Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 8, Nov. 2024
Manuscript ID ZUMJ-2408-3542 (R1) DOI . 10.21608/zumj.2024.315909.3542
ORIGINAL ARTICLE

Value of Assessment of Serum Interleukin-6 in Epileptic Patients

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Submit Date 27-08-2024
Revise Date 12-09-2024
Accept Date 13-09-2024

ABSTRACT

Background: The immune system has been a hotspot for epilepsy researchers during the past decade. The outcome of this is an ever-increasing body of knowledge about the role of several immunological variables in the development of epilepsy and seizures epileptogenesis.

Methods: We carried out this case-control study in the Neurology Clinic and Neurology Department, Faculty of Medicine, Zagazig University Hospitals,on 224 persons categorized into two groups: 112 epileptics and 112 controls. Comprehensive evaluations were conducted on all patients, including electroencephalograms, brain MRIs, standard laboratory tests, as well as serum interleukin-6 (IL-6) levels that were assessed by an enzyme-linked immunosorbent assay (ELISA).

Results: Patients with epilepsy had a significantly elevated serum IL-6 level compared to the control group (P<0.001). Astatistically significant difference was detected between drug-responsive and drug-non-responsive patients as regard IL-6, as the mean level of IL-6 was higher among drug-non-responsive patients (P=0.02).Also, IL-6 level was significantly higher among patients with generalized tonic-clonic seizures (P=0.02). The median level of IL-6 was significantly higher among patients who received polytherapy compared with those on monotherapy (P=0.001). Also, the median IL-6 level was significantly higher among patients who had generalized epileptiform activity compared with those who had partial-onset seizures(P=0.01).

Conclusions: The correlation between serum IL-6 levels and epilepsy was statistically significant. Epileptic seizures could induce the production of IL-6, and a high concentration of IL-6 could be an obvious neurotoxic and pro convulsion factor.

Keywords: Interleukin-6; Seizure; Refractory epilepsy; Neuroinflammation.

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INTRODUCTION

More than 70 million people across the globe could experience epilepsy, making it one of the most prevalent and severe brain disorders. Both newborns and the elderly are at a higher risk than younger age groups when it comes to its incidence. The intricate genetic architecture of the most prevalent forms of epilepsy is being revealed by advances in genomic technology, which is causing paradigm shifts [1,2].

An immunological response, neuro-inflammation, protects the central nervous system (CNS), but it can be detrimental when stimulated to dangerous levels. The neuroinflammation process is initiated in the brain in response to stressors in order to reduce neuronal damage and neurode-generation. To maintain synaptic plasticity and enhance neurogenesis, cytokine production and toll-like receptor activation are the principal mechanisms that can be utilized. Concurrently, there are a number of pathways that are set in motion to control and alleviate neuroinflammation. But in other instances, neurodegeneration and other negative outcomes are brought about by protracted inflammation and overexpression of cytokines by highly activated glial cells. Therefore, acute neuroinflammation protects brain tissue while also stimulating neurogenesis and repair. But persistent inflammation can damage CNS tissues [3-5].

All cells in the CNS, including neurons and glial cells, are impacted by neuro-inflammation, which can be caused by brain injury or systemic inflammation. It changes the brain's signaling pathways. The brain becomes susceptible to ictogenesis and epileptogenesis due to neuronal hyperexcitability caused by imbalanced mediators and elevated mediators associated with inflammation [6-9].

This work aimedto assess the possible relationship between interleukin-6 (IL-6) and epilepsy and its relationship with refractory epilepsy.

METHODS

This case-control study included 224 individuals divided into two groups. Group 1 (the epilepsy group)included 112 adult patients with idiopathic epilepsy, whose ages ranged from 19 to 63 years with a mean of 35.9±11.4. 58% of them were males and 42%were females. Group 2 (the control group) included 112 apparently healthy individuals who visited our clinics. Their ages ranged from 19 to 58 years with a mean of 33.6±10.5. 54.5% of them were males and 45.5% were females.

Furthermore, the epilepsy group was subdivided into two subgroups:drug-responsive and drug-resistant groups. The drug-responsive group included 52 patients, whose ages ranged from 23 to 50 years with a mean of 33.9±7.83. 61.5% of them were males and 38.5% were females. The drug-resistant group included 60 patients, whose ages ranged from 19 to 36 years with a mean of 37.6±13.6. 55% of them were males and 45% were females. Patients in the latter subgroup were diagnosed with refractory epilepsy, according to the International League Against Epilepsy (ILAE), when seizure independence was not achieved after sufficient trials of two antiepileptic medications that were well-tolerated, selected, and delivered [10].

The Academic and Ethical Committee at Zagazig University gave their approval to the study (IRB#10661). Every single participant gave their written informed consent. All procedures followed here adhere to the guidelines laid out in the Declaration of Helsinki, which is part of the World Medical Association's Code of Ethics for Research Involving Humans.

Inclusion criteria

The current study included patients older than 18 years of both genders diagnosed with idiopathic epilepsy based on patient and witness history in accordance with the ILAE criteria[11].

Exclusion criteria

Patients with secondary epilepsy (diagnosed by history taken from patients and/or relatives and confirmed by MRI brain), patients aged 18 or less, patients with special epileptic syndrome, patients with severe adverse drug reactions or history of alcohol or drug abuse, patients receiving epileptogenic drugs, patients with severe mental or psychiatric diseases, people with severe infections or inflammatory diseases, pregnant or breastfeeding women, and those with uncontrolled diabetes mellitus, hypertension, cardiovascular disease, kidney disease, liver disease, neoplasms, or connective tissue disorders were all excluded as these conditions may be associated with elevated serum IL-6 levels.

History and clinical evaluation

Epileptic patients have been subjected to detailed history taking and neurological examination with a focus on family history, prenatal, natal, and postnatal history, developmental history, age of epilepsy onset, frequency of attacks per month, time of the last attack and its duration before blood sampling, history of status epilepticus, medications used in treatment either monotherapy or polytherapy, and type of seizures divided according to the ILAE into generalized, focal, and epilepsy syndromes.

Laboratory investigations

All patients and healthy controls were subjected to full routine lab investigations, including a complete blood picture, kidney and liver function tests, blood glucose level, serum electrolyte level,erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). The serum level of IL-6 was assessed by an enzyme-linked immunosorbent assay (ELISA).

Electroencephalography

Electroencephalography (EEG) was done using the 10-20 system, with 22scalp electrodes and 16 channels (alvar-model) EEG equipment, with various provocative methods, including photic stimulation, hyperventilation, and sleep deprivation, for 60 minutes. It was done for all epileptic patients for the interictal phase to confirm and classify type of epilepsy and for follow-up in cases of drug-resistant epilepsy.

Radiological investigations

Magnetic Resonance Imaging (MRI) of the brainwas performed using PhilipsAchevia 1.5T MRI machine. It was done for all epileptic patients to exclude secondary epilepsy.

***Statistical analysis*:**

Data were gathered, tabulated, and analyzed using SPSS (statistical package for social science) version 20.0 (SPSS Inc., Chicago, IL, USA). Quantitative data was shown as mean ± standard deviation (SD), median, and interquartilerange (IQR), whereas qualitative

data was expressed as numbers and percentages. The Mann-Whitney U test, Chi-square test, Fisher exact test, and Kruskal-Wallis test were used for data analysis.To indicate significant results, the *P* value was set at less than 0.05, and for highly significant results, it was set at less than 0.001.

RESULTS

Table (1) shows, as regard type of seizures, the most frequent type was generalized tonic-clonic seizures (GTCS), which was detected among 80.4% of patients, while the least frequent types were focal seizures and focal with secondary GTCS, which were detected among 9.8% of patients for each.

Table (2) shows a non-significant difference between drug-responsive and drug-resistantgroups as regards age, sex, family history of epilepsy, age at onset of illness, duration of disease, and type of seizures.

Table (3) shows a statistically significant difference between drug-responsive and drug-resistant patients as regard IL-6, as the mean level of IL-6 was higher among drug-resistant patients (*P*=0.02), and it was significantly higher among patients with GTCS (*P*=0.02). Also, the median level of IL-6 was significantly higher among patients who received polytherapy (*P*=0.001).

Table (4) shows a statistically significant increase in the value of IL-6 among epileptic patients (*P*<0.001) when compared to the control group.

Table (5) shows a statistically significant difference between drug-responsive and drug-resistant patients as regard IL-6, as the mean of IL-6 was higher among drug-resistant patients (*P*=0.002).

Table 1: Seizures characteristics among the epilepsy group

Variables		**Epilepsy group (n=112)**
Type of seizures *(N.%)*	Generalized tonic-clonic seizures	90 (80.4%)
	Focal seizures	11 (9.8%)
	Focal with 2ry generalization	11 (9.8%)
History of status epilepticus *(N.%)*	Absent	77 (68.8%)
	Present	35 (31.3%)
Frequency *(/month)*	Median (IQR)	3 (4)
	Range	(0.08 – 90)

Table 2: Demographic and clinical data of drug-responsive and drug-resistant epileptic patients

Variables		**Drug-responsive (n=52)**	**Drug-resistant (n=60)**	***P* value**
Age *(years)*	*Mean ± SD*	33.9 ± 7.83	37.6 ± 13.6	0.28[1]
	Range	(23 – 50)	(19 – 63)	
Sex *(N.%)*	Male	32 (61.5%)	33 (55%)	0.48[2]
	Female	20 (38.5%)	27 (45%)	
Family history of epilepsy *(N.%)*	Absent	36 (69.2%)	46 (76.7%)	0.38[2]
	Present	16 (30.8%)	14 (23.3%)	

Variables		Drug-responsive (n=52)	Drug-resistant (n=60)	*P* value
Age at onset *(years)*	*Median (IQR)*	21 (19)	22 (15)	0.76[1]
	Range	(2 – 33)	(3 – 51)	
Duration *(years)*	*Median (IQR)*	20 (16)	13 (11)	0.17[1]
	Range	(1 – 39)	(4 – 34)	
Type of seizures *(N.%)*	GTCS	44 (84.6%)	46 (76.7%)	0.12[3]
	Focal seizures	6 (11.5%)	5 (8.3%)	
	Focal with 2ry generalization	2 (3.8%)	9 (15%)	
History of status epilepticus *(N.%)*	Absent	46 (88.5%)	39 (65%)	**0.003[2]**
	Present	6 (11.5%)	21 (35%)	
Frequency *(/month)*	*Median (IQR)*	1 (2.83)	4 (3.75)	**<0.001[1]**
	Range	(0.08 – 12)	0.3 (90)	
Type of treatment *(N. %)*	No therapy	0 (0%)	0 (0%)	**<0.001[3]**
	Monotherapy	39 (75%)	0 (0%)	
	Polytherapy	13 (25%)	60 (100%)	

[1]*Mann-Whitney U test*
[2]*Chi-square test*
[3]*Fisher exact test*
P value >0.05 was considered non-significant
P value ≤0.05 was considered significant

Table 3: Association of IL-6 with demographic and clinical data among the epilepsy group

Variables		IL-6 *Median (IQR)*	P Value
Sex	Male	2.21 (2.09)	0.54[1]
	Female	2.81 (1.35)	
Family history of epilepsy	Absent	2.74 (1.79)	0.84[1]
	Present	2.44 (1.87)	
Type of seizures	GTCS	7.6 (26.25)	**0.02[2]**
	Focal seizures	1.02 (2.17)	
	Focal with 2ry generalization	2.66 (1.65)	
History of status epilepticus	Absent	2.66 (2.09)	0.85[1]
	Present	2.36 (1.87)	
Type of treatment	Monotherapy	1.77 (2.99)	**0.001[1]**
	Polytherapy	2.81 (4.79)	
EEG findings	Normal	1.47 (1.05)	**0.02[2]**
	Focal	1.09 (1.65)	
	GEA	2.96 (3.82)	

[1]*Mann-Whitney U test*
[2]*Kruskal-Wallis test,*
P value >0.05 was considered non-significant
P value ≤0.05 was considered significant

Table 4: IL-6 among the studied groups

Variables		Control group (n=112)	Epilepsy group (n=112)	P Value
IL-6 *(pg/ml)*	*Median (IQR)*	0.17 (0.16)	2.66 (1.79)	**<0.001**[1]
	Range	(0.01 – 0.47)	(0.27 – 48.43)	

[1]*Mann-Whitney U test,*
P value ≤0.05 was considered significant

Table 5: IL-6 among drug-responsive and drug-resistant patients

Variables		Drug-responsive (n=52)	Drug-resistant (n=60)	P Value
IL-6 *(pg/ml)*	*Median (IQR)*	2.14 (1.5)	3.11 (5.83)	**0.002**[1]
	Range	(0.27 – 7.9)	(0.42 – 48.43)	

[1]*Mann-Whitney U test,*
P value ≤0.05 was considered significant

Seizure recurrence is the predominant symptom of epilepsy, a complicated and multifaceted neurological illness [11]. Evidence from clinical trials shows that epileptic foci of brain tissue experience immune activation in individuals with epilepsy, lending credence to the complex link between the immune system and epilepsy. Seizures trigger an inflammatory immunological cascade by activating glial cells around epileptic foci to release inflammatory mediators. Recent evidence suggests that neuroinflammation may have a role in the development of epilepsy and seizures [12].

Inflammatory and immunological mediators play important roles in epileptogenesis and the onset of seizures, according to experimental data. Specifically, it has been demonstrated that cytokines such as IL-1β, IL-6, tumor necrosis factor-α (TNF-α), and toll-like receptor-4 play a role in the origin of seizures and epileptogenesis[13].

In our study, we found that IL-6 was significantly higher among epileptic patients compared to the control group. This was in agreement withseveral otherstudiessinceEzer et al. [14], Tao et al. [15],and Milano et al.[16] reported that patients with epilepsy had higher levels of IL-6 in their serum compared to healthy controls, which may indicate that IL-6 synthesis is increased or that IL-6 metabolism is decreased in these individuals.

In a review of 66 studies involving 1934 patients, de Vries et al. [17] came to the conclusion that IL-1β, IL-6, IL-10, interferon-γ (IFN-γ), and TNF-α were the most studied cytokines in relation to epilepsy and that IL-6, IL-17, and cerebrospinal fluid (CSF) IL1β were elevated in cases of human epilepsy.

On the other hand, the function of IL-6 in neuroinflammation and seizure activity has been the subject of contradictory research in the last several years. There was a statistically significant correlation between elevated IL-6 levels and post-traumatic stress disorder (PTSD), according to Choudhary et al. [12].

Reducing NMDA-mediated neurotoxicity and promoting neuronal differentiation and survival are two effects that IL-6 has been shown to have. Although definitive information about the expression and function of IL-6 in regions of the brain that are known to be epileptogenic is lacking, it is reasonable to assume that higher levels of IL6 in plasma and cerebrospinal fluid are linked to an increased propensity to induce seizures [11].

According to Lehtimaki et al. [18], the CSF compartment and endothelial cells of brain arteries are the primary sources of elevated serum cytokine levels. An individual's threshold for seizures is lowered by elevated levels of pro-inflammatory cytokines in the brain, lending credence to the idea that neuroinflammation plays a role in epileptogenesis[19,20].

Our findings demonstrated that IL-6 was

significantly higher among drug-resistant epilepsy patients compared to drug-responsive patients.On the other hand, IL-6 was higher in patients with a history of status epilepticus than in those without a history of status epilepticus.However, this difference was not statistically significant.

In consistency, Milano et al. [16] reported that the percentage of monocytes positive for IL-6 was greater in drug-resistant patients compared to drug-responsive individuals.

Similarly to our study,El-Fayomy et al. [21] found that when comparing the control group to their patients with refractory epilepsy, they found significantly increased serum levels of IL-6 (P=0.024).

Potere et al. [22] found that drug-resistant epilepsy (DRE) patients with focal epilepsy had higher IL-6 levels and more severe seizureswhen compared with patients with generalized seizures.Sinha et al. [23] found that IL-6 was positively correlated with status epilepticus (P<0.05).

Seizures, according to recent research, accelerate glial cell activation, which in turn increases inflammatory mediator synthesis and promotes an inflammatory process [24].Theneuromodulatory actions of these inflammatory mediators cause alterations in the connection and function of neurons. As a result, there is a possibility that seizures and pro-inflammatory cytokines exacerbate each other, leading to neuronal hyperexcitability and an increased risk of seizures [25].

The blood-brain barrier is disrupted, and seizure activity is maintained when repetitive or prolonged seizures trigger an inflammatory cascade linked to an increase in IL-6 levels [26].

Pletalo et al.[27,28]reported that elevated levels of IL-6 in the serum or CSF were strongly correlated with the severity of seizures (P<0.05).

Compared to individuals with focal epilepsy or focal with secondary generalization, our study indicated that patients with generalized tonic-clonic convulsion had considerably greater levels of IL-6.

Tawfik et al.[29]discovered that individuals suffering from idiopathic generalized tonic-clonic epilepsy exhibited elevated levels of the inflammatory cytokines IL-2, TNF-, and IL-6. The beginning of generalized or tonic-clonic seizures is associated with a quick increase in IL-6 cytokine levels in both plasma and CSF [30].

El-Fayoumy et al. [21] found that patients with focal epilepsy had a higher mean level of IL-6. There was a small but non-significant difference between patients with complex partial seizures and those with focal with secondary generalization or generalized tonic-clonic fits.

Study limitations

The study was conducted in a single hospital, specifically Zagazig University Hospital, limiting the generalizability of the findings to other hospitals both within Egypt and internationally. Furthermore, the study focused on the IL-6 level only with no other markers of neuroinflammation. Further larger studies are also needed to validate the current study findings.

CONCLUSION

Seizures and epilepsy may be intimately linked to elevated IL-6 blood expression. IL-6 could be a significant independent indictor for drug resistance among epileptic patients.

Conflict of interest: None.

Financial disclosures: None.

REFERENCES

1. **Thijs RD, Surges R, O'Brien TJ, Sander JW.** Epilepsy in adults. Lancet. 2019;393(10172):689-701.
2. **Dos Santos IRC, Dias MNC, Gomes-Leal W**. Microglial activation and adult neurogenesis after brain stroke. Neural Regen Res. 2021;16(3):456-9.
3. Rana A, Musto AE. The role of inflammation in the development of epilepsy. J Neuroinflammation. 2018;15(1):1-12.
4. **Uludag IF, Bilgin S, Zorlu Y, Tuna G, Kirkali G**. Interleukin-6, interleukin-1 beta and interleukin-1 receptor antagonist levels in epileptic seizures. Seizure. 2013;22(6):457-61.
5. **Kauffman MA, Moron DG, Consalvo D, Bello R, Kochen S**. Association study between interleukin 1 beta gene and epileptic disorders: a HuGe review and meta-analysis. Genet Med. 2008;10(2):83-8.
6. **Nowak M, Bauer S, Haag A, Cepok S, Todorova-Rudolph A, Tackenberg B, et al.** Interictal alterations of cytokines and leukocytes in patients with active epilepsy. Brain Behav Immun. 2011;25(3):423-8.
7. **Rothaug M, Becker-Pauly C, Rose-John S.** The role of interleukin-6 signaling in nervous tissue. Biochim Biophys Acta. 2016;1863(6 Pt A):1218-27.

8. **Alapirtti T, Rinta S, Hulkkonen J, Mäkinen R, Keränen T, Peltola J.** Interleukin-6, interleukin-1 receptor antagonist and interleukin-1beta production in patients with focal epilepsy: A video-EEG study. J Neurol Sci. 2009;280(1-2):94-7.
9. **Kishimoto T, Kang S, Tanaka T**. IL-6: A new era for the treatment of autoimmune inflammatory diseases. In: Nakao K, Minato N, Uemoto S, eds. Innovative medicine: basic research and development. Tokyo: Springer; 2015.131-47.
10. **Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Allen Hauser W, Mathern G, et al**. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies [published correction appears in Epilepsia. 2010 Sep;51(9):1922]. Epilepsia. 2010;51(6):1069-77.
11. **Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L,et al**. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):512-21.
12. **Choudhary A, Varshney R, Kumar A, Kaushik K.** A Prospective study of novel therapeutic targets interleukin 6, tumor necrosis factor α, and interferon γ as predictive biomarkers for the development of posttraumatic epilepsy. World Neurosurg X. 2021;12:100107.
13. **Ishikawa N, Kobayashi Y, Fujii Y, Kobayashi M.** Increased interleukin-6 and high-sensitivity C-reactive protein levels in pediatric epilepsy patients with frequent, refractory generalized motor seizures. Seizure. 2015;25:136-40.
14. **Ezer R, Ertaşoğlu Toydemir H, Gökyiğit FM.** The relationship between interleukin-6 and epileptic seizure. Ortadogu Tıp Derg. 2020;12(2):225-32.
15. **Tao H, Gong Y, Yu Q, Zhou H, Liu Y.** Elevated serum matrix metalloproteinase-9, interleukin-6, hypersensitive C-reactive protein, and homocysteine levels in patients with epilepsy. J Interferon Cytokine Res. 2020;40(3):152-8.
16. **Milano C, Montali M, Barachini S, Burzi IS, Pratesi F, Petrozzi L, et al**. Increased production of inflammatory cytokines by circulating monocytes in mesial temporal lobe epilepsy: A possible role in drug resistance. J Neuroimmunol. 2024;386:578272.
17. **de Vries EE, van den Munckhof B, Braun KP, van Royen-Kerkhof A, de Jager W, Jansen FE.** Inflammatory mediators in human epilepsy: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2016;63:177-90.
18. **Lehtimäki KA, Keränen T, Huhtala H, Hurme M, Ollikainen J, Honkaniemi J, et al.** Regulation of IL-6 system in cerebrospinal fluid and serum compartments by seizures: the effect of seizure type and duration. J Neuroimmunol. 2004;152(1-2):121-5.
19. **Virta M, Hurme M, Helminen M**. Increased frequency of interleukin-1beta (-511) allele 2 in febrile seizures. Pediatr Neurol. 2002;26(3):192-5.
20. **Librizzi L, Noè F, Vezzani A, de Curtis M, Ravizza T**. Seizure-induced brain-borne inflammation sustains seizure recurrence and blood-brain barrier damage. Ann Neurol. 2012;72(1):82-90.
21. **El-Fayoumy N, El-Massry HH, Montasser M, Ragab A, Mohamed R, Alim S**. Role of interleukin-6 in refractory epilepsy. ESNPN. 2016; 53 (4): 238.
22. **Potere N, Batticciotto A, Vecchié A, Porreca E, Cappelli A, Abbate A, et al**. The role of IL-6 and IL-6 blockade in COVID-19. Expert Rev Clin Immunol. 2021;17(6):601-18.
23. **Sinha S, Patil SA, Jayalekshmy V, Satishchandra P.** Do cytokines have any role in epilepsy? Epilepsy Res. 2008;82(2-3):171-6.
24. **Vezzani A, French J, Bartfai T, Baram TZ**. The role of inflammation in epilepsy. Nat Rev Neurol. 2011;7(1):31-40.
25. **Kothur K, Bandodkar S, Wienholt L, Chu S, Pope A, Gill D,et al**. Etiology is the key determinant of neuroinflammation in epilepsy: Elevation of cerebrospinal fluid cytokines and chemokines in febrile infection-related epilepsy syndrome and febrile status epilepticus. Epilepsia. 2019;60(8):1678-88.
26. **Li G, Bauer S, Nowak M, Norwood B, Tackenberg B, Rosenow F, et al.** Cytokines and epilepsy. Seizure. 2011;20(3):249-56.
27. **Peltola J, Palmio J, Korhonen L, Suhonen J, Miettinen A, Hurme M,et al**. Interleukin-6 and interleukin-1 receptor antagonist in cerebrospinal fluid from patients with recent tonic-clonic seizures. Epilepsy Res. 2000;41(3):205-11.
28. **Peltola J, Laaksonen J, Haapala AM, Hurme M, Rainesalo S, Keränen T.** Indicators of inflammation after recent tonic-clonic epileptic seizures correlate with plasma interleukin-6 levels. Seizure. 2002;11(1):44-6.
29. **Tawfik T, Yehia M, Kishk N, Shalaby N, Shehata R.** Role of inflammatory mediators in idiopathic generalized tonic clonic epilepsy. ESNPN. 2014; 51: 195-9.
30. **Lehtimäki KA, Keränen T, Palmio J, Mäkinen R, Hurme M, Honkaniemi J,et al.** Increased plasma levels of cytokines after seizures in localization-related epilepsy. Acta Neurol Scand. 2007;116(4):226-30.

Citation:

Amer, M., Abdelrheem, E., Lotfy, S., Hashim, N. Value of assessment of serum Interleukin -6 in Epileptic Patients. *Zagazig University Medical Journal*, 2024; (4449-4456): -. doi: 10.21608/zumj.2024.315909.3542