Original Research Article

A cross-sectional study of cognitive dysfunctions in type 2 diabetes mellitus

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Abstract

Introduction: Diabetes mellitus is a chronic metabolic disease characterized by hyperglycemia that affects various body systems. For this progressive, incurable condition, the best scenario after diagnosis is good metabolic control and risk factor management to forestall vascular and neuropathic complications. People with diabetes often develop diverse microvascular, macrovascular, and neuropathic complications that erode the quality of life, making diabetes a major concern for much of the developed and developing world.**Materials and Methods:** This is a cross-sectional, comparative study. Subjects for the study were selected from the in-patient admissions made under various specialties at the Department of Psychiatry, Midnapore Medical College. Resi-Monirampore, Barrackpore, Kolkata. After obtaining institutional ethical committee clearance and informed consent from the patients, 60 patients who were diagnosed as having type 2 diabetes and 60 non-diabetic controls, matched to age, gender, education, and socio-economic status, were chosen by convenience sampling. The control group was selected from relatives of the patients admitted under various specialties.**Results:** A total of 120 subjects comprising 60 patients diagnosed as having type 2 DM and 60 non-diabetic controls were included in the study. There is no significant difference between the age of the control group and cases. There was a significant difference between the mean BMI value of the controls and cases ($p=0.012 < 0.05$). Results indicated that diabetics were significantly overweight with respect to their non-diabetic counterparts. As expected, there was a very high significant difference between random blood sugar values between the two groups. **Conclusion:** The genesis and pattern of cognitive deficits in the diabetic population are complex. However, it appears from this study that such deficits do exist and are associated with advancing age, longer duration of poorly controlled diabetes, higher HbA1cvalues, and the combined use of Insulin and Oral Hypoglycaemic Agents rather than OHA alone. Further studies which evaluate other aspects of cognitive functions such as vasomotor coordination, psychomotor speed, motor persistence, and mental flexibility, which are likely to be affected earlier than the cognitive impairments captured in this study, are required. Even modest reductions in cognitive function result in substantially increased risks of dementia over several years. Hence, prevention and control of type 2 diabetes have critical public health consequences.

Keywords: Diabetes mellitus, OHA, HbA1.

Introduction

Diabetes mellitus is a chronic metabolic disease characterized by hyperglycemia that affects various body systems. For this progressive, incurable condition, the best scenario after diagnosis is good metabolic control and risk factor management to forestall vascular and neuropathic complications[1].People with diabetes often develop diverse microvascular, macrovascular, and neuropathic complications that erode the quality of life, making diabetes a major concern for much of the developed and developing world. The increasing population and increasing sedentary lifestyle worldwide have led to a rise in diabetes, with a 72% increase in the disease projected by 2030[2].The impaired insulin metabolism in patients with diabetes results in widespread morbidities involving the retinal, renal, cardiovascular, and peripheral nervous systems and affects cognition[3].Elevated blood glucose levels not only cause brain malfunction but also promote the synthesis of sorbitol, which damages blood vessels and causes degeneration of the nerves. Oxidative stress, microvascular vasculopathy, inflammation, and dyslipidemia are other key mediators resulting in neuropathology that can lead to dementia or cognitive impairment[4].Patients are said to be cognitively impaired when they have difficulty remembering, learning new things, concentrating, or making decisions that affect everyday life. Cognitive impairment, especially for people with chronic diseases, is likely to be an obstacle to providing appropriate medical treatment, as patients' understanding of the need for treatment, regular follow-up, and self-care can be limited by the cognitive dysfunction[5]. Cognitive functions that enable complex behaviors are particularly important for patients with diabetes. Cognitive impairment might result in nonadherence to diet, medication, and exercise. Older patients with diabetes and concomitant cognitive dysfunction may be unable to follow complicated regimens (e.g., multiple daily insulin injections with or without a sliding scale, multiple oral medications, or a complex dietary regimen). These patients may be at increased risk of treatment complications (e.g., omission of meals leading to hypoglycemia or incorrect dose or timing of insulin injections and/or oral medications). Cognitive impairment also increases the risk of major cardiovascular events and all-cause mortality[6].Studies about the relationship between cognitive impairment and diabetes mellitus are inconclusive because of inconsistent reports. The inconsistency in findings may be attributable to differences in study design, study subjects, duration or severity of diabetes, and the tools used for assessment of cognitive impairment. One such tool, the Montreal Cognitive Assessment (MoCA), was developed to screen for mild cognitive impairment, but few studies have reported using the MoCA

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in community settings. A pilot study from Canada reported the MoCA to be a better screening tool than the Standardized Mini-Mental State Examination for mild cognitive impairment in the diabetic population.Although diabetes is considered a risk factor for cognitive impairment, the cognitive function of patients with type 2 diabetes is not usually evaluated in routine clinical care. The purpose of this study was to screen for mild cognitive impairment among patients with diabetes in the state of Karnataka in southwestern India.

Materials and methods

This is a cross-sectional, comparative study. Subjects for the study were selected from the in-patient admissions made under various specialties at the Department of Psychiatry, Midnapore Medical College. Resi-Monirampore, Barrackpore, Kolkata.

Sampling Technique: After obtaining institutional ethical committee clearance, 60 patients who were diagnosed as having type 2 diabetes and 60 non-diabetic controls, matched to age, gender, education, and socio-economic status, were chosen by convenience sampling. The control group was selected from relatives of the patients admitted under various specialties.

Sampling Procedure: Initial contact was made in the hospital wards, and suitable subjects satisfying the inclusion and exclusion criteria were identified. Informed consent was obtained from those who were willing to participate in the study. The purpose of the study was explained to the participants, and they were informed that refusal to participate would not affect the ongoing treatment or outcome adversely.

Demographic details of the subjects were collected using the socio-demographic and clinical data proforma designed especially for the study. The cognitive functions of subjects chosen for the study were assessed using Standardized Mini-Mental State Examination (SMMSE) and Brief Cognitive Rating Scale (BCRS). Investigations like haemogram, random blood sugar, fasting blood sugar, postprandial blood sugar, glycosylated hemoglobin, lipid profile, liver function tests, renal function tests, and ECG, which were available, were recorded.

Inclusion Criteria for Cases: Patients with type 2 diabetes in the age group of 30-65 years, with a minimum education level of 8^{th} standard, as diagnosed by the Department of Internal Medicine, based on blood sugar estimations as per World Health Organisation recommendation of Fasting Blood Sugar ≥ 126mg/dL and 2-hours postprandial blood sugar ≥ 200mg/dL.

Exclusion Criteria for Cases: Type 2diabetics more than 65 years of age were excluded. Similarly, patients with chronic diseases which may cause cognitive impairment such as hypertension, neurodegenerative diseases like dementia, and organic mental disorders, those with a history of substance abuse, with a past or current history of psychiatric disorders were also excluded. Inclusion Criteria for Controls Non-diabetic subjects in the age group of 30-65 years with a minimum education level of 8^{th} standard were included as controls. Exclusion Criteria for Controls Patients with chronic diseases which may cause cognitive impairment such as hypertension, neurodegenerative diseases like dementia, and organic mental disorders, those with a history of substance abuse, with past or current history of psychiatric disorders were excluded. Standardized Mini-Mental State Examination (SMMSE) The SMMSE is a bedside screening test for cognitive impairment, derived from the Mini-Mental State Examination (MMSE)[7], the most widely used instrument to measure cognitive impairment. SMMSE has attempted to build on the advantages of MMSE, namely ease of administration and scoring, while addressing its shortcomings, viz. intra-rater and inter-rater variance. SMMSE is administered by a trained rater or clinician and takes about 5 –10 minutes. It contains 12 items that are asked in sequence and generate a total score of 30. The scores of less than 18 indicate severe cognitive impairment while 18-23 point to mild impairment and scores above 24 is reflective of no impairment. SMMSE has clearer instructions than MMSE and has a time limit for the answers, commensurate with the cognitive tasks. It has good content and concurrent validity and is organized into discrete subsections measuring orientation, registration, attention, and concentration, recall, language, and construction. But the subsections and individuals items cannot be viewed as measures of specific aspects of cognition because factor analytic studies typically yield a two-factor solution. Because of the non-specific nature of the individual subsection scores of SMMSE, it should be followed by a more comprehensive assessment, as attempted in the current study. Brief Cognitive Rating Scale (BCRS) BCRS is designed specifically to assess the syndrome of cognitive decline. As a clinical rating instrument, BCRS merges the judgment and skill of the clinician with objective rating criteria. Consequently, stable data can be obtained on subjects with cognitive impairment who may be only variably cooperative and attentive. BCRS assesses the magnitude of cognitive impairment on five clinical axes; each scored on a Likert scale of 1 to 7 using specified criteria. The axes represented are concentration, recent memory, past memory, orientation, and functioning/ self-care. Items are scored on the basis of a structured clinical interview conducted in the presence of a primary caregiver.

Statistical Analysis: The data were analyzed for statistical significance by using the chi-square test for categorical variables, ANOVA, Student's t-test, and Mann-Whitney U test for continuous numerical variables. Carl Pearson's coefficient of correlation was used to find out the correlation between the variables.

Results

A total of 120 subjects comprising of 60 patients diagnosed as having type 2 DM and 60 non-diabetic controls were included in the study. There is no significant difference between the age of the control group and cases. There was a significant difference between the mean BMI value of the controls and cases ($p=0.012 < 0.05$). Results indicated that diabetics were significantly overweight with respect to their non-diabetic counterparts. As expected, there was a very high significant difference between random blood sugar values between the two groups. In SMMSE, the mean total score obtained by the control group was 28.06 with a standard deviation of 1.05, while that obtained by the cases group was 24.27 with a standard deviation of 1.11. The difference between the two groups was very highly significant. Results indicated circumscribed areas of cognitive dysfunction in type 2 diabetic patients with respect to controls. Table 3 depicts data on BCRS, which show significant impairment in diabetic patients with respect to controls except in the functioning and self-care domain

Table 1: Random Blood Sugar

	Group	N	Mean	SD	Z
RBS	Control	60	112.20	9.21	5.4121
	Cases	60	278.16	89.91	P:0.001

Table 2: Standardized Mini-Mental State Examination

	Group	Mean	SD	t
Orientation	Control	9.30	0.59	6.62
	Case	8.36	0.49	
Registration	Control	3.0	0.00	6.59
	Case	2.40	0.49	
Attention	Control	4.20	0.61	9.41
	Case	2.76	0.56	
Recall	Control	2.66	0.47	5.45
	Case	2.06	0.36	
Language	Control	8.0	0.00	0.00
	Case	8.0	0.00	
Construction	Control	0.83	0.37	1.76
	Case	0.63	0.49	
Total Score	Control	28.06	1.04	13.61
	Case	24.26	1.11	

Table 3: Brief cognitive Rating Scale

	Group	Mean	SD	t
Concentration	Control	1.43	0.50	8.70
	Case	2.56	0.50	
Recent memory	Control	1.23	0.43	5.24
	Case	1.80	0.40	
Past Memory	Control	1.00	0.00	5.75
	Case	1.53	0.50	
Orientation	Control	1.00	0.00	2.11
	Case	1.26	0.69	
Functioning and Self-care	Control	1.00	0.00	1.79
	Case	1.10	0.30	
Total Score	Control	1.13	0.13	7.49
	Case	1.64	0.35	

Table 4: Duration of Diabetes mellitus Vs. cognitive tests

	HbA1c%	Mean Score	SD	F	P
SMMSE	<5	27.36	1.74	32.35	0.001
	5-10	24.30	1.03		
	>10	23.77	0.97		
BCRS	<5	1.20	0.20	26.96	0.001
	5-10	1.64	0.34		
	>10	1.82	0.36		

Table 5: HbA1C % vs Cognitive tests (cases)

	HbA1c%	Mean Score	SD	F	P
SMMSE	6.3-8.3	25.40	0.54	5.89	0.007
	8.3-10.3	24.35	1.08		
	>10.3	23.63	0.92		
BCRS	6.3-8.3	1.32	0.10	5.535	0.01
	8.3-10.3	1.60	0.27		
	>10.3	1.80	0.39		

Discussion

This study has tried to address these issues by investigating cognitive functions in type 2 DM patients matched against non-diabetic controls with respect to age, gender, education, and socio-economic status. The study revealed that there is statistically significant cognitive impairment in type 2 diabetes patients compared with controls which persisted even after correction for confounding factors. Cognitive tests were administered to the subjects within 2 hours after the last meal ingestion. This precaution was taken because type 2 DM patients are prone to develop discrete episodes of hypoglycemia as an adverse effect of medications prescribed to achieve normoglycemia. Since hypoglycemia is known to affect cognitive functions adversely, cognitive testing during such hypoglycaemic episodes might lead to spurious results[8].There was a statistically significant difference between the body mass index of diabetics and non-diabetics in the current study. This was in agreement with results from a previous study[9].However, there was an essential difference. The mean BMI (23.41) of diabetics in the current study was still within normal limits (BMI: 18-24), unlike in many studies in which the BMI of diabetic patients was in the range of obesity. This assumes importance because the findings by Elias et al. from the Framingham investigation of obesity and cognitive function identified obesity as a risk factor for cognitive dysfunction independently of diabetes, total cholesterol, alcohol consumption, cigarette smoking, hypertension, and stroke. The fact that, in the current study, diabetic subjects were not obese eliminated a potential confounding factor and gave further credence to the hypothesis at the beginning of the study, i.e., cognitive deficits observed are due to the intrinsic effect of diabetes[9].Both of these methods are not above reproach because SMMSE is affected by age and education. SMMSE is less than ideal when those with mild cognitive impairment are evaluated, as it might miss these subjects, which very well could have been the case with the current study. Another possibility is that since SMMSE is biased toward verbal items and does not adequately measure other cognitive functions such as the ability to attend to relevant input, ability to solve abstract problems, psychomotor speed, and visuospatial ability, cognitive functions that would have been the first to be affected by diabetes[10].This means that SMMSE should not be used in lieu of a more comprehensive neuropsychological assessment of cognitive function, a major strength of the current study, which assessed the subjects in further detail with BCRS.

Conclusion

The genesis and pattern of cognitive deficits in the diabetic population are complex. However, it appears from this study that such deficits do exist and are associated with advancing age, longer duration of poorly controlled diabetes, higher HbA1cvalues, and the combined use of Insulin and Oral Hypoglycaemic Agents rather than OHA alone. Further studies which evaluate other aspects of cognitive functions such as vasomotor coordination, psychomotor speed, motor persistence, and mental flexibility, which are likely to be affected earlier than the cognitive impairments captured in this study, are required. Even modest reductions in cognitive function result in substantially increased risks of dementia over several years. Hence, prevention and control of type 2 diabetes have critical public health consequences.

Conflict of Interest: Nil
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