Diabetes Mellitus Type 2 as a Major Risk Factor of Developing Alzheimer’s Disease in Pakistani Population

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ABSTRACT

Background: Diabetes mellitus type-2 (DMT2) could increase the risk of Alzheimer’s disease (AD) specifically related dementia, through several biological pathways, but the relationship between DM and the development of AD remains uncertain.

Objectives: The aim of the present study was to explore the status of diabetes as one of the major risk factors of cognitive decline and dementia in AD and to compare the risk of developing AD among subjects with and without DM.

Methods: The baseline examination was conducted from January 2008 to October 2010 on 611 subjects of both sexes who were above 50 years of age, to detect the prevalent cases of dementia. The Mini-Mental State Examination (MMSE) was done on all of these subjects. At each follow-up, random blood glucose levels were determined; all participants underwent a comprehensive clinical examination

Results: The study shows that risk of “dementia” increases with age, duration of diabetes and relevant conditions e.g. obesity. The risk of “Dementia increases with duration of diabetes and the chi-square tests verify the claim. The calculated chi-square test statistics value was found to be 130.26 with degrees of freedom 9, corresponding p-value is (<0.005). It was also found that obese diabetics had higher risk of developing AD, as well as those having borderline diabetes were also at the higher risk.

Conclusion: The present study revealed that DMT2 is one of the major risk factors that would increase the risk of AD; but along with other factors like obesity, lifestyle and aging, it can lead to AD and related pathological conditions in individuals markedly characterized by dementia and cognitive decline.

Key words: Diabetes mellitus type-2 (DMT2), alzheimer’s disease (AD), dementia, cognitive decline, obesity.

INTRODUCTION

Incidence rates for AD have been studied extensively throughout the world.1-4 Studies from various populations although have consistently shown an association between diabetes and cognitive deficits or dementia,4-5 but the precise relationship remains unclear. Insulin resistance is present in most diabetic patients and is associated with compensatory hyperinsulinemia, which is one of the suggested mechanisms to explain the increased risk of Alzheimer’s disease in diabetic patients.6-8 Now-a-days Type-2 DM is common in old age5,9 that can be a risk factor for dementia and cognitive decline.10,11 Few evidences also support the association of borderline diabetics and risk of dementia and Alzheimer’s disease.12 Besides adding many complications in body, diabetes can contribute to poor memory and lessen cerebral intellectual functions in an assortment of ways. The complications related to it and its pathophysiology as obesity, daily stress, aging and unhealthy lifestyles may worsen the hyperglycemia that is reported to be among a few reasons that put our population at higher risk of memory and thinking problems as we grow older.13 The findings are of great concern, as prevalence of diabetes is alarmingly increasing in Pakistan27 and hence may contribute to the growing number of Alzheimer’s cases in coming years.

OBJECTIVES

To explore the status of diabetes as one of the major risk factors of cognitive decline and dementia in AD.

To compare the risk of developing AD among subjects with and without DM.

METHODOLOGY

a Males and females of 50 years and above.
b Complaints of memory loss reflected in everyday problems such as difficulty in remembering names of the individuals following introduction, misplacing objects, difficulty remembering multiple items to be purchased or multiple tasks to be performed, problems remembering telephone numbers or zip codes and difficulty recalling information quickly or following direction. Onset of memory loss should be described as a gradual phenomenon, without sudden worsening in recent months.

c Presence of dementia with and without diabetes.

This study included 611 subjects who were above 50 years of age, to detect the prevalence of dementia. The Mini-Mental State Examination (MMSE) was done on all of these subjects. We considered the range from zero to 30, in which 27-30 was normal cognition, 21-26 was mild dementia while 10-20 was considered as moderate dementia and patient of severe dementia scored < 10. Non-diabetic older patients (n=324) and diabetics (n=287) were selected (Age >50Yrs) for this study. All preliminary diagnosed AD participants underwent a comprehensive clinical examination and cognitive tests, as detected previously. The diagnosis of AD was similar to that of international criteria and required gradual onset, progressive deterioration and lack of any other specific causes of dementia. The Mini-Mental State Examination (MMSE) was done on all of these subjects, while our criterion for identifying Alzheimer’s disease was similar to those used by the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA). At each follow-up random blood glucose level was determined, the virtually pain free method was used by using ACCU-CHEK-Active. Patients were monitored for degrees of cognitive impairment and dementia. Statistical analysis was based on incident tables to evaluate the association between the presence or absence of dementia with or without diabetes and was determined by chi-square test for independence between variables.

RESULTS

The risk of “Dementia” increases with duration of diabetes and the chi-square tests verify the claim. The calculated chi-square test statistics value was found to be 130.26 with degrees of freedom 9, corresponding p-value is (<0.005).

DISCUSSION

In Pakistan, diabetes is reported as a common metabolic disorder, along with other risk factors like obesity and cardiovascular problems. However in older individuals dementia is a cognitive problem when observed neurologically in diabetic patients with AD. It was hypothesized earlier that perhaps the changes in the insulin receptors in diabetes, obesity and related insulin resistance may contribute to decreased sensitivity to insulin that can reduce synaptic plasticity in aging. These effects appear to be due to raised brain insulin level as observed in aging, obesity and diabetes which decreases the clearance of Aβ amyloid thus increasing amyloid toxicity. But there is a continuous lack of knowledge about mechanisms that can lead to impaired cognitive function in hyperglycemic patients. According to the recent studies, the association between diabetes and dementia is unlikely to be due to the potential confusing effects of demographic variables such as age or sex, educational level or socioeconomic status (Shafqat, 2008). Moreover the kind of usual
neuropsychological routines observed in these patients may be the result of various interrelated pathological processes developed with the duration of disease, such as damaging effects of hyperglycemia on the brain that can be linked with complications of cerebrovascular disease which is known to be the major cause of the decline in processing, perception & reaction time. It has been suggested that duration of diabetes is responsible for changes in insulin signaling that may be a major cause of hyperglycemic brain cells leading to damaging effects like damaged blood vessels, nerve cell death or the acquisition of amyloid deposits. Our data revealed that the older population with diabetes having obesity reported memory problems mostly when compared with non-diabetic and non-obese individuals. In our population though the actual number of diabetic patients is higher but patients who developed dementia are less and this has limited the statistical analysis for the identification of such risk factors for dementia in this subgroup. In the present study, we found that clinical cognitive decline was also becoming a common occurrence in a sample of older individuals with base line diabetes and was predicted by decline in cognitive functions. These findings are of potential clinical importance and further confirmatory studies are needed in both diabetic and non-diabetic populations. However, the control over increasing trend of obesity and diabetes or hyperglycemia can help our population minimize the detrimental effects on brain and its functions.

CONCLUSION

Our study revealed that “Type-2 Diabetes” is a major factor (disease) that will increase the risk of AD in Pakistan; along with other factors like obesity, lifestyle and aging. Prolonged duration of diabetes can lead to AD and related pathological conditions in individuals markedly characterized by dementia and cognitive decline. Several limitations of our study warrant further discussion. Our epidemiological observations, coupled with emerging experimental evidence, support a possible role of diabetes in the pathogenesis of AD. Our data also raise the possibility that obesity and related factors like gender, age and lifestyles might provide a link and could be useful for early detection of risk and prevention of AD and its related dementia.

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