

# Incidence of Epilepsy and Evaluation of Associated Disorders in Elderly People of Amirkola, North of Iran

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## Abstract

**Introduction:** The aim of this study was to determine the incidence of epilepsy in the elderly and investigating the disorders associated with its occurrence.

**Methods and Materials:** This cross-sectional study using a census sampling method, is a part of a comprehensive and cohort research of "Amirkola Health and Ageing Project". Cognitive impairment using Mini Mental State Examination (M.M.S.E). and psychiatric diseases based on relevant tests such as Geriatric Depression Scale G.D.S. Physical activity was measured based on the standard physical activity questionnaire for elderly Physical Activity Scale for Elderly(PASE). All data were analyzed using chi-square test and logistic regression in SPSS v23 software.

**Results:** Of 1482 participants 35 subjects were epileptic. the incidence was 2.36 in 1,000 of the elderly. Significant association between Parkinson's Disease( $p=0.001$ ), falls ( $p=0.001$ ), depression( $p=0.001$ ), hyperphosphoremia( $p= 0.039$ ) and hypokalaemia ( $p= 0.031$ ) concluded with epilepsy. Past history of stroke and serum (triglyceride,LDL) level in epileptic were more than the no epileptics.

**Conclusion:** significant association between Parkinson's Disease, frequency of fall, depression and correlation of history of stroke, increased serum triglyceride level and higher serum level of LDL with epilepsy concluded.

**Key words:** Elderly, epilepsy, stroke, Parkinson's disease, fall

## Introduction

Seizure is a temporary neurological symptom and sign caused by abnormal, paroxysmal and hypersynchronous electrical neuronal activity of cerebral cortex. Epilepsy is a group of disorders in which repeated epileptic seizures occur spontaneously, with an overall incidence of about 1% of the population (1). Although the incidence of epilepsy is high in the first few years of life, the prevalence of epilepsy in older people has risen in recent years compared with other age groups. Due to the increasing population of the older adults in different societies, the incidence of epilepsy increases as the elderly people age. In the elderly group, after stroke and dementia, epilepsy is the most common neurological disease (2), and also one of the important causes of death in this age group (3), older people with epilepsy have a mortality rate 2-3 times higher than those elderly without epilepsy (4).

The known underlying causes of epilepsy and seizure triggers in older people are strokes, dementia, brain tumors, head trauma, infectious diseases such as meningitis or encephalitis (5,6). Toxins and the complications of drugs used in these ages and herbal medicines, metabolic problems, such as hypoglycemia and hypocalcemia, can also be considered as accelerating epileptic episodes in this age (7, 8, 9). There is no consensus on whether the association of factors such as cognitive impairment or psychiatric disorders in epilepsy of elderly people can be considered as an etiologic factor or its complications (8). Among the other specifics of the elderly epilepsy, more complications of the anti-epileptic drugs are in this age group (10, 11).

Furthermore, the other issue of older people with epilepsy is the fact that the causes and clinical manifestations of seizures are different when we compared the older individuals with the younger ones. Moreover, an atypical and uncommon clinical manifestation of epilepsy in the elderly will cause the diagnosis of epileptic seizures difficult in the older people (12,13). With this in mind, the diagnosis of epileptic seizures in the elderly should be more precise to justify the initiation of anti-epileptic drugs (14). In studies on the causes of epileptic seizures in the elderly, about one third to half of the cases remains without etiology (15).

Considering the differences in causes and factors associated with epilepsy and its complications in the elderly, and that a lot of financial burden is imposed on families and communities, thus a research on elderly epilepsy has become more important in recent years.

By identifying the causes and factors related to epilepsy and how to prevent them, it is possible to reduce the incidence of epilepsy in this age group and help greatly in improving their quality of life, reducing emotional burden on the patients' families because of fear of seizures and dangers in these fragile years of their life.

On the other hand, it can help to improve the economic situation of the patients' families and their communities by reducing the financial burden of taking care of these patients and treating the complications caused by these disorders (such as fractures), and most importantly, to reduce the mortality rate of the elderly due to the disease. Considering all the above, the aim of this study was to determine the incidence of epilepsy in the elderly and the causes associated with its occurrence in the elderly population of Amirkola.

### **Methods and Materials:**

This cross-sectional study using a census sampling method, is a part of a comprehensive and cohort research of "Amirkola Health and Ageing Project" (A.H.A.P). The Project (89291) began in 2011-2012 in Amirkola, city located near the Caspian Sea, northern Iran and is still ongoing. This study was approved by the Ethics Committee of the Babol University of Medical Sciences (9503032, 4227). A written consent was received from each participant before data collection phase. In this study, 1616 elderly people (60 years and above) were enrolled and whose information is available at the Center for Research on Social Factors Affecting Health (Babol University of Medical Sciences). The elderly population was divided into three age groups: 60-69 years, 70 to 79 years, and 80 years and over. To collect the information needed for this study, the first questionnaire was completed by the participants or if necessary by their companions. This questionnaire contains demographic questions that include age, gender, education, occupation, marital status, and medical history which is collected self-declaration.

For illiterate patients, all questions were read by the interviewer and tried to resolve any ambiguities in understanding the questions. The first stage of the Ageing project also evaluates and records the weight, height, blood pressure, BMI, according to the findings of the questionnaire and the medical records of the trained personnel. The diagnosis of epilepsy in the elderly and the onset of it and the use of the anti-epileptic drug in this study were self-explanatory that in all studied cases confirmed by the neurologist responsible for this study.

History of stroke, Ischemic Heart Disease (I.H.D.), and head trauma, dementia, brain tumors and other neurological disorders such as Parkinson's disease are among the information in the questionnaire completed for all elderly people. Cognitive impairment using Mini Mental State Examination (M.M.S.E). and psychiatric diseases based on relevant tests such as Geriatric Depression Scale G.D.S. and other tests are done and the final confirmation of these cases is with the specialists of these diseases in (A.H.A.P).

The elderly's weight was measured with participants wearing with light clothes. Body mass index was measured and recorded according to the height and weight of the patients. The normal weight of elderlies with BMI (25-29), the overweight older people with BMI ( $\geq 30$ ) and elderlies as a weight loss with BMI ( $< 25$ ). Physical activity was measured based on the standard physical activity questionnaire for elderly Physical Activity Scale for Elderly(PASE). C.B.C. and the serum levels of vitamin D, Zinc, Copper, Phosphorus Calcium, Sodium and Potassium were investigated in this study. The exact criteria for defining the diseases and associated factors, the questionnaires used and the normal amount of laboratory tests performed at the(A.H.A.), comprehensive health center of the elderly, Amirkola has been available and accessible (16).

The criteria for entering the study were elderly people having at least two seizures during the last year before the interview. Elderly people previously diagnosed with epilepsy were excluded, other exclusion criteria were; syncope, fall, confusion states, and other differential diagnosis of epileptic seizures, metabolic disorders such as hypoglycemia, transient global amnesia, migraine attacks with aura, transient ischemic attacks(T.I.A) and sleep disorders (parasomnia).Alcohol consumption, sleep deprivation,( provocative seizure factors) were excluded as a cause of epilepsy (17).

### **Statistical analysis:**

For statistical analysis, the elderly people were divided into two main groups; the first group included patients who had been diagnosed with epilepsy and the second group was normal, including those who did not have epilepsy, but were similar in age and gender to the patient group. Collected data were entered into the software SPSS (23), and statistical analysis was performed. Chi-square test and t-test were used to evaluate the association between related

disorders with epilepsy. Using logistic regression analysis, other variables affecting epilepsy were controlled. A  $p < 0.05$  indicated a meaningful level.

### Results:

Of the 1482 participants over the age of 60, 35 participants were epileptic. Hence, the prevalence of epilepsy was 2.36 in 1,000 participants. 825 elderly people (55.7%) were males, and 657 (44.3% females), 21 cases of 35 elderly epileptic patients (60%) were females, while less frequency of female than male in studied elderly people, frequency of epilepsy in elderly women was non-significantly higher than elderly men ( $p = 0.08$ ). Table 1 shows characteristics of elderly patients with and without epilepsy. Distribution of demographic and clinical characteristics and their associations with epilepsy in the elderly individuals by the calculation of odds ratio (OR) with 95% confidence interval (95% CI) that are demonstrated in Table 2.

The mean age of epileptic elderly based on table 1 was (67.5 + 7.5). The difference between the mean age of epileptic and non-epileptic elderly patients (69.1 + 7.2) was not significant while the frequency of epilepsy in elderly age more than 70 was higher than the group less than 70 years non-significantly ( $p = 0.20$ ).

Sixty-seven elderly people had history of stroke of which 6% had epilepsy, while 11% of epileptic elderly had history of stroke. Although the proportion of epilepsy in the participants with history of stroke was higher than those without stroke, but the difference did not have a statistically significant level (6% versus 2%, OR = 2.8, 95% CI, 0.97-8.27,  $p = 0.07$ ).

Proportions of epilepsy in the elderly, with and without Parkinson's Disease were 12.5% and 2.3%, respectively (Table 2), indicating a significant association between Parkinson's Disease and epilepsy (OR = 6.25, 95% CI = 1.35-28.4,  $p = 0.001$ ). Similarly, there was a positive association between history of falls and depression with epilepsy. Falls occurred in 20% of epileptic patients versus 6.2% of those without epilepsy (OR = 3.81, 95% CI = 1.62-8.97,  $p = 0.001$ ). Moreover, the occurrence of epilepsy in depressed elderly was twice higher in non-depressed people (3.7% vs. 1.4%), (OR = 2.68, 95% CI = 1.32-5.43,  $p = 0.001$ ).

As shown in Table 1, serum levels of phosphorous was significantly higher in epileptic patients compared to healthy people ( $p = 0.039$ ) and also the serum levels of potassium was significantly

lower compared to healthy people ( $p= 0.031$ ). In addition, there was a trend towards a higher level of serum triglyceride in epileptic patients compared to healthy people ( $p= 0.054$ ). On the other hand, the proportions of epilepsy in the elderly, with and without hypertriglyceridemia were (3.2% vs. 1.7%), indicating a non-significant association between the higher level of serum triglycerides and epilepsy  $OR= 1.96$ ,  $95\%CI= 0.99-3.88$ ,  $p=0.06$ .

Similarly, there was non-significantly higher serum level of LDL in epileptic elderly compared to healthy people ( $p = 0.057$ ), while there was not any significant association between serum level of HDL in two studied groups ( $p = 0.45$ ). The difference between BMI of epileptic and non-epileptic elderly patients was not significant ( $p=0.84$ ), while as shown in table 2, the incidence of epilepsy was higher in lower B.M.I. elderly ( $p=0.003$ ) and so on obese subjects ( $p=0.019$ ) compared with normal weight elderly.

According to the data, epilepsy incidence decreased with educational level progression but it was not significant ( $p= 0.93$ ). By considering the other data, patients with and without epilepsy were similar regarding demographic features like marital status, total physical activity, MMSE (Mini Mental State Examination), also there was no statistically significant association between epilepsy in the elderly with cardiovascular disease, hypertension, metabolic syndrome, diabetes mellitus, smoking, and several other measured biochemical characteristics and variables.

### **Discussion:**

In this study, the incidence of epilepsy in elderly people was 2.36 per 1000. In a study among the US Medicare beneficiaries, the annual incidence of epilepsy in the elderly was 2.4/1000 persons that was similar to our results their prevalence rate was 10.8/1000 (18). In other studies different incidence had report so as in study by Giussan et al, the prevalence of epilepsy was 4.57 per 1,000. The incidence was 53.41 per hundred thousand and the highest incidence of epilepsy was among the the elderly (19). In a study on epilepsy in Finland, the incidence of epilepsy in the elderly has increased by 3.5% per year (20). In other studies, there are reports of varying rates of incidence and prevalence of epilepsy in the elderly, but overall, these rates are higher in the elderly than in any other periods of life.

In our study also, the incidence of epilepsy increased with the age, while mean age of epileptic elderly ( $67.5 + 7.5$ ) which was less than previous studies in this field (21). Perhaps one of the

reasons for lower age onset of epilepsy in the elderly in this area may be due to lower age onset of stroke, which is the common cause of epileptic seizures in older adults. In other similar studies, the incidence ranges from 1 to 3 per 1,000 person-years in people with epilepsy, and the incidence rate of this study is in the average of these rates. It should be concluded that the indicators for health care status of the elderly population are generally acceptable in this area.

The incidence of epilepsy in our study elderly population with history of stroke was 6%, while 11% of epileptic elderly had history of stroke. However, the proportion of epilepsy in older adults with history of stroke was higher than those without history of stroke, although the difference did not reach a statistical significant level in most other studies, stroke is the common cause of seizures in the elderly population (22). In a retrospective cohort study (23), the diagnosis of epilepsy was given to a total of 10843 elderly people for the first time. In these older adults, the common causes of epilepsy were: strokes, dementia, brain tumors and other central nervous system diseases. Similar results have been reported in other studies with regard to the incidence of post stroke seizures in the elderly. (24).

In a previous study in Babol (a city nearby Amirkola) in northern Iran (25), the incidence of seizure in 250 cases of stroke was 42 (17.3%) during the two-year follow up. In 14 seizure cases, the episodes were repeated.

Finally, in this study, (5.6%) cases of stroke suffered from epilepsy that was similar to findings of this study. In the epidemiological study of elderly epilepsy in Iran, it was reported that 24% of the causes of elderly epilepsy were related to stroke (26). Given that stroke is a predominantly "elderly illness" and also because strokes are somewhat preventable, engaging in preventive measures to reduce the incidence of stroke, definitely can reduce complications caused by stroke such as epilepsy in elderly people.

Another important finding of this study was the significant association between Parkinson's disease and epilepsy in the elderly of this area of investigation. In comparison with other studies in this field, the amount of this companion has been higher in current study (27). Some researchers believe that Parkinson's Disease associated with epilepsy in the elderly is more likely due to the combination of comorbid brain disorders with P.D. (28), while in several reports point to the problem of misdiagnosis of non-motor epilepsy with non-motor manifestations of P.D.

(29) and others point to low rate of this association, the cause of this association is attributed to the abnormal intra cortical excitability in P.D. (30).

In other reports, it has been concluded that although there is no direct correlation between Parkinson's disease and epilepsy in the elderly Pathological changes that found in the P.D patient's brain including cortical thinning and architectural changes may be epileptogenic (31). Nonetheless, it seems some justifications are necessary for the causes of this significant association with the current study, in particular if these findings are confirmed in later studies in other areas.

According to the findings of this study, the frequency of fall in aging epileptic people was triple the rate compared to non- epileptic cases. Although seizure attacks may lead to fall, some acute seizures may occur following a traumatic brain injury due to falling. Another cause of the fall in the elderly can be the side effects of taking some medications. The difficulty of diagnosing epilepsy in the elderly (32) also leads to this association between fall and seizure which is poorly documented.

Nevertheless, there are reports that a genetic basis (ApoE4 allele) is related to the risk of posttraumatic epilepsy (33) , but in practice, the older adults suffer more likely the risk of acute seizure following a traumatic brain injury than young adults (34). It is clear that preventing and treating each one can reduce other occurrences (35). The findings of this study showed that the frequency of epilepsy in elderly patients with depression was twice as high more than those elderly without depression.

In Ettinger et al.'s study, it was shown that psychiatric disorders such as depression, anxiety, psychosis and substance abuse in elderly patients who were referred for the new-onset epilepsy was more than the control group (36).

Other studies disclosed that depression is the most common comorbid psychiatric disorder in patients with epilepsy (37), and lifetime prevalence of depression in association with epilepsy is as high as 55%. (38). Knowledge of the relationship between depression and epilepsy in the elderly is important. This association is also a two-way, of which preventive or therapeutic measures for each of them can have a positive effect on the others. Yet epilepsy treatment is usually done, but due to fear of exacerbation of epileptic seizure attacks due to side-effects of

antidepressant drugs, treatment for depression is less done in elderly epileptics. Certainly, untreated depression in different ways can exacerbate epileptic seizures and reduce the quality of life and even increase the mortality rate of these patients,

Cognitive impairment in our study did not correlate significantly with the occurrence of epilepsy in the elderly, but mean score of M.M.S.E. in epileptic elderly was lower than non-epileptics. Most studies show that in cases of cognitive impairment, the occurrence of epileptic seizures had increased (39,40).

There was a trend towards a higher level of serum triglycerides in the elderly epileptic patients compared to healthy people. In other studies, hypertriglyceridemia as a dyslipidemia in epileptic patients was reported (41). The cause of dyslipidemia in this study was attributed to using enzyme-inducer anti-epileptic drugs.

Given the high levels of triglyceride and L.D. L. (known risk factors of atherosclerosis) in current study, can these risk factors play a role in the development of epilepsy in the elderly, a question that needs to be answered.

One of the findings of this study was the trend of lower level of education in elderly epileptics compared with non-epileptics. In many studies (42,43), the same results were obtained. However, educated people are more aware of the disease and the ways to prevent it.

Although lower occurrence of epilepsy was seen in our study elderly population with normal weight, the occurrence of epilepsy was higher in low B.M.I. and obese elderly. Results from other studies in this field are similar to our findings (44). With these findings, to have good weight has been advised to the elderly, to prevention of this disease, but also, in many other diseases in this era of life.

In clinical daily practice, electrolyte disturbances such as (hyponatremia, hypocalcemia, and hypomagnesemia) can manifest with seizures (46,46), but our findings of hyperphosphoremia and hypokalemia being more in elderly epileptics compared to healthy elderly people cannot be justified. In the event of getting similar results from other studies in this field, there should be an underlying cause for these findings. Ultimately, these findings may be helpful in preventing or treating these patients.

Despite current study was a community-based study as a strong point, but there were limitations. One of the limitations of this study was the small sample size of elderly epileptics, which made it difficult to compare the relevant variables in the epileptic and non-epileptic elderly groups. Failure to distinguish the clinical epileptic syndromes such as Complex Partial Seizures (CPS) from other epileptic seizure syndromes was one of the other limitations of this study leading to not differentiating the types of epileptic seizures attacks. In addition, in the present study, the types of strokes had not been determined which became a limitation of this study.

Further studies are needed to investigate the probability of other accompanying diseases, or identifying new biological markers or genetic predisposition to epileptic seizures in the elderly people.

#### Conclusion:

The incidence of epilepsy in elderly people was 2.36 per 1000. The ratio was higher in older age. The mean age of elderly epileptics was less than the most previous studies. Proportion of epilepsy in subjects with history of stroke was higher than those without history of stroke. Significant association between Parkinson's disease and epilepsy in the elderly of this area was another important finding of this study. Frequency of fall and depression in elderly epileptics was triple and double, respectively as compared to non-epileptic cases. Lack of association between cognitive impairment with occurrence of elderly epilepsy was another finding of the study. A trend towards a higher level of serum triglycerides and L.D.L was observed in epileptic elderly. We cannot justify the high serum level of phosphorus and low serum levels of potassium in these elderly epileptics.

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#### Authors' Contributions:

AlijanAhmadiAhangar and Seyed Reza Hosseini, designed the study, supervised the study approved the final version. Payam Saadat was involved in preparation of the manuscript. Ali Bijhani, participated in data analysis. Mohsen Khalili and Shayan Alijanpour collected the data.

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