Original Article

AN OBSERVATIONAL STUDY FROM EASTERN INDIA ON THE RISK FACTORS, COMORBIDITIES, AND SOCIETAL FACTORS LINKED WITH ALZHEIMER'S DISEASE

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Abstract

Background: Alzheimer Disease (AD), the most prevalent form of dementia in the world, is a progressive neurological condition that lowers quality of life and puts a strain on carers. Several linked comorbidities as well as social and risk factors can be addressed and controlled, if necessary, despite the fact that the condition cannot be totally prevented with current medication.

Aim: Our study makes an effort to define and clarify the relative frequency of these characteristics in patients who present with AD vs those who present with other neurologic issues.

Methods: This study comprised 324 cases of Alzheimer's disease, including 208 men and 116 women.

Results: The findings indicate etiologic variables and chances for prompt intervention. Diabetes, hyperlipidemia, cerebrovascular illness, and depression are substantially linked with dementia. The association between hypertension and dietary factors, occupational factors, or marital status was insignificant. The study's total aged population with its prevalent comorbidities and confounding variables is one of its limitations.

Conclusion: In order to prevent or delay the onset of dementia, this study concludes that it is crucial to address modifiable risk factors.

INTRODUCTION

Alzheimer disease (AD) is a neurodegenerative disorder that causes behavioural changes, amyloid and tau build-up in the brain, and gradually progressing cognitive and functional deficits. Deficits in short-term memory, executive and visuospatial dysfunction, and praxis are the most typical cognitive symptoms of AD [1, 2, 3]. There are a few less common AD types that have been identified with comparatively preserved memory. Although recent developments in amyloid imaging and genetics show great promise for facilitating early and presymptomatic

diagnosis of AD and its discrimination from other neurodegenerative disorders, clinical assessment, including cognitive testing, remains crucial for the diagnosis and staging of AD [4, 5].

In the current study, we conducted a cross-sectional and retrospective analysis of environmental, social, nutritional, and occupational factors in a cohort of AD patients who presented to the Neurology OPD of a teaching hospital that mostly serves semi-urban and rural patients. According to the majority of published studies, AD accounts for 70% of dementia cases on average [1]. This illness has a significant negative influence on the patient's quality of life as well as that of their families and caregivers. It starts with memory and language problems, moves on to affect visuospatial abilities, and eventually results in difficult-to-control behavioural and psychotic manifestations [2]. The slow but inevitable advancement of the illness in patients results in personality collapse, financial loss for the family, and extremely high levels of stress for caretakers [3].

Recent discoveries have given these patients some hope for an illness that was previously thought to be nearly incurable [4]. However, environmental, social, occupational, nutritional, and dietary aspects should be taken into consideration because they may provide us ways to prevent the disease or at the very least provide us with insights into the various modes of pathogenesis of this disease [5]. The relative impact of these characteristics is highlighted in this observational, retrospective study based on how frequently patients with Alzheimer's disease present to the Neurology OPD of a major teaching hospital in Odisha. The role of education, occupation, and cognitive reserve as risk factors for AD has been examined in a number of sizable studies [6, 7]. These characteristics, as well as dietary and nutritional aspects [8] (including vegetarianism), educational attainment, employment position, marital status, living alone versus with family, depression, sleep, and other factors, have all been studied in our patients. In our study cohort, we also briefly examined the effects of obesity, dyslipidemia, hypertension, and diabetes mellitus [9].

METHODOLOGY

From July 2019 to June 2022, this study was conducted in an IMS & SUM Hospital in Bhubaneswar, which is in the eastern Indian state of Odisha. A total of 324 Alzheimer's disease cases- 208 men and 116 women- were examined. The average age of the men was 67 years, compared to 75 for the women. Comparisons were made using control populations, which were selected from the general public restricted to people 60 years of age and older who visited the Neurology OPD for any concern.

The following variables were taken into account, and the necessary records were kept a) manual versus intellectual occupation; b) rural versus urban; c) cerebral vascular disease; d) type 2 diabetes; e) hypertension; f) obesity; g) dyslipidemia; h) smoking; I vegetarianism; j) marital status; l) lack of adequate nocturnal sleep; m) physical activity; n) other dietary variables. O) serum vitamin D concentrations p) oestrogen replacement treatment in females

Taking the patient's history, performing a physical and neurological examination, and consulting previous medical records and conducting any necessary biochemical tests were some of the methods used to gather information. The Social Psychology Network's programme Research Randomizer was used to randomly assign research and control groups.

Diagnosis

Patients in our study were categorised using the NINCDS-ADRDA Criteria for the diagnosis of AD [10]. This section was omitted from the study because it was deemed too complicated to classify patients according to the cognitive domain that was most impaired. The existence of notable behavioural manifestations was also disregarded.

If the patient resided in a region where agriculture is the primary economic activity, this was taken into account. If there was past clinical or imaging evidence of an ischemic stroke at any time, cerebrovascular disease was

assumed to be present. The patient's subjective evaluation served as the basis for determining how much sleep they got at night. Similar rules apply to physical activity, where patients were categorised as physically active or inactive based on their own opinions as well as their physical activity for work and play. Other dietary determinants included consumption of fish and milk, as well as fruits and vegetables high in antioxidants. The amount of protein in the diet was also analysed. Other parameters were established using common diagnostic and cut-off standards.

RESULTS

In comparison to the overall patient population at the OPD, which consisted of patients, 64% of patients were from cities. 94% of patients worked in white collar jobs currently or in the past, whereas the remaining 6% were in manual labor-intensive jobs like agriculture. However, the percentage of manual and non-manual occupations was nearly evenly distributed in the control group.

In the patient population, 42% had type 2 diabetes, compared to 15% in the control group. 80% of AD patients and 75% of the control group both had hypertension. Compared to the control group, which had only 35% of patients with AD, 84% of patients had dyslipidemia. Obesity, which is characterised by a Body Mass Index (BMI) above 30, affected 3% of AD patients and 5% of the control group. The prevalence of cerebrovascular disease, which is indicated by a prior ischemic stroke, was 36% in the control group and 85% in AD patients. For primarily religious and cultural reasons, only about 5% of the AD cohort identified as vegetarians, compared to 2% in the control group.

Following is the marital status: The control population had a marriage rate of 92%, while only 78% of the research sample was married. The remaining participants were primarily widowed or single. As determined by a psychiatrist, 65% of the study population had a current or prior diagnosis of depression, compared to 23% in the control group. Compared to 32% of patients in the control group, 63% of study group participants reported having insufficient or fragmented nocturnal sleep.

Due to poor understanding and incomplete medical records, it was challenging to evaluate oestrogen replacement therapy; therefore, an average estimate was made among female patients and controls, of course, which produced a result of 2% in both the study and control groups. A arbitrary cut-off level of either LDL-C greater than 120 mg/dL or triglycerides greater than 180 mg/dL was used to determine dyslipidemia. Dyslipidemia was discovered to be present in 56% of AD patients compared to 24% of controls. 43% of controls and 88% of patients both had vitamin D deficiencies.

According to the patients' own subjective evaluations, physical activity was assessed. Compared to 68% of the control group, just 14% of AD patients reported engaging in regular physical exercise. Diverse dietary parameters were evaluated on an individual basis, with 16% of AD patients reporting dietary fats, inadequate protein intake, inadequate or no consumption of green leafy vegetables, and inadequate or no consumption of fruit, in contrast to none of the participants in the control group.

DISCUSSION

We discovered that the following factors had significantly different occurrences in the study and control groups, suggesting that they may either be contributing factors to AD or dementia in general in our patients or that they may be predisposing factors that make it possible for the patient's cognitive reserve to be impacted to the point where dementia is detectable.

When compared to the control group, patients in the AD group were shown to have around twice the prevalence of type 2 diabetes. Numerous animal investigations have demonstrated how the γsecretases and as well as Aβ clearance are stimulated by both insulin resistance and insulin deprivation [11]. The Rotterdam Study [12] conducted in the 1990s discovered that type 2 diabetes nearly increased the risk of dementia and AD.

Neurofibrillary tangle (NFT) formation is a result of hyperphosphorylation of tau protein due to insulin resistance [13].

According to the Honolulu-Asia Aging Study, diabetes in old age was associated with a higher risk of AD (relative risk: 1.8) and AD pathology on autopsy, especially in individuals carrying the APOE-ε4 allele [14]. There is some proof that the metabolic syndrome, which includes abdominal obesity, hypertriglyceridemia, insulin resistance, and hypertension, may have a stronger relationship with AD than diabetes alone [14]. However, we only focused on the individual components in our study and did not take into account the clustering effect of the metabolic syndrome. In addition, non-enzymatic glycation of the A peptide may occur, making it a more neurotoxic AGE than its unglycated version [15].

Due to the high prevalence of hypertension in the age group selected for both the study and control groups, we could not identify any significant differences in the prevalence of hypertension between AD and control patients. It is frequently counterintuitive how hypertension and dementia are related. On the one hand, people with dementia have lower blood pressure than healthy people do [16], but longitudinal studies have shown that high blood pressure is linked to a higher risk of dementia later in life. This syndrome is known as dementia and midlife hypertension.

In contrast to controls, patients with AD in our study were found to have dyslipidemia more than twice as frequently. This is consistent with earlier research, including one study [17] that discovered 10% higher cholesterol levels in AD patients compared to healthy persons. The blood brain barrier's integrity is mostly compromised by high blood cholesterol, which increases the risk of dementia. Increased Aβ-peptide deposition, NFT production, neuroinflammation, malfunction of cholinergic pathways, and microhaemorrhages are some effects of dyslipidemia. When obesity was taken into account, we did not see any significant differences. This may have been caused by the low prevalence of obesity among the patients visiting our OPD, which is in line with local demographics. Studies on the relationship between fat and dementia have produced a variety of results. According to a significant study by Fitzpatrick et al. [20], obesity increases the risk of dementia in middle age (hazard ratio - HR: 1.39; 95% CI: 1.03-18.7) but decreases the risk in later life (HR: 0.63; 95% CI: 0.44-0.91).

In our investigation, dementia and cerebral vascular disease were highly correlated. This is also consistent with other research that found significant small vessel arteriolosclerotic disease and amyloid angiopathy in post-mortem examinations of AD patients' brains. According to the so-called "two stroke" explanation of AD, the initial stroke led to oligemia in the brain tissue, which in turn induced amyloidogenic and non-amyloidogenic pathways to destroy neurons. Aβ peptide accumulates as a result of increased APP expression and processing in the amyloidogenic pathway [21]. The blood-brain barrier is damaged, which reduces the amount of A peptide that is cleared.

The majority of people who visit our OPD are married, thus the minor difference in marital status between the study and control groups that we discovered is probably meaningful. In 2009 [22], Hkansson et al. demonstrated that widowed or never-married people had an increased risk of getting dementia from any cause, particularly if they carry the APOE 4 allele. This has also been related to married people experiencing depression less frequently.

When compared to the controls, we discovered that our dementia patients had a more than twofold higher incidence of depression. The topic of whether depression is a result, cause, or coincidence in terms of dementia has been explored in earlier studies [23] but without clear resolution.

Even though we did not precisely quantify the differences between cases and controls with reference to this variable, it was difficult to objectively evaluate these factors based on the history taking, which is why we did not accurately quantify the occurrence of insomnia, coupled with psychosis, and behavioural agitation in our AD patients. Studies have linked sleep problems, particularly REM sleep disturbances, to an increased risk of dementia [24, 25]. Other variables we looked at included dietary variables like vegetarianism, consumption of dairy products, consumption of fruits and green leafy vegetables, and serum vitamin D levels. These variables did not significantly differ between the study and control groups in our study beyond a few percentage points, so they are not tabulated or further discussed.

Our study included some drawbacks that might make it harder to draw conclusions regarding the significance of the parameters under investigation and how they relate to Alzheimer's disease. One, individuals with a variety of illnesses who presented to the OPD with a variety of neurologic complaints, not all of which were connected to cognitive dysfunction, made up the population from which the study and control groups were chosen. Second, both the participants in the study and the control group were elderly. Thirdly, the perception of dementia in these people is likely to have a higher threshold than in highly educated and affluent people, in whom family members or the patient himself/herself is able to recognize the onset of cognitive impairment at an earlier stage. The general mass of patients in our OPD come primarily from the lower middle and lower socioeconomic groups.

CONCLUSION

Numerous investigative and observational research have assessed the impact of risk factors that can be changed or partially changed in cross-sectional Alzheimer's disease. Late middle age, the period before the onset of cognitive decline, is of utmost importance since risk factors including diabetes mellitus, hypertension, adequate treatment of depressive disorders, hyperlipidemia, and a healthy balanced diet and active lifestyle may all be changed at this time. This study emphasises the significance of taking advantage of these chances to at least partially offset or postpone the onset of dementia in the future. Beyond that, good management of illnesses like diabetes and hypertension will significantly lengthen these patients' lives and improve their general quality of life, regardless of the onset of dementia.

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