilgim yok □

S-17) Gribal bir enfeksiyon geçirdiğinizde herhangi bir ilaç kullanır mısınız?

Evet □ Hayır □

Evet ise: Bu ilaçların isimlerini belirtiniz.

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S-18) Epileptik insanlar spor yapabilirler mi?

Evet □ Hayır □ Bilgim yok □

Evet ise: Hangi tür sporları yapabilirler?

Futbol □

Basketbol □

Tenis □

Su sporları □

Yürüyüş □

Koşu □

S-19) Epilepsi hastalığı herhangi bir zeka geriliği yaratır mı?

Evet □ Hayır □ Bilgim yok □

S-20) Epilepsi hastalığı kişinin uyku düzeniyle alakalı mıdır?

Evet □ Hayır □ Bilgim yok □

S-21) Diğer hangi tür ilaçların epileptik nöbetleri artıracağı hakkında bir bilginiz var mı?

Evet □ Hayır □

Evet ise: Nöbetleri artıracağını bildiğiniz ilaç türlerine örnek veriniz.

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S-22) Epilepsi her yaşta görülebilir mi?

Evet □ Hayır □ Bilgim yok □

S-23) Epilepsi hastalığı ile bilgileri en çok nereden edindiniz?

Televizyon □ Gazete □ Doktor □

Eczacı □ İnternet □ Eş-Dost □

APPENDIX 2

EPILEPSY INFORMATION FORM

Name-Surname: **Education level:** Primary □

Sex: Intermediate □

Age: University □

Profession: Master/Doctorate □

Q-1) Have you got epilepsy disease?

Yes □ No □

If Yes: Which drugs do you use?

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If you said "NO" to the fist question, pass to the third question.

Q-2) Are your seizures under control?

Yes □ No □

Q-3) Is there any disadvantages to epileptic person to drink fizzy drinks like coke?

Yes □ No □ No idea □

Q-4) Is there any restrictions to epileptic person to take a driving licence and to drive a car?

Yes □ No □ No idea □

Q-5) Can a male with epilepsy do military service?

Yes □ No □ No idea □

Q-6) Is there any harm to epileptic patients to take an alcohol?

Yes □ No □ No idea □

Q-7) Is there any effects of smoking of an epileptic person to the disease?

Yes □ No □ No idea □

Q-8) Is the usage time of antiepileptic drugs important?

Yes □ No □ No idea □

Q-9) Can epilepsy effect social life and cause psychiatric problems??

Yes □ No □ No idea □

Q-10) Is epilepsy contagious?

Yes □ No □ No idea □

Q-11) Can epilepsy be treated completely?

Yes □ No □ No idea □

Q-12) Is there any restrictions on pregnancy of an epileptic female?

Yes □ No □ No idea □

Q-13) Can an epileptic female give birth normally?

Yes □ No □ No idea □

Q-14) Can a problem appear in a baby birth, in the case of a pregnancy of an epileptic female?

Yes □ No □ No idea □

Q-15) Can epilepsy appear in a baby of epileptic person?

Yes □ No □ No idea □

Q-16) Is there any effects of drinks like tea and coffee to the disease?

Yes □ No □ No idea □

Q-17) When you have a gribal infection, do you use any drugs?

Yes □ No □

If Yes: write the name of these drugs.

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Q-18) Can epileptic people do sports?

Yes □ No □ No idea □

If Yes: Which type of sports can they do?

Football □

Basketball □

Tennis □

Water sports □

Tracking □

Jogging □

Q-19) Does epilepsy cause mental retardation?

Yes □ No □ No idea □

Q-20) Is epilepsy related with the sleep pattern of the patient?

Yes □ No □ No idea □

Q-21) Have you got any idea which type of drugs increase the frequency of epileptic seizures?

Yes □ No □

If Yes: Give examples to type of drugs that increase the frequency of seizures.

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Q-22) Can epilepsy be shown at any age?

Yes □ No □ No idea □

Q-23) where did you get information about epilepsy, mostly?

Television □ Newspaper □ Doctor □

Pharmacist □ Internet □ Neighbour □

CURRICULUM VITAE

CAGLAR MACIT

Caglar Macit was born on 23/10/1983 in Ankara-Turkey. He finished primary school in Nigde. In 1992, he started to Nigde Anatolian High School and graduated from there in 2002. He won a place at Yeditepe University Faculty of Pharmacy, in 2002 summer. When he studied in fourth class of the faculty, he was elected class representative. He graduated with a B.Sc. (Pharm.) degree in 2007 and the name of his graduation project is “AGESFREE STIMULUS”. After graduation, he started to work as a Research and Teaching Assistant in the Clinical Pharmacy Department in Yeditepe University Faculty of Pharmacy. In the same year, he started his M. Sc. Degree in Clinical Pharmacy Programme and his M. Sc. Thesis entitled “Assessment of the Knowledge about Epilepsy among Epileptic Patients, Nonepileptic Patients and Community Pharmacists and The Provision of Education on Epilepsy” under the supervision of Assist. Prof. Dr. Philip Martin Clark in the Department of Clinical Pharmacy in Yeditepe University and also co-advisor of Prof. Dr. Canan Aykut Bingol in the Department of Neurological Sciences in Yeditepe University Hospital. He has a lot of poster presentations in national and international meetings and seminars. Caglar Macit is currently employed as Research and Teaching Assistant in Yeditepe University, Faculty of Pharmacy, Department of Clinical Pharmacy.