Incidence of Epilepsy among elderly Sudanese patients with Alzheimer's disease: A prospective cohort study on 480 patients, Khartoum, Sudan, 2019

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Abstract

Background: An increased prevalence of epilepsy had been documented with dementia. Alzheimer's disease and epilepsy often coexist.

Objective: The aim of this study to assess incidence rates of epilepsy among Sudanese patients with Alzheimer's disease.

Methods: This is a prospective cohort study. We followed 480 patients aged more than 65 years with diagnosis of Alzheimer's disease between May 2006 and May 2019 looking for coexist epilepsy.

Results: Regarding Alzheimer's disease female were affected more than male (60%). 10% of our patients have epilepsy. Generalize epilepsy was the most common type (62%). Epilepsy was more common with late onset Alzheimer's disease. Abnormal EEG was detected in 20% of our studied group. Abnormal Brain MRI in form of cerebral atrophy was observed in 60 % of patients with Alzheimer's disease and epilepsy.

Conclusion: Patients with Alzheimer's disease have an increased risk of developing epilepsy. There is strong relation between disease duration and development of epilepsy.

1. Introduction

Epilepsy is a common chronic neurological disorder which is characterized by recurrent unprovoked seizures. Epilepsy has been classified into focal, focal to bilateral, generalized & of unknown onset according to the new operational classification applied by ILAE 2017.[1] Epilepsy is either idiopathic, when there is no underlying cause, or secondary when there is underlying cause. The incidence and prevalence of epilepsy increase with age, and are highest in patients over 65 years.[1] The causes and clinical manifestations of epilepsy differ in elderly and affect the diagnostic approach.[2]

The most common type of seizure in elderly patients with epilepsy is a focal seizure but unlike other age groups it originates from extra temporal regions or the frontal lobe.[3] Older patients with seizures may be more frequently misdiagnosed. The diagnosis and treatment of epilepsy in the elderly will become a greater concern because the number of elderly is rapidly increasing, the complexities of diagnosis are more challenging, the incidence of positive EEG in the elderly is less than that in the young epileptic patients, and drug therapy is affected by interactions and altered pharmacokinetics.[4] The elderly patients often have more severe and prolonged postictal symptoms than younger individuals.[4]

Dementias of non-vascular origin give rise to seizures. Dementia is present in 9 to 17 percent of older adults with epilepsy.[5] Dementia may coexist and possibly interact with other causes of epilepsy. Alzheimer's disease is the most common form of [dementia](#) (60%). Alzheimer's causes the progressive and irreversible deterioration of cognitive function, manifesting with the loss of memory and the gradual decline in the ability to think or reason.[6] The disease is most commonly seen in the elderly and is believed to affect anywhere from 4 percent to 12 percent of people over age 65. Alzheimer's disease is

caused by the gradual accumulation of a protein, known as **beta-amyloid**, in the brain. As the protein molecules begin to stick together, they create lesions (plaques) that interrupt the nerve pathways central to cognitive and motor function.[7]

Alzheimer disease (AD) is a significant risk factor for epilepsy in the elderly. Alzheimer's disease and epilepsy often coexist. Between 10 to 20 percent of patients with AD will develop seizures.[8] There is a high risk of epilepsy in Alzheimer disease, particularly when mutations occur in the amyloid precursor protein\beta amyloid gene pathway.[9] Those with early onset Alzheimer disease have also been reported to have a higher risk of developing epilepsy. The severity of seizures also appears closely linked to the advancing stages of Alzheimer's. Alzheimer and epilepsy pose a significant burden on the affected individuals, their families and care givers.[10]

The aim of this study was to assess incidence rates of epilepsy in Sudanese patients with Alzheimer's disease (AD) seen in Daoud Charity Neurological Referral Clinic,, Sheik Mohamed Kheir Charity Neurological Referral Clinic, Ibrahim Malik Teaching Hospital, El Shaab Teaching Hospital and Prof. Abbasher private clinic in the period between May 2006-May 2019.

2. Material And Methods

Study design: A prospective cohort study.

Duration of the study: 13 years

Population Sample: 480 participants from different areas of Sudan were interviewed.

Inclusion Criteria: includes

- 1) Age $\geq$ 65 years;
- 2) History of $\geq$ 1 unprovoked seizure;
- 3) Nationality: Sudanese;
- 4) Patient with Alzheimer s disease who attend Banat charity neurological referral clinic.

Exclusion Criteria:

- 1) Age < 65 years;
- 2) History of <1 unprovoked seizure.

Study area:

Subjects with Alzheimer's disease were randomly recruited in Daoud's charity Neurological Referral Clinic, Ibrahim Malik Teaching Hospital(100 bedded hospital), El Shaab Teaching Hospital (El Shaab Teaching

Hospital is a 240 bedded hospital that has two neurological unites with 43 beds and an intensive care unit), Sheik Mohamed Kheir Charity Neurological Referral Clinic and Prof. Abbasher private Neurological Clinic.

Data collection:

Data collection and Tools:

Interview with Pre-tested Questionnaires. For each subject, the following data were collected: age, marital status, occupation, residency, educational level, employment, duration of diagnosis of Alzheimer's disease, age at seizure onset, seizure type, number of seizures before enrollment, etc.

Data analysis:

All collected data was entered into the computer using the statistical package program for social science (SPSS) to analyze the data via simple descriptive statistics. (Analyzer is specialized personnel in SPSS).

Ethical concern:

Written informed consent was obtained from all study participants relatives. The study was approved by the local ethics committee.

3. Results And Discussion

The study population consisted of 480 patients with Alzheimer's disease (AD). Females constituted 60% of the total number of the patients. The age of the patients range from 65 year to 98 year. During the period of follow up out of 480 patients 48 were labeled as epileptic (10%). 10% of our patients have positive family history of Alzheimer's disease (AD). Almost 10% of our studied group experiences repeated attacks of convulsions during the first two years after being diagnosed as having Alzheimer's disease. Generalized epilepsy was observed in 30 patients (62%) while focal epilepsy was reported in 18 patients (58%).

Out of 48 patients with Alzheimer's disease and epilepsy only 10 patients (20%) had abnormal EEG. Abnormal Brain MRI in form of cerebral atrophy (mainly front parietal) was observed in 60 % of patients with Alzheimer's disease and epilepsy.

Seizure is a sudden disruption of the brain's normal electrical activity accompanied by altered consciousness and/or other neurological and behavioral manifestations. Epilepsy is a condition characterized by recurrent seizures. The most important classification depends on the clinical presentation and spread of electrical activity e.g. generalized epilepsy or focal epilepsy.[11] Epilepsy is either; idiopathic when there is no underlying cause or secondary if there is an underlying cause. Underlying factors can be identified in a greater proportion of elderly patients than younger patients,

including cerebrovascular disease, trauma, dementia and tumors, a significant portion (one- third to one-half) are of unknown etiology.[12]

Alzheimer's disease (AD) is a chronic neurodegenerative disease that usually starts slowly and gradually worsens over time. It is the cause of 60% of cases of dementia. The disease process is associated with plaques and neurofibrillary tangles in the brain. The cause of Alzheimer's disease is poorly understood except for 1%-5% of cases where genetic differences have been identified (autosomal dominant inheritance).[13]

Our study is a multicenter study, two referral charity clinics, one private neurological clinic and two neurological hospitals. Almost 480 patients with Alzheimer's disease (AD) were included in the study. Like what was mentioned in the literature 60% of our patients were female.[14] The sex and gender gap is clearly clinically relevant when it comes to dementia care and health policy. The influences on observed sex and gender differences are complex. There are many factors which are likely contributing to this puzzle, relating to both sex (reproduction, sex hormones), gender (social roles, identities and opportunities) and the interaction between the two (e.g. epigenetic). Some researchers argue that sex differences in AD is due to the fact that women live longer than men and since AD incidence and prevalence increase with age so more women would live long enough to develop dementia.[15] The age distribution of our study group range from 65-98 years. Most individuals with the disease are 65 or older, although individuals may develop familial or early onset Alzheimer's disease, as early as their 30s and 40s. The likelihood of developing Alzheimer's disease double about every five years after age 65. After the age 85, the risk reaches nearly 50 percent so the greatest risk factor for Alzheimer's disease is advanced age.[15] The vast majority of Alzheimer's disease cases have a late onset disease. The Average life expectancy after diagnosis is eight to ten years. In some cases however, it can be as short as three years or as long as twenty years.

During the period of the follow up out of 480 patients, 48 labeled as epileptic (10%). this is similar to what was mentioned in the literature.[16] Alzheimer disease (AD) and epilepsy are disorders commonly seen in the elderly. From a clinical aspect, patients with AD have an increased risk of developing seizures and epilepsy; thus AD may be an important cause of epilepsy in the elderly. Compared with healthy individuals of the same age, patients with sporadic AD have a 6- to 10-fold increased risk of developing clinical seizures during the course of their illness. In early-onset familial AD (EOFAD), epilepsy occurs more often than in sporadic AD. Seizure prevalence seems to increase with AD duration. AD severity seems to constitute another risk factor for seizures. People who have AD in combination with a seizure disorder suffer greater cognitive decline and more rapid progression of symptoms than those with AD alone.[17] Patients with Alzheimer's disease should be assessed carefully for epileptiform activity and silent seizures if they present with fluctuations in cognition, rapidly progressive cognitive decline.

Characterization of the clinical manifestations of seizures is usually based on information derived from the patient or the caregiver. The diagnosis of seizures in patients with AD is not always easy, there are many difficulties in establishing the diagnosis in this group of patients, since confirmation of a seizure

requires a consistent clinical history which is difficult to achieve in patients with a dementia condition owing to difficulties remembering and/or reporting the event.

Generalized epilepsy was found to be the most common type among our studied group, there are few studies in the literature evaluating what type of seizures happen more often in AD. It was stated that both generalized seizures and complex partial seizures(focal with impairment) are likely to occur, but focal seizures with/without secondary generalization tend to predominate.[18] In the predominant seizure subtype in patients with Alzheimer's disease (non-motor complex partial seizures), some symptoms of these seizures can overlap with cognitive features of Alzheimer's disease, but they can often be distinguished as epileptic events by their recurrent and stereotyped nature, and supported by epileptiform activity on EEG.

Like what was reported by researchers worldwide a small number of our patients exhibited EEG abnormalities.[19] The sensitivity of scalp EEG recordings to detect epileptiform activity depends on the type of EEG protocol that is used. In patients with Alzheimer's disease, epileptiform activity is commonly detected in electrodes that surround frontotemporal and temporal brain regions. EEG in patients with dementia and epilepsy may well be less important in the determination of type of epilepsy. Like what was reported by other researchers a considerable number of our studied group showed an evidence of brain atrophy when they were examined using Brain MRI. A brain scan using magnetic resonance imaging (MRI) is generally included in the standard evaluation for Alzheimer's disease and other forms of dementia.[20] This scans can also show the loss of brain mass associated with Alzheimer's disease. Beta-amyloid, considered a hallmark of the disease, show up as dark areas in MRI scans of the brain. AD is characterized by an insidious onset and inexorable progression of atrophy that is first manifest in the medial temporal lobe. The entorhinal cortex is typically the earliest site of atrophy, closely followed by the hippocampus, amygdala, and parahippocampus.[21] MRI can measure the size and amount of cells in the [hippocampus](#), an area of the brain that typically shows [atrophy \(shrinkage\)](#) during the course of Alzheimer's disease. MRI scans of the brain with Alzheimer's disease may also show parietal atrophy. The parietal lobe of the brain is located in the upper back portion of the brain and is responsible for several different functions including visual perception, ordering and calculation, and the sense of our body's location.[22] In the early stages of Alzheimer's disease, an MRI scan of the brain may be normal.

Conclusion: Patients with Alzheimer's disease have an increased risk of developing epilepsy. There is strong relation between disease duration and development of epilepsy.

Declarations

Conflict of interest:

Authors confirmed that there are no competing interests.

Funding:

There were no funds

Informed consent:

Both written and verbal consents were from each patients relatives before starting of the study.

Ethical approval:

The study was approved by the local ethics committee. Ethical approval was sought from the State Ministry of Health.

Ethical Publication Statement:

All authors gave their consent for publication.

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