

ASSOCIATION BETWEEN RISK FACTORS AND NEW-ONSE SEIZURES IN OLD AGE POPULATION

ABSTRACT

Objective: To determine the association between risk factors and new-onset seizures in old age population at a tertiary care hospital, Karachi.

Methods: A case control study on old age patients of > 60 years visited emergency department (ED) either with new onset seizure or without seizure were conducted at ED of Ziauddin University Hospital Karachi. 154 consecutive old age patients were distributed into two groups i.e., case group (77 old age patients of new onset seizure (32 male and 45 female) and control group (77 old age patients without seizure (40 male and 37 female)). Risk factors including stroke, dementia, head trauma, metabolic causes, brain tumor, infection of central nervous system (CNS), depression and anxiety were evaluated.

Results: Out of 154 old age patients, male was 32 (41.6%) and 40 (51.9%) and female was 45 (58.4%) and 37 (48.1%) in case and control group respectively. Type of seizure in control group was generalized tonic-clonic seizure (GTCS) in 51 (66.2%) patients and focal seizure in 26 (33.8%) patients. Comorbidities were diabetes mellitus (DM) in 76 (98.7%) and 59 (76.6%) patients, hypertension (HTN) in 72 (93.5%) and 63 (81.8%) patients and ischemic heart disease (IHD) in 39 (50.6%) and 25 (32.5%) patients. Risk factors were stroke in 23 (29.9%) and 16 (20.8%) patients, dementia in 3 (3.9%) and 0 (0.0%) patients, head trauma in 0 (0.0%) and 33 (42.9%) patients, metabolic causes in 27 (35.1%) and 27 (35.1%) patients, brain tumor in 6 (7.8%) and 0 (0.0%) patients, CNS infection in 17 (22.1%) and 1 (1.3%) patients and depression in 2 (2.6%) and 0 (0.0%) patients.

Conclusion: New-onset seizures are significantly associated with age, diabetes mellitus, hypertension, ischemic heart disease, brain tumor and CNS infection.

Keywords: Seizures, stroke, dementia, infection, depression.

1. INTRODUCTION

Seizures are one of the most common diseases of the nervous system in the elderly, second to dementia stroke [1]. Geriatric seizures include:

- 1) Pre-elderly (< 60 years old) epilepsy continuing to old age stage.
- 2) New-onset seizures in the elderly.

Seizures, especially late-onset seizures significantly impact the quality of life of older people and increases the health care resource burden on our society [2].

A recent epidemiological study showed that the average annual incidence of seizures in the elderly aged 65 years and above is up to 240 per 100,000 [3]. Nearly 25% of people newly diagnosed with seizures are under age of 20 and the same proportion of newly diagnosed patients is over the age of 60 [4]. Old age stage is a peak period for developing epilepsy and seizures [5]. The incidence of epilepsy and seizures is higher in the elderly (≥ 60 years old) than in other age groups [6, 7]. It has been estimated that the annual incidence is 85 per 100,000 for people aged 65–69 years, 159 per 100,000 for people aged over 80 years, and 80.8 per 100,000 people in the over all age groups [8].

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Commented [IS2]: it is desirable to indicate the ethnicity of the studied patients

Commented [IS3]: since the size of the abstract is limited, this information is not required here

Commented [IS4]: this information should be transferred to methods (in the description of case and control groups), and only in absolute values, there is no need to write percentages

Commented [IS5]: In the abstract, I recommend writing only percentages with 95% CI boundaries for frequencies

Commented [IS6]: It is not clear which seizures were in the "case" group. From this sentence, it turns out that there were no differences in the samples according to the type of seizures. "Patients" were in both study groups. Only from the names of the formed groups and reading the manuscript it becomes clear that there were no cases of seizures in the control group.

Commented [IS7]: This information is not very well presented. For example, write as follows, "we found statistically significant differences between the groups of patients with and without seizures (control) for the following risk factors (in women): diabetes ...% (95% CI ...-...) vs ...% (95% CI ...-...) in control (p-value = ...); hypertension ...% (95% CI ...-...) vs ...% (95% CI ...-...) (p-value = ...) and so on. And similarly write for men ..

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With increasing age, the prevalence and incidence of epilepsy and seizures increases correspondingly [9]. The existence of some special causes may contribute to the high incidence of epilepsy and seizures in the elderly. It is reported that an underlying etiology can be found in nearly 50% of elderly patients [10]. Younger patients with epilepsy and seizures often show a genetic cause. However, new-onset seizures in the elderly is mainly the consequence of accumulated injuries to the brain and other secondary factors [11-14].

Studies have shown that seizures affect approximately 1 to 2% of the elderly population, and the incidence increases progressively with the advance in age. These cases of epilepsy can occur due to an acute cerebral seizure or have no apparent precipitator [15].

On the other hand regarding diagnosis, there is consensus in the literature that epileptic seizures (ES) are more difficult to diagnose in the elderly for various reasons such as the difficulty in obtaining an accurate clinical history, a frequently atypical ictal presentation, difficulty in making a differential diagnosis between an epileptic and non-epileptic event [16] and due the occurrence of comorbidities [17].

Seizures are considered to be one of the commonest neurological affections in the elderly and considering the fact that the population of the elderly is on the rise, remedial public health measures to address this issue becomes mandatory which is unfortunately abysmal in developing countries. No national publication was found which should address this entity and on the contrary only a few international publications on epilepsy in this age range were found including one important Brazilian study.

New-onset seizures in elderly people often has an underlying etiology, including cerebrovascular diseases, primary neuron degenerative disorders, intracerebral tumors and traumatic head injury [5]. Stroke and other cerebrovascular diseases are the most important risk factors for new-onset epilepsy and seizures in the elderly, which account for 30%–50% in all identified etiologies [20-22]. Stroke is an important cause of epilepsy and seizures [23]. Primary neurodegenerative disorders like Alzheimer's disease (AD) account for around 10%–20% of all identified causes in older people [24].

Head trauma is a common cause of intractable epilepsy and seizures, accounting for 10%–20% of symptomatic seizures in the general population and 5% of all epilepsies [25]. Brain tumor is a common cause of epilepsy and seizures second only to cerebrovascular disease in the elderly, accounting for nearly 10%–30% in all causes of geriatric epilepsy and seizures [3]. Acute symptomatic seizure can occur as a result of CNS insult by infection or inflammation [18,19]. Beside neurological causes there are many metabolic causes of seizures including electrolyte imbalance, increased or decreased glucose and renal or hepatic impairment. In a population-based case-control study on first unprovoked seizures, an association with AD was found in 11% of patients (17/145), leading to a six-fold increase compared to patients without dementia [26]. Sherzai et al. [27] found a 6.9% AD prevalence among patients hospitalised for seizures in a nationwide US sample compared to the healthy elderly population, which is higher than that for other types of dementias, incident stroke (HR, 3.38; 95% CI, 2.78-4.10) and dementia (HR, 2.56; 95% CI, 2.11-3.12) were associated with an increased risk of late-onset epilepsy, while higher levels of physical activity (HR, 0.90; 95% CI, 0.83-0.98) and moderate alcohol intake (HR, 0.72; 95% CI, 0.57-0.90) were associated with a lower risk. The risk of developing unprovoked epileptic seizures was highest less than 2 years before and up to 2 years after a first psychiatric diagnosis [28, 29].

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MATERIAL AND METHODS

STUDY SETTING:

The study was performed at DR Ziauddin University Hospital North Nazimabad Campus, Karachi.

This case control study was conducted in six month of duration.

Data collection procedure:

Patients meeting the inclusion criteria attending outpatient department (OPD) and emergency room (ER) were enrolled in the study. Prior to inclusion patients or informants were explained about benefits of the study and informed written consent was taken.

An approval from the institutional ethics committee was taken prior to commencement of this study. Brief history regarding duration of seizures, co-morbidity (diabetes mellitus, hypertension and ischemic heart disease), history of trauma was taken, and detailed clinical examination was done. Patients were divided into two group case and control as per operational definition. EEG (for clinical documentation) and brain imaging (CTscan and/or MRI) were done to identify the risk factors of new onset seizures and association between risk factors and new onset seizures.

Blood workup like random blood sugar (RBS), urea/creatinine/electrolytes (UCES), liver function tests (LFTS), prothrombin time (PT), international normalization ratio (INR), serum albumin, calcium and magnesium were performed. This information along with demographics was entered in the proforma attached as annexure. Exclusion criteria was followed strictly to avoid confounding variables.

For example, Table. Characteristic of studied groups of patients

Characteristic/ Feature	Patients with new onset seizure (case group, N = 77)		Patients without seizure (control group, N = 77)		p-value
	male	female	male	female	
Total, % (95%CI) (n)	41.6 (31.2-52.7) (32)	58.4 (47.3-68.9) (45)	51.9 (41.0-62.8) (40)	48.1 (37.3-59.0) (37)	0.196
Mean age, years (M±SD)					
Age distribution:					
61-70					
71-80					
81-90					
Mean duration of disease (seizure), months (M±SD)			no	no	
Type of seizure:					
generalized tonic-clonic, % (95%CI) (n)	% (95%CI:) (n)	% (95%CI:) (n)	no	no	...
Focal, % (95%CI) (n)	% (95%CI:) (n)	% (95%CI:) (n)			

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Commented [IS12]: Descriptive information on the composition of the studied groups (number, sex, age) should be transferred here from the "Results" section. Better as one table. See the example in the text.

Commented [IS13]: Here authors can see the significance of differences between men and women

Commented [IS14]: There are no links to tables inside the text.

TABLE1: AGE DISTRIBUTION IN CASE AND CONTROL

Age (years)	CASE		CONTROL	
	N	%	N	%
61-70	48	62.3	58	75.3

71-80	22	28.6	17	22.1
81-90	7	9.1	2	2.6
Total	77	100	77	100.0
Pearson Correlation coefficient				P-Value
				0.04*

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UNDER PEER REVIEW

STATISTICAL ANALYSIS For example: In statistical analysis the clinical variables were compared two groups: case and control. These cohorts were stratified into two parts according to the presence/absence of risk factors. Differences between groups were performed using the contingency tables (2 by 2, 2 by 3, 2 by 4) with Chi-square-test (for large samples) or Fisher's Exact test (for small samples). In cases of statistically significant differences between the control and case groups we calculated the odds ratio (OR), and the Phi-coefficient of association. OR were calculated with a 95% confidence interval (95% CI) All statistical analysis was two-tailed, and Bonferroni's corrected, p -values < 0.05 were considered statistically significant. All data are shown as n (%) and 95% CI. The age of subjects at the time of the study and the age at onset of seizures are indicated as the mean and standard deviation ($M \pm SD$). Statistical analyses were conducted using statistical software: <http://...>

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Results:

A total of 154 old age patients visited ed were selected for study on the basis of inclusion and exclusion criteria. Consecutive old age patients were distributed into two groups i.e., case group (77 old age patients of new onset seizure) and control group (77 old age patients without seizure).

Mean age of old age patients in case group (new onset seizure group) was 69.7 ± 7.6 (61-90) years and in control group (without seizure group) was 66.8 ± 6.0 (61-82) years.

Mean duration of disease in old age patients in case group (new onset seizure group) was 3.4 ± 1.6 (1-6) months and in control group (without seizure group) no duration of disease due to absence of seizure.

Gender of old age patients in case group (new onset seizure group) was male 32 (41.6%) and female 45 (58.4%) and in control group (without seizure group) was 40 (51.9%) and female 37 (48.1%). **Pearson correlation coefficient was applied that shows p -value = 0.196 of $\phi = 0.1$.**

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Age distribution of old age patients in case group (new onset seizure group) was 61-70 years with 48 (62.3%) patients, 71-80 years with 22 (28.6%) patients and 81-90 years with 7 (9.1%) patients and in control group (without seizure group) was 61-70 years with 58 (75.3%) patients, 71-80 years with 17 (22.1%) patients and 81-90 years with 2 (2.6%) patients. **Pearson correlation coefficient was applied that shows p -value of 0.04*.**

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Duration of disease distribution in old age patients in case group (new onset seizure group) was 1-3 months with 45 (59.2%) patients and 4-6 months with 31 (40.8%) patients and in control group (without seizure group) no duration of disease due to absence of seizure. **Pearson correlation coefficient was not computable.**

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Type of seizure in old age patients in case group (new onset seizure group) was generalized tonic-clonic seizure (gtcs) in 51 (66.2%) patients and focal seizure in 26 (33.8%) patients and in control group (without seizure group) no type of seizure due to absence of seizure. **Pearson correlation coefficient was not computable.**

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Commented [IS21]: this information belongs to the "Materials and Methods" section.

Diabetes mellitus in old age patients in case group (new onset seizure group) was present in 76 (98.7%) patients and absent in 1 (1.3%) patients and in control group (without seizure group) was present in 59 (76.6%) patients and absent in 18 (23.4%) patients. **Pearson correlation coefficient was applied that shows p -value of 0.001*.**

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Hypertension in old age patients in case group (new onset seizure group) was present in 72 (93.5%) patients and absent in 5 (6.5%) patients and in control group (without seizure group) was present in 63 (81.8%) patients and absent in 14 (18.2%) patients. **Pearson correlation coefficient was applied that shows p-value of 0.02*.**

Ischemic heart disease (IHD) in old age patients in case group (new onset seizure group) was present in 39 (50.6%) patients and absent in 38 (49.4%) patients and in control group (without seizure group) was present in 25 (32.5%) patients and absent in 52 (67.5%) patients. **Pearson correlation coefficient was applied that shows p-value of 0.02*.**

Stroke in old age patients in case group (new onset seizure group) was present in 23 (29.9%) patients and absent in 54 (70.1%) patients and in control group (without seizure group) was present in 16 (20.8%) patients and absent in 61 (79.2%) patients. **Pearson correlation coefficient was applied that shows p-value of 0.1.**

Dementia in old age patients in case group (new onset seizure group) was present in 3 (3.9%) patients and absent in 74 (96.1%) patients and in control group (without seizure group) was present in 0 (0.0%) patients and absent in 77 (100.0%) patients. **Pearson correlation coefficient was applied that shows p-value of 0.08.**

Head trauma in old age patients in case group (new onset seizure group) was present in 0 (0.0%) patients and absent in 77 (100.0%) patients and in control group (without seizure group) was present in 33 (42.9%) patients and absent in 44 (57.1%) patients. **Pearson correlation coefficient was applied that shows p-value of 0.001*.**

Metabolic causes in old age patients in case group (new onset seizure group) was present in 27 (35.1%) patients and absent in 50 (64.9%) patients and in control group (without seizure group) was present in 27 (35.1%) patients and absent in 50 (64.9%) patients. Pearson correlation coefficient was applied that shows p-value of 1.0.

Types of metabolic causes in old age patients in case group (new onset seizure group) were hypoglycemia in 12 (44.4%) patients, hyponatremia in 9 (33.3%) patients, hypernatremia in 1 (3.7%) patients, hypocalcemia in 1 (3.7%) patients, hepatic encephalopathy in 3 (11.1%) patients and uremic encephalopathy in 1 (3.7%) patients and in control group (without seizure group) were hypoglycemia in 6 (22.2%) patients, hyperglycemia in 4 (14.8%) patients, hyponatremia in 11 (40.7%) patients, hypocalcemia in 1 (3.7%) patients, hepatic encephalopathy in 3 (11.1%) patients and uremic encephalopathy in 2 (7.4%) patients. Pearson correlation coefficient was applied that shows p-value of 0.4.

Brain tumor in old age patients in case group (new onset seizure group) was present in 6 (7.8%) patients and absent in 71 (92.2%) patients and in control group (without seizure group) was present in 0 (0.0%) patients and absent in 77 (100.0%) patients. Pearson correlation coefficient was applied that shows p-value of 0.01*.

Types of brain tumor in old age patients in case group (new onset seizure group) were primary brain tumor in 2 (33.3%) patients and secondary brain tumor in 4 (66.7%) patients and in control group (without seizure group) no type of brain tumor due to absence of brain tumor. Pearson correlation coefficient was not computable.

Infection of central nervous system (cns) in old age patients in case group (new onset seizure group) was present in 17 (22.1%) patients and absent in 60 (77.9%) patients and in control group (without seizure group) was present in 1 (1.3%) patients and absent in 76 (98.7%) patients. Pearson correlation coefficient was applied that shows p-value of 0.001*.

Depression in old age patients in case group (new onset seizure group) was present in 2 (2.6%) patients and absent in 75 (97.4%) patients and in control group (without seizure group) was present in 0 (0.0%) patients and absent in 77 (100.0%) patients. Pearson correlation coefficient was applied that shows p-value of 0.1.

Commented [IS23]: This information partially duplicates what is in the tables 2-8 below. Therefore, I recommend leaving only tables, which will be clearer to the readers. But these tables will need to make some changes, namely, indicate the p-value for each risk factor separately, and not totally in the group. Where statistically significant differences are found, calculate the odds ratio (OR) and 95% CI for it, and also indicate the phi- value of the association coefficient. I gave an example of such a table in the text of the manuscript.



Commented [IS24]: table 1 was moved above to the section "materials and methods"

TABLE2: TYPES OF METABOLIC CAUSES DISTRIBUTION IN CASE AND CONTROL

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Types of metabolic causes	CASE		CONTROL	
	N	%	N	%
Hypoglycemia	12	44.4	6	22.2
Hyperglycemia	0	0	4	14.8
Hyponatremia	9	33.3	11	40.7
Hypertatremia	1	3.7	0	0
Hypocalcemia	1	3.7	1	3.7
Hepatic encephalopathy	3	11.1	3	11.1
Uremic encephalopathy	1	3.7	2	7.4
Total	27	100.0	27	100.0
Pearson correlation coefficient			P-VALUE	
			0.4	

For example, Table 2. Risk factors associated with new onset seizures among men old age.

Risk factor	Patients with new onset seizure		Patients without seizure		p-value		Odd Ratio (95%CI)	Phi coefficient association
	n	Frequency, % (95%CI)	n	Frequency, % (95%CI)	Ch2-Pearson	Fisher exact probability test		
Diabetes								
Hypertension								
Ischemic heart disease								
Infection of central nervous system								
Brain tumor								
Head trauma								
Stroke								
Dementia								
Depression								
Hepatic encephalopathy								
Uremic encephalopathy								
Hypoglycemia								
Hyperglycemia								
Hyponatremia								
Hypertatremia								
Hypocalcemia								
Hypercalcemia								
Prothrombin time								
Total, N								

For example, Table 3. Risk factors associated with new onset seizures among women old age.

Risk factor	Patients with new onset seizure		Patients without seizure		p-value		Odd Ratio (95%CI)	Phi coefficient association
	n	Frequency, % (95%CI)	n	Frequency, % (95%CI)	Ch ² -Pearson	Fisher exact probability test		
Diabetes								
Hypertension								
Ischemic heart disease								
Infection of central nervous system								
Brain tumor								
Head trauma								
Stroke								
Dementia								
Depression								
Hepatic encephalopathy								
Uremic encephalopathy								
Hypoglycemia								
Hyperglycemia								
Hyponatremia								
Hypnatremia								
Hypocalcemia								
Hypercalcemia								
Prothrombin time								
Total, N								

TABLE 3: BRAIN TUMOR DISTRIBUTION IN CASE AND CONTROL

BRAIN TUMOR	CASE		CONTROL	
	N	%	N	%
YES	6	7.8	0	0.0
NO	71	92.2	77	100.0
TOTAL	77	100.0	77	100.0
PEARSON CORRELATION COEFFICIENT			P-VALUE	
			0.4	

TABLE 4: CNS INFECTION DISTRIBUTION IN CASE AND CONTROL

CNS INFECTION	CASE		CONTROL	
	N	%	N	%
YES	17	22.1	1	1.3
NO	60	77.9	76	98.7
TOTAL	77	100.0	77	100
PEARSON CORRELATION COEFFICIENT			P-VALUE	
			0.001	

TABLE 5: DEPRESSION DISTRIBUTION IN CASE AND CONTROL

DEPRESSION	CASE		CONTROL	
	N	%	N	%
YES	2	2.6	0	0
NO	75	97.4	77	100
TOTAL	77	100.0	77	100.0
PEARSON CORRELATION COEFFICIENT			P-VALUE	
			0.1	

TABLE 6: HEAD TRAUMA DISTRIBUTION IN CASE AND CONTROL

HEAD TRAUMA	CASE		CONTROL	
	N	%	N	%
YES	0	0.0	33	42.9
NO	77	100	44	57.1
TOTAL	77	100.0	77	100.0
PEARSON CORRELATION COEFFICIENT			P-VALUE	
			0.001	

TABLE 7: DEMENTIA DISTRIBUTION IN CASE AND CONTROL

DEMETIA	CASE		CONTROL	
	N	%	N	%
YES	3	3.9	0	0.0
NO	74	96.1	77	100
TOTAL	77	100.0	77	100.0
PEARSON CORRELATION COEFFICIENT			P-VALUE	
			0.08	

TABLE 8: STROKE DISTRIBUTION IN CASE AND CONTROL

STOKE	CASE		CONTROL	
	N	%	N	%
YES	23	29.9	16	20.8
NO	54	70.1	61	79.2
TOTAL	77	100.0	77	100.0
PEARSON CORRELATION COEFFICIENT			P-VALUE	
			0.1	

Discussion:

Elder population is most rapidly growing throughout the world and exposed to different chronic diseases and neurological disorder. Incidence as well as prevalence of epilepsy is much higher in elder population as compared to youngsters. A large population of elders with epilepsy always remain undiagnosed due to failure in obtaining clinical history, absence of eye witness, atypical presentation of seizure and difficulty in differentiation between epileptic and non-epileptic events [1, 80, 81].

Globally, diagnosis of epilepsy in elder is always a big challenge for physicians for provide optimal health care and enhanced the quality of life of elders. Therefore, identification of comorbidities and risk factors is very important for early and accurate diagnosis of epilepsy in elders. Therefore, current research was designed in tertiary care hospital of Karachi for determining the association between risk factors and new-onset seizures in old age population.

In current study, 154 older age patients were selected and distributed into two groups i.e., case group (77 old age patients of new onset seizure) and control group (77 old age patients without seizure). Most of them were female 45 (58.4%) diagnosed with new onset seizure as compared to male 32 (41.6%). Mean age of patients in new onset seizure group was high 69.7 ± 7.6 (61-90) years. Age is always an important factor in elders, as the age increased risk of developing epilepsy also increased. All the studies on elder population confirms the higher mean age of elders suffering from epilepsy such as; Shariff EM, et al. and Phabphal K, et al. Reports the 70.12 ± 8.72 and 73.07 ± 9.97 years as mean age of epileptic patients [34, 82].

In current study, most of the patients were suffering from generalized tonic-clonic seizure (GTCS) with 51 (66.2%) patients followed by focal seizure with 26 (33.8%) patients with mean duration of disease in new onset seizure group was 3.4 ± 1.6 (1-6) months.

In current study, commonly reported comorbidities in seizure and non-seizure group were; diabetes mellitus in 76 (98.7%) and 59 (76.6%) patients ($p=0.001^*$), hypertension in 72 (93.5%) and 63 (81.8%) patients ($p=0.02^*$) and IHD in 39 (50.6%) and 25 (32.5%) patients ($p=0.02^*$).

In current study, commonly reported risk factors in seizure and non-seizure group were; stroke in 23 (29.9%) and 16 (20.8%) patients ($p=0.1$), dementia in 3 (3.9%) and 0 (0.0%) patients ($p=0.08$), head trauma in 0 (0.0%) and 33 (42.9%) patients ($p=0.001^*$), metabolic causes in 27 (35.1%) and 27 (35.1%) patients ($p=1.0$), brain tumor in 6 (7.8%) and 0 (0.0%) patients ($p=0.01^*$), CNS infection in 17 (22.1%) and 1 (1.3%) patients ($p=0.001^*$) and depression in 2 (2.6%) and 0 (0.0%) patients ($p=0.1$). Notable risk factors were metabolic disorder 27 (35.1%), stroke 23 (29.9%) and CNS infection in 17 (22.1%) followed by brain tumor 6 (7.8%), dementia 3 (3.9%) and depression 2 (2.6%).

Different studies reported the different prevalence of different risk factors significantly or non-significantly associated with epilepsy of elders. Shariff EM, et al. reported the stroke as most commonly diagnosed factor in 58% patients, occult CVD in 22.7%, tumors in 16.8% patients and others (infection, trauma, etc.) in 2.5% patients [34]. Another study by Guo Y, et al. also reported the stroke as most commonly diagnosed factor in 48.7% patients, brain injury 17.5% patients, tumor in 9.7% patients, dementia in 7.0% patients and CNS infection in 3.8% patients [83].

Stroke is considered as the most commonly diagnosed risk factor throughout the world responsible for developing epilepsy in elders. Our study finding also stroke is considered as the most commonly diagnosed risk factor throughout the world responsible for developing epilepsy in elders. Our study finding also reported the stroke as second common cause of epilepsy in elders. CNS infection and brain tumors are also the important risk factors behind the epilepsy of elders. Our study finding also confirms that CNS infection and brain tumors both are actively playing their role in emerging of new onset seizure in elders.

Conclusion:

New-onset seizures are significantly associated with age, diabetes mellitus, hypertension, ischemic heart disease, brain tumor and CNS infection. Most commonly reported risk factors in new onset seizure were metabolic causes, stroke and CNS infection followed by brain tumor, dementia and depression.

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Commented [IS27]: This has already been said. In the discussion, these figures do not need to be cited.

Commented [IS28]: This cannot be said, because the age of patients in the control group is within the same range. To do such a conclusion, it was necessary to compare the frequency of seizures in cohorts of young, middle and old age patients.

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Commented [IS30]: It is not necessary in the "Discussion" to repeat the numbers that are already in the "Results", authors just need to do a conclusion and compare the obtained data with previously published results

Commented [IS31]: Based on the data presented in the manuscript, one cannot talk about the association of seizures with age. Perhaps this will be more pronounced if the authors present data separately for men and women.

Consent:

As per international standards or university standards, patients written consent has been collected and preserved by the author(s).

Ethical approval:

As per international standards or university standards, written ethical approval has been collected and preserved by the author(s).

Abbreviations

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References:

1. Brodie MJ, Elder AT, Kwan P. Epilepsy in later life. *Lancet Neurol.* 2009 Nov 1;8(11):1019-30.
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