Study of cognitive functions and their association with depression in type II diabetes mellitus

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Abstract

Introduction: Individuals with diabetes have higher risk of developing depression, cognitive impairment, and dementia compared to those who do not have diabetes. The present study aims to assess the level of cognitive functions and the presence of depression in diabetes patients and healthy controls. The study also explores the level of cognition among the normal control, diabetes without depression, and diabetes with depression. **Methods:** In the present study, the presence of depression and the level of cognitive functions of 59 cases of diabetes mellitus type-2 were compared with an age- and gender-matched control group of 40 individuals. Clinical and demographic details were recorded on a semi-structured performa. Montreal Cognitive Assessment (MoCA) and Patient Health Questionnaire-9 (PHQ-9) were applied to both diabetes patients and healthy controls to assess the level of cognitive functions and the presence of depression, respectively. **Results:** On applying odds ratio (OR), it was observed in the present study that there were 93.50% more chances [OR 1.935 with 95% confidence interval (CI) being 0.481–7.789] of depression among diabetic cases as compared to the control group. Similarly, the chance of MoCA score being less than 26 was twice among the diabetic group as compared to the control group (OR 2.208 with 95% CI being 0.702–6.946). On application of the Chi-square test, the association of depression was significant with HBA1C level, level of education, and presence of complications. **Conclusions:** Patients with diabetes had almost double the risk of developing depression and poor cognitive functions as compared to the healthy control. High HbA1C level, level of education, and presence of complication in diabetes had a positive statistical association with depression. Thus, it is advisable to investigate patients with diabetes for the presence of depression and cognitive dysfunction by applying simple tools.

Keywords: Cognitive functions, depression, diabetes

Introduction

Diabetes mellitus is a persistent metabolic disorder marked by high blood sugar levels that have an impact on multiple bodily systems including cardiovascular, renal, retinal, and peripheral nervous systems and cognitive functions.[1,2]

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Cognitive decline may have a widespread impact on quality of life of the individuals with DM. It may interfere with the compliance of the treatment, leading to poor control of the disease and subsequent complications. Cognitive functions are important in pursuing daily activities of life, which gets adversely affected with cognitive decline in diabetes. Individuals with diabetes have a 1.5 times higher risk of experiencing cognitive impairment and dementia compared to those who do not have diabetes.[3,4]

If a diabetic person has cognitive impairment, it could raise the possibility of treatment complications, such as the development

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of hypoglycaemia due to missed meals or incorrect dosage or timing of diabetes medications.[5,6] It is important to detect cognitive decline early to address the situation effectively. Various studies[7,8] have indicated that type-2 diabetes mellitus (T2DM) patients have a higher prevalence of depression, with symptoms including decreased energy, changes in appetite, and sadness.[9] Studies have suggested that depression may have adverse effects on people with T2DM, such as poor glycaemic control, eating habits, and exercise.[10,11] Although diabetes is considered a high risk factor for cognitive impairment, the cognitive functions of diabetic patients are not routinely assessed in clinical care. Researchers have used various tools, including the Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Hopkins Verbal Learning Test, Addenbrooke's Cognitive Examination-Revised, Clock-Drawing Test, Six-Item Cognitive Impairment Test, and others, to evaluate cognitive functions.[12] However, a few studies from India have used the MoCA score, which has been considered as a better tool for assessing subjects with mild cognitive impairment (MCI).

The present study was planned with the following aims and objectives:
1. To assess the presence of depression and the level of cognition in diabetes patients.
2. To compare the level of cognition among the control, subjects of diabetes with depression and without depression.
3. To assess the association of depression and cognitive functions with the socio-demographic and clinical parameters in diabetes.

Material and Methods

This cross-sectional comparative study was conducted in collaboration between the Department of Psychiatry and Diabetes Clinic of Department of Medicine in a tertiary care referral hospital. The hospital is a multi-specialty treatment facility centre catering to the health needs of a defined group of the population from the entire province. Diabetes patients are evaluated in detail in routine clinical practice, and all relevant biochemical tests are performed.

The study sample comprised 59 cases of diabetes between the ages of 18 and 70 years attending the outpatient department (OPD) of a diabetes clinic. Forty (40) healthy controls were also enrolled to make a comparison group. The sample size was calculated at 80% study power and an α-error of 0.05 assuming a standard deviation of 46.47mg/dl for fasting blood sugar as found in reference study. For a minimal detectable mean difference of 36 mg/dl between the two groups, 27 subjects in each group are required. [13] Considering 10% attrition rate, it was rounded off to 30 subjects in each group.Utmost care was taken to ensure the homogeneity of the sample population by recruiting the close relatives or friends of the patients as a control group. The purpose of the study was revealed to the participants, and consent was obtained. Ethical committee approval was taken for the study.

Diabetes was defined as either requiring oral or injectable anti-diabetic medication or fasting blood sugar $\geq$ 126 mg/dl or 2 hour postprandial blood sugar $\geq$ 200 mg/dl or HbA1C $\geq$ 6.5 %.

The participants were excluded from the study if they were known (1) to have current substance use disorder using Diagnostic and Statistical Manual, Fourth edition (DSM-IV) criteria; (2) to have current or past psychosis or mania or any other mental disorder using DSM-IV criteria except existing major depressive disorder (MDD); and (3) to have a major medical or surgical problem before the diagnosis of diabetes.

Measures

A detailed evaluation of socio-demographic and clinical profiles was made on specially designed semi-structured instruments by interviewing the participants and from the medical records. This included duration of illness, duration of treatment, type of treatment, BMI, complications due to diabetes, blood sugar fasting, and HbA1C levels. Participants were also assessed for the presence of depression and cognitive impairment by applying the Patient Health Questionnaire-9 (PHQ-9) and MoCA, respectively. Participants who scored 10 or above on PHQ-9 were further evaluated by a psychiatrist.

The PHQ-9 is a self-report version of PRIME-MD11 that evaluates the presence of major depressive disorder (MDD) using modified criteria from the DSM-IV.[14] There is a strong agreement observed between the diagnosis made using the PHQ-9 and those made by independent psychiatry professionals (κ = 0.65 for the diagnosis of any one or more PHQ disorder; overall accuracy: 85%; sensitivity: 75%; specificity: 90%). In this particular study, the Hindi version of the PHQ-9 was utilized. It has been validated in the Indian population and is considered a reliable tool for diagnosing depression.

The PHQ-9 serves a dual purpose as it not only establishes a provisional diagnosis of depressive disorder but also provides a score indicating the severity of symptoms. In the case of diagnosing depression, we defined clinically significant depression as a PHQ-9 score of 10 or higher.

The MoCA questionnaire[15] is capable of identifying mild cognitive impairment in individuals with limited education and can assess various cognitive domains such as visual perception, executive functioning, language, attention, memory, and orientation. The test-retest reliability of the MoCA-B was found to be 0.91 (P < .001), and it exhibited good internal consistency with a value of 0.82. The highest achievable score on the MoCA is 30 points, with a score of 26 or higher considered within the normal range.

Data analysis

All data collected were entered into Microsoft Excel 2013 worksheets in the form of master charts. These data were classified and analysed as per the aims and objectives. Categorical

variables were tabulated using frequencies and percentages. Inferential statistics such as Chi-square test were used to find out association of socio-demographic and clinical variables with depression and MoCA scores among diabetic cases, and odds ratio was calculated to compare the presence of depression and MoCA scores of the T2DM group with those of the control group. Medcalc 20.2 version software was used for analysis of the data.

Results

The present study compared the presence of depression and cognitive functions in 59 diabetic cases to those of a control group of 40 individuals matched by age and gender. Among the diabetic cases, 49 were male and 10 were female, 23 subjects comprised the age group of less than 40 years and 40-60 years respectively, while 13 subjects were over 60 years of age. Half of the cases had at least secondary level education. Only one subject had a BMI less than 18.5, while 30 were in the normal range and 28 were overweight or obese. The majority of subjects had been diagnosed with diabetes for more than 2 years and had no complications at the time of the study [Table 1].

The odds ratio (OR) analysis showed that diabetic cases had a 93.50% greater chance of depression than the control group [OR 1.935, 95% confidence interval (CI) 0.481–7.789)], and had double the risk of having MoCA score less than 26 (OR 2.208, 95% CI 0.702–6.946) [Table 2]. Further analysis showed that depression was more common in diabetic subjects with an HBa1c greater than 8, those with education upto secondary level, and those with diabetic complications. The Chi-square test revealed a significant association between depression and HBa1c level, education, and the presence of complications. Additionally, depression was more commonly observed in males, those over 60 years old, and those diagnosed with diabetes for more than 2 years, but these observations were not statistically significant [Table 3].

Analysis of MoCA scores showed that all diabetic subjects over 60 years old, a BMI less than 18.5, diabetic complications, and depression had scores less than 26. However statistically it was not significant.

Discussion

In the present study, the presence of depression and the cognition level of 59 cases of diabetes were compared with age- and gender-matched 40 healthy controls.

Prevalence of depression in diabetic versus control

In the present study, the application of OR revealed that diabetics were 93.50% more likely to have depression than the control group (OR 1.935 with 95% CI 0.481–7.789). The prevalence of depression among diabetics was found to be 13.56%, which was higher than that of the control group (7.5%). Previous studies have also reported a higher risk of depression in individuals with

Table 1: Association of socio-demographic and clinical variables with depression among diabetic cases

Variables	Depression				Total
	No	%	Yes	%	
Age					
<40 yr	20	86.96	3	13.04	23
40-60 yr	21	91.30	2	8.70	23
>60 yr	10	76.92	3	23.08	13
Chi-square test		1.474 at 2DF; *P*=0.479 NS			
Gender					
Male	42	85.71	7	14.29	49
Female	9	90.00	1	10.00	10
Chi-square test		0.113 at 1DF; *P*=0.737 NS			
Education					
Up to Secondary	21	75	7	25	28
> Secondary	30	96.77	1	3.23	31
Chi-square Test		4.238 at 1 DF; *P*=0.040S			
Duration Code					
<2 yr	12	85.71	2	14.29	14
2-5 yr	19	86.36	3	13.64	22
>5 yr	20	86.96	3	13.04	23
Chi-square Test		0.012 at 2DF; *P*=0.994 NS			
BMI					
<18.5	1	100.00	0	0.00	1
18.5-24.9	26	86.67	4	13.33	30
25 or >25	24	85.71	4	14.29	28
Chi-square Test		0.171 at 2 DF; *P*=0.918 NS			
HBA1c Level					
<6.5	10	100.00	0	0.00	10
6.5-8	26	96.30	1	3.70	27
>8	15	68.18	7	31.82	22
Chi-square Test		10.064 at 2 DF; *P*=0.007 S			
Complication					
No	44	91.67	4	8.33	48
Yes	7	63.64	4	36.36	11
Chi-square Test		3.846 at 1DF; *P*=0.050 S			
MoCA Score					
<26	45	84.91	8	15.09	53
≥26	6	100.00	0	0.00	6
Chi-square Test		0.156 at 1 DF; *P*=0.693 NS			

diabetes. Anderson *et al.*[16] found that the risk of depression was twice as high in individuals with diabetes compared to those without diabetes. Another community-based cohort study showed that the prevalence and incidence of depressive disorders were higher in diabetic patients compared to the general population.[17]

Certain risk factors such as poor diet, inactivity, irregular sleep patterns, and a low socio-economic status can activate shared physiological pathways that cause and promote depression and diabetes.[18] Chronic stress can stimulate the sympathetic nervous system and hypothalamic-pituitary-adrenal axis, leading to increased cortisol and adrenaline/noradrenaline production, which can trigger depression (dopamine dysfunction), diabetes (insulin resistance), or both (disruption of hippocampal neurogenesis).[19]

Table 2: Comparison of depression and MoCA scores between diabetic group and control group

	Depression					Odds ratio (95% Confidence Interval)
	Yes	%	No	%	Total	
Diabetic Cases	8	13.56	51	86.44	59	1.935 (0.481-7.789)
Control	3	7.5	37	92.50	40	
	MoCA Scores					
	<26	%	≥26	%	Total	
Diabetic Cases	53	89.83	6	10.17	59	2.208 (0.702 to 6.946)
Control	32	80.00	8	20.00	40	

Table 3: Association of socio-demographic and clinical variables with MoCA score among diabetic cases

Variables	MoCA Score				Total
	<26	%	≥26	%	
Age					
<40 yr	20	86.96	3	13.04	23
40-60 yr	20	86.96	3	13.04	23
>60 yr	13	100.00	0	0.00	13
Chi-square Test	1.888 at 2 DF; *P*=0.389 NS				
Gender					
Male	44	89.80	5	10.20	49
Female	9	90.00	1	10.00	10
Chi-square Test	0.308 at 1 DF; *P*=0.579 NS				
Education					
Up to Secondary	26	92.86	2	7.14	28
> Secondary	27	87.10	4	12.90	31
Chi-square Test	0.090 at 1 DF; *P*=0.764 NS				
BMI					
<18.5	1	100.00	0	0.00	1
18.5-24.9	27	90.00	3	10.00	30
25 or >25	25	89.29	3	10.71	28
Chi-square Test	0.123 at 2 DF; *P*=0.940 NS				
Duration					
< 2yr	11	78.57	3	21.43	14
2-5 yr	20	90.91	2	9.09	22
>5 yr	22	95.65	1	4.35	23
Chi-square Test	2.824 at 2 DF; *P*=0.244 NS				
HBA1c Level					
<6.5	9	90.00	1	10.00	10
6.5-8	23	85.19	4	14.81	27
>8	21	95.45	1	4.55	22
Chi-square Test	1.400 at 2 DF; *P*=0.497 NS				
Complication					
No	42	87.50	6	12.50	48
Yes	11	100.00	0	0.00	11
Chi-square Test	0.468 at 1 DF; *P*=0.494 NS				
Depression					
No	45	88.24	6	11.76	51
Yes	8	100.00	0	0.00	8
Chi-square Test	0.156 at 1 DF; *P*=0.693 NS				

Association of depression with HbA1c level

The current study found a correlation between depression and HbA1c >8, which is in line with previous studies that also linked depression and hyperglycaemia in T2DM patients.[19] The exact mechanism for this association is not fully understood, but it is possible that increased mental stress in depressed patients leads to elevated blood glucose levels due to poor self-care behaviours. This is supported by earlier research indicating that depressive symptoms and mental stress are linked to unhealthy eating habits, low physical activity levels, and high blood glucose levels.[20]

Education level and depression

The study found a significant association between lower levels of education and the presence of depression among diabetic patients. This finding is consistent with previous research that has shown a similar relationship.[21] Interestingly, another study conducted among African-American men found a paradoxical result, showing that although education was beneficial, those who graduated high school were at a higher risk of developing depressive symptoms during a 25-year follow-up period.[22]

Association between diabetes complication and depression

The occurrence of depression was higher among diabetic individuals who had complications as compared to those without complications. Previous research has also found similar results.[23] Moreover, a systematic review and meta-analysis has demonstrated that having diabetes complications can elevate the likelihood of experiencing depressive disorders.[24] This could be because both diabetes complications and depression share certain biological mechanisms such as inadequate glycaemic control, inflammatory conditions, and activation of the sympathetic nervous system.[25] Essentially, they may be different expressions of the same underlying pathological processes.[26]

Association between diabetes and cognitive functions

The study sample of diabetic patients had almost twice the chance of having an MoCA score less than 26 compared to the control group (OR 2.208 with 95% CI being 0.702–6.946). Studies have reported a higher prevalence of cognitive impairment among Type II diabetic patients than non-diabetics.[27] Other studies as Gao *et al.*[28] in China and Bashir *et al.*[29] in Nigeria reported the prevalence of MCI as 13.5% and 88.5%, respectively, among T2DM individuals. The prevalence of MCI has been found to vary across different studies, which may be due to differences in demographics, sampling procedures, diagnostic criteria, educational level, and age of participants.

The complex mechanism behind cognitive impairment in diabetic patients includes various factors such as cerebrovascular disease,[30] changing blood glucose levels, insulin resistance, hypertension, depression, and other physical and psychological factors.[31] Chronic hyperglycaemia can also cause neuronal injury through advanced glycation end products that cause oxidative damage.[32] Other factors that can cause cognitive impairment include micro-angiopathy, oxidative stress, inflammation, and dyslipidemia.[5] Expression of the enzyme that breaks down insulin and the occurrence of very low blood sugar levels are other suggested mechanisms of poor cognition in these patients.[33] Cognitive functions also have been considered to be adversely affected by longer duration and poor glycaemic control.[34]

Although the decline in cognitive function in T2DM patients with depression was not statistically significant when compared to those without depression, all T2DM patients with depression had MoCA scores less than 26. Previous studies[27] have suggested that depression may be a risk factor for MCI, possibly through reducing synaptic plasticity and increasing pro-inflammatory cytokines.[35]

Conclusions

Patients with diabetes had almost double the risk of developing depression and poor cognitive functions as compared to healthy controls. A high HbA1C level and the presence of complication in diabetes had a positive statistical association with depression.

It is suggestive to investigate all patients with diabetes for the presence of depression and cognitive dysfunction by applying simple tools and timely remedial measures to be applied to improve their quality of life.

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Conflicts of interest
There are no conflicts of interest.

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