ASSOCIATION BETWEEN RISK FACTORS ANDNEW-ONSE SEIZURES IN OLDAGE POPULATION

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ABSTRACT

Background: Seizures are one of the most common diseases of the nervous system in the elderly especially late-onset seizures significantly impact the quality of life of older people. 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.Nearly 25% of people newly diagnosed with seizures. With increasing age, the prevalence and incidence of epilepsy and seizures increases correspondingly. The existence of some special causes may contribute to the high incidence of epilepsy and seizures in the elderly. It is reported that the causes of seizures for example (stroke, cns infections, electrolyte imbalance, metabolic disorders, and neurodegenerative diseases) can be found in nearly 50% of elderly patients. Younger patients with epilepsy and seizures often show a genetic cause. However, new-onset seizures in the elderly are mainly the consequence of accumulated injuries to the brain and other secondary factors.

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) and control group (77 old age patients without seizure). Risk factors including stroke, dementia, head trauma, metabolic causes, brain tumor, and infection of central nervous system (CNS), depression and anxiety were evaluated.

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 and 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 underage 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].

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].

The rationale of the study: is to measure the association between risk factors and new-onset seizures in old

age population, it is clinically plausible to identify association between risk factors & new onset seizures in our

population and surprisingly there have been no local studies published during last 5 years in this regard. As a

large number of the Pakistani population belongs to the rural areas and poor socio economic strata, therefore

most of our patients report very late due to lack of easy access to medical facilities and financial constraints as

compared to other developed countries.

It is important to investigate the status of new onset epilepsy in the elderly patients of our country, so that an

accurate clinical diagnosis is made and also treatment of such patients could be streamlined in an appropriate

direction to prevent further delay and complications.

MATERIALS AND METHODS

STUDY SETTING:

THE STUDY WAS PERFORMED AT DR ZIAUDDIN UNIVERSITY HOSPITAL NORTH NAZIMABAD CAMPUS, KARACHI.

STUDY DESIGN:

CASE CONTROL STUDY.

DURATION OF STUDY:

SIX MONTHS FROM 02-05-2019 TO 01-11-2019.

SAMPLE SIZE:

SOFTWARE: OPEN EPI

SAMPLE SIZE: 154

- CASE GROUP: 77 OLD AGE PATIENTS OF NEW ONSET SEIZURE
- CONTROL GROUP: 77 OLD AGE PATIENTS WITHOUT SEIZURE

FIGURE 6: SAMPLE SIZE CALCULATION

STUDY TECHNIQUE:

NON-PROBABILITY CONSECUTIVE SAMPLING.

SAMPLE SELECTION FOR CASE GROUP

INCLUSION CRITERIA:

- AGE > 60 YEARS
- EITHER GENDER
- PATIENTS WITH NEW ONSET SEIZURES DURING LAST 6 MONTH.

EXCLUSION CRITERIA:

- AGE <60YEARS**.**
- PATIENT OR INFORMANTS NOT GIVING INFORMED CONSENT.

- PATIENTS WHO HAVE BEEN DIAGNOSED AS EPILEPTICS FOR MORE THAN 6 MONTHS.

SAMPLE SELECTION FOR CONTROL GROUP

INCLUSION CRITERIA:

- AGE > 60 YEARS
- EITHER GENDER
- HEALTHY POPULATION WITH RISK OF SEIZURES..

EXCLUSION CRITERIA:

- AGE < 60 YEARS.
- PATIENT OR INFORMANTS NOT GIVING INFORMED CONSENT.

Sample Size for Unmatched Case-Control Study

For:

Two-sided confidence level(1-alpha)	95
Power (% chance of detecting)	80
Ratio of Controls to Cases	1
Hypothetical proportion of controls with exposure	40
Hypothetical proportion of cases with exposure:	62.5
Least extreme Odds Ratio to be detected:	2.50

	Kelsey	Fleiss	Fleiss with CC
Sample Size - Cases	78	77	85
Sample Size - Controls	78	77	85
Total sample size:	156	154	170

References

Kelsey et al., Methods in Observational Epidemiology 2nd Edition, Table 12-15
Fleiss, Statistical Methods for Rates and Proportions, formulas 3.18 &3.19

CC = continuity correction
Results are rounded up to the nearest integer.
Print from the browser menu or select, copy, and paste to other programs.

Results from OpenEpi, Version 3, open source calculator--SSCC

Print from the browser with ctrl-P

or select text to copy and paste to other programs.

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 (CT SCAN 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.

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 OF 0.1.

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*.

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.

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.

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*.

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 APPLIEDTHATSHOWSP**-**VALUEOF 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*.

TYPESOF 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.

TABLE:AGE DISTRIBUTION IN CASE AND CONTROL

	CASE		CONTROL	
Age (years)	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*

TABLE: TYPES OF METABOLIC CAUSES DISTRIBUTION IN CASE AND CONTROL

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**
HYPERNATREMIA	**1**	**3.7**	**0**	**0**
HYPOCALCEMIA	**1**	**3.7**	**1**	**3.7**
HEPATIC ENCEPHALOPATHY	**3**	**11.1**	**3**	**11.1**
UREMICENCEPHALOPATHY	**1**	**3.7**	**2**	**7.4**
TOTAL	**27**	**100.0**	**27**	**100.0**
PEARSON CORRELATION COEFFICIENT			**P-VALUE**	
			0.4	

TABLE: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: GENDER DISTIBUTION IN CASE AND CONTROL

CNS INFECTION	CASE		CONTROL	
	N	%	N	%
MALE	32	41.6	40	51.9
FEMALE	45	58.4	37	48.1
TOTAL	77	100.0	77	100
PEARSON CORRELATION COEFFICIENT			P-VALUE	
			0.1	

TABLE: 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 : 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: 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 YOUNGERS. 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. COMMONLY REPORTED COMORBIDITIES IN SEIZURE AND NON-SEIZURE GROUP WERE; DIABETES MELLITUS, HYPERTENSION AND ISCHEMIC HEART DISEASES AND COMMONLY REPORTED RISK FACTORS WERE; STROKE , DEMENTIA, HEAD TRAUMA, METABOLIC CAUSES BRAIN TUMOR, CNS INFECTION AND DEPRESSION.AND PATIENTS WITH NOTABLE RISK FACTORS WERE METABOLIC DISORDER, STROK, CNS INFECTION FOLLOWED BY BRAIN TUMOR,DEMENTIA AND DEPRESSION

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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CONSENT:

As per international standards or university standards, patient's 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).

Competing interest:

Author has declared that no competing interests exist.

LIST OF ABBREVIATIONS

ED	Emergency Department
CNS	Central Nervous System
GTCS	Generalized Tonic–Clonic Seizure
DM	Diabetes Mellitus
HTN	Hypertension
IHD	Ischemic Heart Disease
ES	Epileptic Seizures
AD	Alzheimer's disease
QOL	Quality of Life
CNS	Central Nervous System
TBI	Traumatic Brain Injury
CVD	Cerebrovascular Disease
CAA	Cerebral Amyloid Angiopathy
PRES	Posterior Reversible Encephalopathy syndrome
RCVS	Reversible cerebral Vasoconstriction Syndrome
AVMs	Arteriovenous Malformations
CADASIL	Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy
MELAS	Mitochondrial Encephalopathy with Lactic Acidosis and Stoke Like Episodes
SE	Status Epilepticus
ECG	Electrocardiogram
EEG	Electroencephalography
MRI	Magnetic resonance imaging
CT	Computed tomography
SPSS	Statistical Package for Social Sciences

REFERENCES:

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

2. Baker GA, Jacoby A, Buck D, Brooks J, Potts P, Chadwick DW. The quality of life of older people with epilepsy: findings from a UK community study. Seizure. 2001 Mar 1;10(2):92-9.

3. Faught E, Richman J, Martin R, Funkhouser E, Foushee R, Kratt P, et al. Incidence and prevalence of epilepsy among older US Medicare beneficiaries. Neurology. 2012 Feb 14;78(7):448-53.

4. Marwat MA, Khan TM, Azeemi MM. Diagnosis and management of epilepsy.Gomal J Med Sci. 2005;3(2):71.

5. Hesdorffer DC, Logroscino G, Benn EK, Katri N, Cascino G, Hauser WA. Estimating risk for developing epilepsy: a population-based study in Rochester, Minnesota. Neurology. 2011 Jan 4;76(1):23-7.

6. Olafsson E, Ludvigsson P, Gudmundsson G, Hesdorffer D, Kjartansson O, Hauser WA. Incidence of unprovoked seizures and epilepsy in Iceland and assessment of the epilepsy syndrome classification: a prospective study. Lancet Neurol. 2005 Oct 1;4(10):627-34.

7. Leppik IE, Birnbaum AK. Epilepsy in the elderly. Ann N Y Acad Sci. 2010 Jan;1184:208-24.

8. Wallace H, Shorvon S, Tallis R. Age-specific incidence and prevalence rates of treated epilepsy in an unselected population of 2 052 922 and age-specific fertility rates of women with epilepsy. Lancet. 1998 Dec 19;352(9145):1970-3.

9. Ghosh S, Jehi LE. New-onset epilepsy in the elderly: challenges for the internist. Cleve Clin J Med. 2014 Aug 1;81(8):490-8.

10. Liu S, Yu W, Lü Y. The causes of new-onset epilepsy and seizures in the elderly.Neuropsychiatr Dis Treat. 2016;12:1425.

11. Tanaka A, Akamatsu N, Shouzaki T, Toyota T, Yamano M, Nakagawa M, et al. Clinical characteristics and treatment responses in new-onset epilepsy in the elderly. Seizure. 2013 Nov 1;22(9):772-5.

12. Spencer D. Seizures and epileptiform activity in early Alzheimer disease: how hard should we be looking? seizures in Alzheimer disease. Epilepsy Curr. 2014 Mar;14(2):73-5.

13. Smith N, Tiwari D. Epilepsy in older people. Rev ClinGerontol. 2015;25(1):53-9.

14. Assis TMR, Bacellar A, Costa G, Nascimento OJM. Mortality predictors of epilepsy and epileptic seizures among hospitalized elderly.ArqNeuropsiquiatr. 2015 Jun;73(6):510-5.

15. Stephen LJ, Brodie MJ. Special problems: Adults and elderly. Epilepsia. 2008 Jan;49:45-9.

16. Ramsay RE, Pryor FM. Epilepsy in the elderly. Neurology. 2000;55(5 Suppl 1):S9-14.

17. Massengo SA, Ondze B, Bastard J, Guiziou C, Velmans N, Rajabally YA. Elderly patients with epileptic seizures: in-patient observational study of two French community hospitals. Seizure. 2011 Apr 1;20(3):231-9.

18. Stefan H, May TW, Pfäfflin M, Brandt C, Füratsch N, Schmitz B, et al. Epilepsy in the elderly: comparing clinical characteristics with younger patients. ActaNeurol Scand. 2014 May;129(5):283-93.

19. Khan A, Chiragh S, Irfan M, Sherin A. Frequency of seizures and epilepsy after ischaemic stroke. J Postgrad Med Instit. 2008;22(2):124-9.

20. Sibia RS, Kumar A, Sharma H. Seizure in later life: an ode to the elderly. Int J Res Med Sci. 2014 Oct;2:1393-5.

21. Hommet C, Mondon K, Camus V, De Toffol B, Constans T. Epilepsy and dementia in the elderly. Dement GeriatrCognDisord. 2008;25(4):293-300.

22. Pitkanen A, Bolkvadze T. Head trauma and epilepsy. In: Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV, editors. Jasper's Basic Mechanisms of the Epilepsies. 4th ed. Bethesda (MD): National Center for Biotechnology Information (US); 2012.

23. Assis TR, Bacellar A, Costa G, Nascimento OJ. Etiological prevalence of epilepsy and epileptic seizures in hospitalized elderly in a Brazilian tertiary center-Salvador – Brazil.ArqNeuropsiquiatr. 2015 Feb;73(2):83-9.

24. Tedrus GM, Fonseca LC, Nogueira Junior E, Pazetto D. Epilepsy with onset at over 50 years of age: clinical and electroencephalographic characteristics. ArqNeuropsiquiatr. 2012 Oct;70(10):780-5.

25. Beghi E, Carpio A, Forsgren L, Hesdorffer DC, Malmgren K, Sander JW, et al. Recommendation for a definition of acute symptomatic seizure. Epilepsia. 2010 Apr;51(4):671-5.

26. Hesdorffer DC, Hauser WA, Annegers JF, Kokmen E, Rocca WA. Dementia and adult-onset unprovoked seizures.Neurology. 1996 Mar;46(3):727-30.

27. Sherzai D, Losey T, Vega S, Sherzai A. Seizures and dementia in the elderly: Nationwide Inpatient Sample 1999–2008. Epilepsy Behav. 2014 Jul 1;36:53-6.

28. Johnson EL, Krauss GL, Lee AK, Schneider AL, Dearborn JL, Kucharska-Newton AM, et al. Association between midlife risk factors and late-onset epilepsy: results from the atherosclerosis risk in communities study. JAMA Neurol. 2018 Nov 1;75(11):1375-82.

29. Adelöw C, Andersson T, Ahlbom A, Tomson T. Hospitalization for psychiatric disorders before and after onset of unprovoked seizures/epilepsy. Neurology. 2012 Feb 7;78(6):396-401.

30. Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, Zalutsky R. How common are the "common" neurologic disorders?.Neurology. 2007 Jan 30;68(5):326-37.

31. Sirven JI. Acute and chronic seizures in patients older than 60 years. Mayo Clin Proceed. 2001;76(2):175-83.

32. Thijs RD, Surges R, O'Brien TJ, Sander JW.Epilepsy in adults.Lancet. 2019 Feb 16;393(10172):689-701.

33. Hanby MF, Al-Bachari S, Makin F, Vidyasagar R, Parkes LM, Emsley HC. Structural and physiological MRI correlates of occult cerebrovascular disease in late-onset epilepsy. NeuroimageClin. 2015;9(1):128-33.

34. Shariff EM, AlKhamis FA. New onset epilepsy in the elderly: clinical, radiological and electroencephalographic features and treatment responses. Neurosciences. 2017 Apr;22(2):102-6.

35. Forsgren L, Beghi E, Oun A, Sillanpää M. The epidemiology of epilepsy in Europe–a systematic review.Eur J Neurol. 2005 Apr;12(4):245-53.

36. Pugh MJ, Knoefel JE, Mortensen EM, Amuan ME, Berlowitz DR, Van Cott AC. New-onset epilepsy risk factors in older veterans. J Am Geriatr Soc. 2009 Feb;57(2):237-42.

37. Stefan H. Epilepsy in the elderly: facts and challenges. ActaNeurol Scand. 2011 Oct;124(4):223-37.

38. Lhatoo SD, Johnson AL, Goodridge DH, Macdonald BK, Sander JW, Shorvon SD. Mortality in epilepsy in the first 11 to 14 years after diagnosis: multivariate analysis of a long-term, prospective, population-based cohort. Ann. Neurol. 2001 Mar 1;49(3):336-44.

39. Lees A. Retrospective study of seizure-related injuries in older people: a 10-year observation. Epilepsy Behav. 2010 Nov 1;19(3):441-4.

40. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014 Apr;55(4):475-82.

41. Epidemiology Commission of the International League Against Epilepsy. The burden of premature mortality of epilepsy in high-income countries: a systematic review from the Mortality Task Force of the International League Against Epilepsy. Epilepsia. 2017 Jan;58(1):17-26.

42. Nwani PO, Nwosu MC, Nwosu MN. Epidemiology of acute symptomatic seizures among adult medical admissions. Epilepsy Res Treat. 2016;2016.

43. Landwehr R, Liszka R. Acute symptomatic seizures in geriatric patients with multiple risk factors-a diagnostic challenge. Curr Aging Sci. 2017 Nov 1;10(4):263-9.

44. Brodie MJ, Schachter SC, Kwan P. Fast facts: epilepsy. Karger Medical and Scientific Publishers; 2012 Mar 1.

45. Ramsay RE, Macias FM, Rowan AJ. Diagnosing epilepsy in the elderly.Int Rev Neurobiol. 2007 Jan 1;81:129-51.

46. Bladin CF, Alexandrov AV, Bellavance A, Bornstein N, Chambers B, Coté R, et al . Seizures after stroke: a prospective multicenter study. Arch Neurol. 2000 Nov 1;57(11):1617-22.

47. Roivainen R, Haapaniemi E, Putaala J, Kaste M, Tatlisumak T. Young adult ischaemic stroke related acute symptomatic and late seizures: risk factors. Eur J Neurol. 2013 Sep;20(9):1247-55.

48. Hsu CJ, Weng WC, Peng SS, Lee WT. Early-onset seizures are correlated with late-onset seizures in children with arterial ischemic stroke. Stroke. 2014 Apr;45(4):1161-3.

49. De Reuck JL. Stroke-related seizures and epilepsy.NeurolNeurochir Pol. 2007;41(2):144-9.

50. Bleck TP. Seven questions about stroke and epilepsy. Epilepsy Curr. 2012 Nov;12(6):225-8.

51. Renú A, Amaro S, Laredo C, Román LS, Llull L, Lopez A, et al. Relevance of blood–brain barrier disruption after endovascular treatment of ischemic stroke: dual-energy computed tomographic study. Stroke. 2015 Mar;46(3):673-9.

52. Cleary P, Shorvon S, Tallis R. Late-onset seizures as a predictor of subsequent stroke. Lancet. 2004 Apr 10;363(9416):1184-6.

53. Imfeld P, Bodmer M, Schuerch M, Jick SS, Meier CR. Seizures in patients with Alzheimer's disease or vascular dementia: A population-based nested case–control analysis. Epilepsia. 2013 Apr;54(4):700-7.

54. Rao SC, Dove G, Cascino GD, Petersen RC. Recurrent seizures in patients with dementia: frequency, seizure types, and treatment outcome. Epilepsy Behav. 2009 Jan 1;14(1):118-20.

55. Hommet C, Verny M. Epilepsy and dementia. Epilepsies. 2009 Jul 1;21(3):245-53.

56. Pandis D, Scarmeas N. Seizures in Alzheimer disease: clinical and epidemiological data. Epilepsy Curr. 2012 Sep;12(5):184-7.

57. Amatniek JC, Hauser WA, DelCastillo-Castaneda C, Jacobs DM, Marder K, Bell K, et al. Incidence and predictors of seizures in patients with Alzheimer's disease. Epilepsia. 2006 May;47(5):867-72.

58. Appel S, Chapman J, Cohen OS, Rosenmann H, Nitsan Z, Blatt I. Seizures in E200K familial and sporadic Creutzfeldt-Jakob disease. ActaNeurol Scand. 2015 Mar;131(3):152-7.

59. Werhahn KJ. Epilepsy in the elderly.DtschArztebl Int. 2009 Feb;106(9):135.

60. Christensen J, Pedersen MG, Pedersen CB, Sidenius P, Olsen J, Vestergaard M. Long-term risk of epilepsy after traumatic brain injury in children and young adults: a population-based cohort study. Lancet. 2009 Mar 28;373(9669):1105-10.

61. Messori A, Polonara G, Carle F, Gesuita R, Salvolini U. Predicting posttraumatic epilepsy with MRI: prospective longitudinal morphologic study in adults. Epilepsia. 2005 Sep;46(9):1472-81.

62. Harden CL. The apolipoprotein E epsilon (epsilon) 4 allele is important for trauma-related epilepsy. Epilepsy Curr. 2004 Jan;4(1):29-30.

63. Lynam LM, Lyons MK, Drazkowski JF, Sirven JI, Noe KH, Zimmerman RS, et al. Frequency of seizures in patients with newly diagnosed brain tumors: a retrospective review. ClinNeurolNeurosurg. 2007 Sep 1;109(7):634-8.

64. Maschio M. Brain tumor-related epilepsy. CurrNeuropharmacol. 2012 Jun 1;10(2):124-33.

65. Pugh MJ, Zeber JE, Copeland LA, Tabares JV, Cramer JA. Psychiatric disease burden profiles among veterans with epilepsy: the association with health services utilization. Psychiatr Serv. 2008 Aug;59(8):925-8.

66. Dunn DW, Austin JK. Differential diagnosis and treatment of psychiatric disorders in children and adolescents with epilepsy.Epilepsy Behav. 2004 Oct 1;5:10-7.

67. Ettinger AB, Copeland LA, Zeber JE, Van Cott AC, Pugh MJ. Are psychiatric disorders independent risk factors for new-onset epilepsy in older individuals?.Epilepsy Behav. 2010 Jan 1;17(1):70-4.

68. Gaitatzis A, Trimble MR, Sander JW. The psychiatric comorbidity of epilepsy.ActaNeurol Scand. 2004 Oct;110(4):207-20.

69. Cramer JA, Blum D, Fanning K, Reed M. The impact of comorbid depression on health resource utilization in a community sample of people with epilepsy.Epilepsy Behav. 2004 Jun 1;5(3):337-42.

70. Cramer JA, Blum D, Reed M, Fanning K; Epilepsy Impact Project Group. The influence of comorbid depression on quality of life for people with epilepsy.Epilepsy Behav. 2003 Oct;4(5):515-21.

71. Zagaria MA. Causes of seizures in the elderly. US Pharm. 2008;33(1):27.

72. Kandar HK, Das SK, Ghosh L, Gupta BK. Epilepsy and its management: A review. J PharmaSci Tech. 2012;1(2):20-6.

73. Annegers JF, Hauser WA, Lee JR, Rocca WA.Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984.Epilepsia. 1995 Apr;36(4):327-33.

74. Holtkamp M, Othman J, Buchheim K, Meierkord H. Predictors and prognosis of refractory status epilepticus treated in a neurological intensive care unit. J NeurolNeurosurg Psychiatry. 2005 Apr 1;76(4):534-9.

75. Pradhan S, Yadav R. Seizures and epilepsy in central nervous system infections. Neurology Asia. 2004;9(S1):4-9.

76. Brodie MJ, Kwan P. Epilepsy in elderly people. Br Med J. 2005 Dec 1;331(7528):1317-22.

77. Chapin J, Naugle R. Geriatric Patients with Epilepsy. In Handbook on the Neuropsychology of Epilepsy.Springer, New York, NY; 2015.

78. 78. Tallis R, Boon P, Perucca E, Stephen L. Epilepsy in elderly people: management issues. Epileptic Disord. 2002 Nov 6;4(2):33-40.

79. McBride AE, Shih TT, Hirsch LJ. Video-EEG monitoring in the elderly: a review of 94 patients. Epilepsia. 2002 Feb;43(2):165-9.

80. Sarkis RA, Schrettner M .Seizures and Epilepsy in the Elderly A focus on multidisciplinary care. Pract Neurol. 2018:36-9.

81. Johnston A, Smith PE. Epilepsy in the elderly. Expert Rev Neurother. 2010 Dec 1;10(12):1899-910.

82. Phabphal K, Geater A, Limapichat K, Sathirapanya P, Setthawatcharawanich S. Risk factors of recurrent seizure, co-morbidities, and mortality in new onset seizure in elderly. Seizure. 2013 Sep 1;22(7):577-80.

83. Guo Y, Yu L, He B, Li S, Zhu Q, Sun H. Aetiological features of elderly patients with newly diagnosed symptomatic epilepsy in Western China. BioMed Res Int. 2018 Apr 24;2018.