Study of Risk Factors of Mild Cognitive Impairment in Patients with Type 2 Diabetes Mellitus

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I. INTRODUCTION

Diabetes mellitus is a severe metabolic disease which can effect multiple organs in the body. It is a complex disorder and several factors related to it, either the disease itself or its treatment, long-term complications and comorbidities can affect the brain[1]. Type 2 diabetes has been consistently associated with increased risk of accelerated cognitive decline[2] and an higher incidence of dementia,[3,4] particularly in older individuals. Patients with Type 2 Diabetes mellitus are almost two times more likely to experience cognitive decline and dementia compared to those with normal glucose tolerance (NGT).[4] Studies have suggested that T2DM effects cognitive domains like verbal memory (verbal fluency, immediate and delayed verbal recall), attention and processing speed, psychomotor ability, and executive functions.[5,6]. Diabetes has also been observed to be related with cognitive decrements such as worsening of abstract reasoning[7], complex motor functioning and working memory[7].

Such decline maybe in part due to an array of tissue response from chronic hyperglycemia, postprandial glucose fluctuations, advanced glycosylated end-products, and altered insulin action and amyloid-beta (Aβ) peptide accumulation[8,9]. Chronic hyperglycemia is implicated, perhaps by promoting the development of cerebral microvascular disease. Inflammation and oxidative stress also appear to be involved in the pathogenesis of cognitive decline. These two factors form a vicious cycle that accelerates brain injury and cognitive impairment.[9]

The spectrum of cognitive decline in type 2 diabetes mellitus ranges from asymptomatic state to dementia. Mild cognitive impairment (MCI) is the intermediate clinical state which generally preceeds dementia in which patients have cognitive complaints and objective disturbances on cognitive tests but their daily functioning is largely preserved. Although people with MCI have a higher dementia risk, the conversion rates reported range from 1% to 25% or more per year.[10] In fact, many persons with MCI convert back to a cognitively normal state.[10]

This transitional and therefore possibly modifiable characteristic makes the state of MCI a promising approach in the development of prevention strategies of dementia. Though association of diabetes with early cognitive decline is vastly studied, risk factors which accelerate it are not completely studied. Hence by identifying the risk factors for MCI, the patients at risk can be identified early and will be benifitted by aggressive management, thus preventing development of dementia. Thus, we investigated the association between various physical and biochemical parameters in patients with type 2 diabetic patients and mild cognitive impairment (MCI).

Objective of the study: To identify risk factors of mild cognitive impairment in type 2 diabetes patients.

II. METHOD OF STUDY

The study was done in Sri Devraj Urs Medical College, Kolar, Karnataka. Type 2 Diabetes mellitus patients presenting to Department of General Medicine were screened to be included in the study. After applying stringent inclusion and exclusion criteria, 206 type 2 diabetic patients were enrolled in the study.

The inclusion criteria were as follows:

- T2DM patients aged 18years and above and volunteer to participate in the study.

T2DM was diagnosed according to diagnostic criteria given by American Diabetes Association.

The exclusion criteria were as follows:

- Patients with other neurological conditions such as history of head trauma, brain tumor, epilepsy, stroke, transient ischemic attack, coma, or presence of dementia before T2DM, parkinson's disease.
- Patients with psychiatric disorders; depression, alcohol dependence, drug dependence, and use of antidepressant or antipsychotic medications, schizophrenia.
- Patients with auditory/visual disorders.

All patients gave their written consent prior to participation, and the study was approved by Institutional Ethical Committee.

Assessment of Variables :

Detailed history was taken from the participants and general and systemic examination was done.

- History including level of physical activity, duration of diabetes, history of hypertension and history of smoking was taken.

Physical activity was determined on the basis; if subject was doing at least 30 min of aerobic exercise in a day, he/she was considered as active and if otherwise as sedentary.

- Anthropometric measurements such as –

-height and weight were measured and body mass index (BMI) was calculated according to Quetelet equation (BMI = weight in kilograms/height in meters squared).

-For waist–hip ratio, waist circumference was measured at the midpoint between the lower margin of ribs and the superior border of the iliac crest. Hip circumference was measured around the widest portion of the buttocks.

-Systolic blood pressure (SBP) and Diastolic blood pressure (DBP) were noted down as a mean of two tests conducted after an interval of 3 min in sitting position after 15 min of rest.

- Laboratory tests were done which includes-

HbA1c, total blood cholesterol, HDL cholesterol,

- Mild cognitive impairment was diagnosed by using the Montreal Cognitive Assessment (MoCA) score. It is a score with total of 30 points. Patients with score of 26 or more were considered as without MCI and less than 26 are considered with MCI.

The scoring by MMSE can be influenced by the effect of age and education level. To avoid any bias, present data were well matched for age and education status

Figure 1shows the data collection protocol after following stringent inclusion and exclusion criteria.

III. STATISTICAL METHODS

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Continuous data was represented as mean and standard deviation. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between group with no cognitive impairment (NCI) group and with MCI. Pearson's correlation was done to find the correlation between two quantitative variables. p value <0.05 was considered as statistically significant.

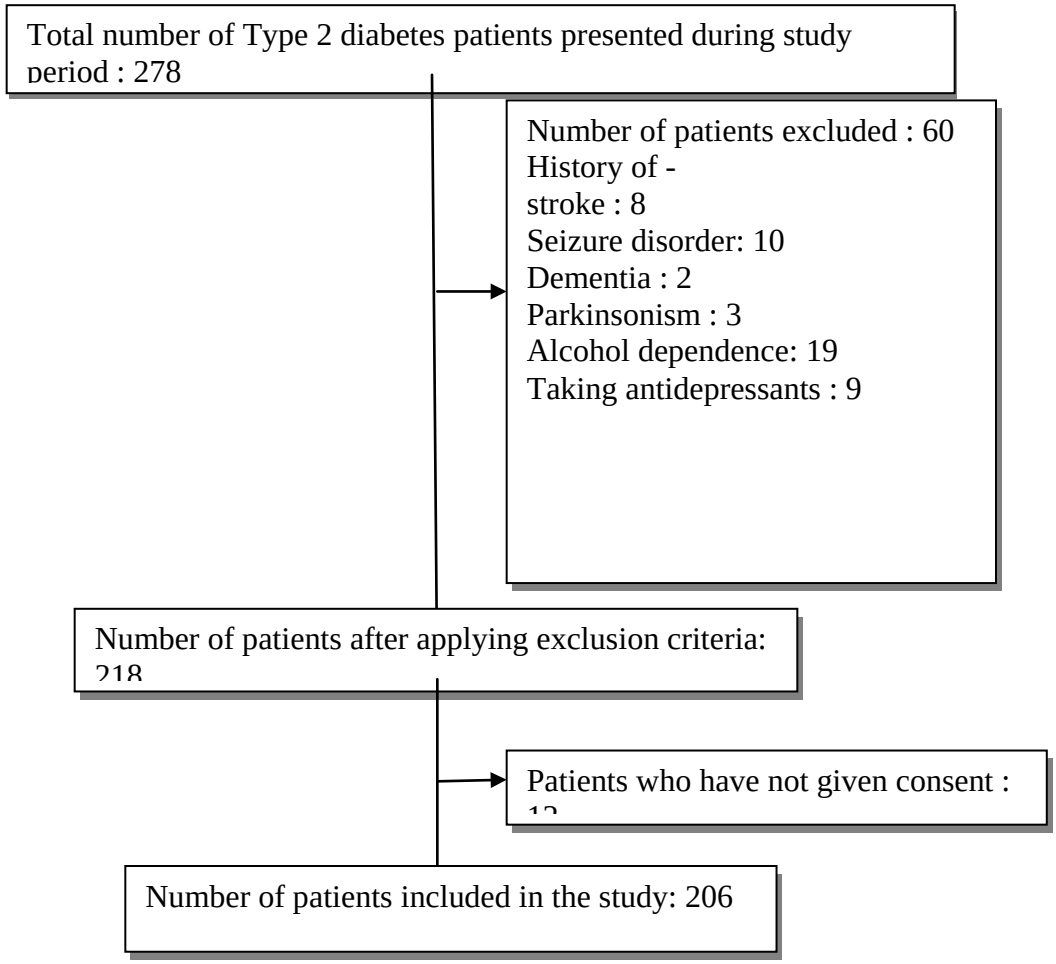

Figure 1: Showing data collection protocol after following stringent inclusion and exclusion criteria

IV. Results

A total of 206 type 2 diabetic patients were enrolled in the study. Participants are aged between 52 - 76 years with mean age of 66 years. 107 (51.9%) were men and 99 (48.1%) were women. The median duration of diabetes was 12 years.

118 (57.3%) patients have MCI(MoCA <26) and 88 (42.7%) do not have MCI (MoCA >26).

When various physical and biochemical variables among study population are compared, there were significant differences in the mean duration of diabetes ([8.09 ± 3.02 y vs. 5.80 ± 4.06 y], p = 0.002), rate of patients with hypertension ([59% vs. 41 %], P=0.025), rate of patients with sedentary life style ([48% vs. 33%], p = 0.001), rate of patients with smoking history, ([37% vs. 29%], p = 0.003), percentage of patients with BMI more than 27 kg/m^2, ([69% vs. 57%], p = 0.045), percentage of patients with waist hip ratio more than 0.85 ([68% vs. 59%], p = 0.004), between group with MCI and without MCI.

Duration of diabetes, presence of associated hypertension, smoking history, high BMI and waist hip ratio positively correlated with MCI whereas physical activity correlated negatively with MCI.

There are no significant differences in the duration of hypertension and SBP, DBP values, levels of HbA1C and blood lipid between group with MCI and without MCI. Though all the variables had a higher rate among group with MCI, the difference was not statistically significant.

Duration of diabetes, presence of associated hypertension, smoking history, BMI , waist hip ratio and physical activity were included in the multivariate logistic regression models to find probability of these variable as risk factors for MCI, pnly duration of diabetes, sedentary life style and smoking history had p less than 0.005. hence, they could be independent risk factors for development of MCI in type 2 diabetes patients.

V. Discussion

In the present study, we studied correlation between various parameters in type 2 diabetic patients and mild cognitive impairment.

Several screening tools are available for detecting cognitive impairment. The Montreal Cognitive Assessment (MoCA) was developed as a 30-point, 10-minute test that evaluates visuospatial and executive function, orientation, language, attention and recall. It is more sensitive (90% vs 18%) than MMSE in detecting mild cognitive impairment with a specificity of 87%. MMSE has a good sensitivity and specificity for the detection of dementia, but for the detection of nondementia cognitive impairment, its sensitivity is only 20%–60%. In order to correct MMSE deficiencies, the MoCA has been introduced into clinical practice.

Our results show that duration of diabetes, lack of physical activity and smoking are independent risk factors for MCI. These findings are in agreement with other studies. [11,12,13.] The findings of another study [11] suggest an association between earlier onset, longer duration, and greater severity of diabetes and MCI. One study[12] proves that compared to never smokers, middle-aged male smokers experienced faster cognitive decline in global cognition and executive function, which is inagreement with our study. Another study [13] points out that practical interventions aimed at reducing and replacing sedentary behavior with intermittent light intensity physical activity can help slow cognitive decline.

Higher prevalence of cognitive decline is alarming, and results of the present study suggest that every diabetic subject should be examined for cognition so that dementia can be prevented or delayed effectively in diabetic patients.

Limitations of the study is that MoCA score which is influenced by age and educational level is used in prospective observational study. Though age and education status are well matched while comparing results in our study, the results are more dependable when done in a case-control type of study.

VI. Conclusion

The longer duration of diabetes, sedentary life style and smoking could be risk factors of MCI in type 2 diabetic patients. The study suggest that lifestyle changes can reduce risk of MCI development in diabetic patients.This finding could have an important impact on the management of cognitive decline in diabetic patients. In absence of curative treatments for dementia with type 2 diabetes mellitus (T2DM), it is worthwhile to target modifiable risk factors so that progression of dementia can be delayed or prevented.

References

[1] Seaquist ER, “The Final Frontier: How Does Diabetes Affect the Brain?, “ in *Diabetes*, 2010;59(1):4-5.

[2] Fontbonne A, Berr C, Ducimetiere P, Alperovitch A, “Changes in cognitive abilities over a 4-year period are unfavourably affected in elderly diabetic subjects: results of the epidemiology of vascular aging study,” Diabetes Care .2005.24: 366–70

[3] Cukierman T, Gerstein HC, Williamson JD , “Cognitive decline and dementia in diabetes—systematic overview of prospective observational studies,”. Diabetologia .2006.48: 2460–9.

[4] Mayeda ER, Haan MN, Yaffe K, Kanaya AM, Neuhaus J. Does type 2 diabetes increase rate of cognitive decline in older Mexican Americans? *Alzheimer disease and associated disorders*. 2015;29(3):206-212.

[5] Cukierman-Yaffe T, Gerstein HC, Williamson JD, Lazar RM, Lovato L, et al. (2009) Action to Control Cardiovascular Risk in Diabetes-Memory in Diabetes (ACCORD-MIND) Investigators

[6] Abbatecola AM, Rizzo MR, Barbieri M, Grella R, Arciello A, et al. (2006) Postprandial plasma glucose excursions and cognitive functioning in aged type 2 diabetics. Neurology 67: 235–40.AM

[7] Yan SD, Chen X, Fu J, Chen M, Zhu H, et al. (1996) RAGE and amyloid-beta peptide neurotoxicity in Alzheimer's diesease. Nature 382: 685–691.

[8] Varun Parkash Singh, Anjana Bali, Nirmal Singh, and Amteshwar Singh Jaggi, Advanced Glycation End Products and Diabetic Complications. Korean J Physiol Pharmacol. 2014 Feb; 18(1): 1–14.

[9] Christopher T. Kodl and Elizabeth R. Seaquist. Cognitive Dysfunction and Diabetes Mellitus Endocr Rev. 2008 Jun; 29(4): 494–511.

[10] Farias ST, Mungas D, Reed BR, Harvey D, DeCarli C. Progression of Mild Cognitive Impairment to Dementia in Clinic- vs Community-Based Cohorts. *Archives of neurology*. 2009;66(9):1151-1157.

[11] Roberts RO, Geda YE, Knopman DS, et al. Duration and Severity of Diabetes Are Associated with Mild Cognitive Impairment. *Archives of neurology*. 2008;65(8):1066-1073.

[12] Michael J. Wheeler, Paddy C. Dempsey, Megan S. Grace, Kathryn A. Ellis, Paul A. Gardiner et al. Sedentary behavior as a risk factor for cognitive decline? A focus on the influence of glycemic control in brain health, Alzheimers Dement (N Y). 2017 Sep; 3(3): 291–300.

[13] Sabia S, Elbaz A, Dugravot A, et al. Impact of smoking on cognitive decline in early old age: the Whitehall II cohort study. *Archives of General Psychiatry*. 2012;69(6):627-635. doi:10.1001/archgenpsychiatry.2011.2016.

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