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Evaluation of Relation between HbA1c Level with Cognitive Disorders and Depression in Type 2 Diabetes Mellitus Patients

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Abstract

BACKGROUND: The role of HbA1c level in cognition decline and depression in type 2 diabetic patients is reported in some studies.

AIM: We evaluated the possible significant relationship between HbA1c level and cognition decline and depression in type 2 diabetic patients.

MATERIAL AND METHODS: This descriptive-analytic study was performed on 512 patients with a different HbA1c level and ages range. All subjects were administered a structured clinical interview. Cognitive functions and depressive disorders were assessed through the Mini-Mental Status Exam (MMSE) and Patient Health Questionnaire-9 (PHQ-9) respectively. Chi-square test was used for relationships between variables.

RESULTS: HbA1c mean in all patients was 7.58%. MMSE score mean in total was 27.28. 83.3% of patients had a depressive disorder, and 8.59% of patients had an MMSE score < 24. There was no significant relationship between HbA1c level and cognitive problems, but there was a significant relationship between recent memory declines with the level of HbA1c (P = 0.03). Also, there was no significant relationship between attention-deficit with HbA1c level.

CONCLUSION: Our finding provides that even though there is no significant difference between HbA1c level and cognitive problems and depression, recent memory state in these patients are more affected than the normal population and these patients have a worse state of depressive disorders.

Introduction

Diabetes mellitus is a chronic long-term illness. All types of diabetes are a global public health problem, particularly type 2 diabetes [1]. The prevalence of diabetes is increasing in many countries around the world. By the year 2025, approximately 380 million people will be diagnosed with type 2 diabetes [1], [2]. In Iran, in 2011, the prevalence of diabetes in the adult population was 11.4% in 2011, with a 35% increase compared to the 2005 reports. It is estimated that by the year 2030, 9.2 million people in Iran will have diabetes [3]. Diabetes mellitus is associated with the poor cognitive function of the brain. Total grey-matter and hippocampus volume affects these associations and reduce it by almost 50% when adjusted, but there was no correlation for white-matter volume [4], [5]. Type 2 diabetes is a known risk factor for the development of depression.

Symptoms and disorders of depression in patients with type 2 diabetes are twice as probable as the general population [6]. A possible relationship between diabetes and cognitive problems has been suggested since the discovery of insulin [7]. It's a controversy about how diabetes can affect cognition and make cognitive problems in patients. Changes in glucose level as hyper or hypoglycemia, an increase in insulin level of resistance to it, oxidative stress and inflammatory cytokine effects and deposition of beta-amyloid are possible mechanisms [8]. Recently, HbA1c has been used as a diagnostic test for diabetes. This is a preferred test for defining glycemic control in people with diabetes. After using HbA1c, as

a demonstration of the glycemic condition of diabetic patients, an inverse correlation has been noted between any cognitive measures and depression with HbA1c levels, which proposing that inadequate glycemic control could be associated with worse cognitive function [9], [10].

The purpose of this study was the use of this marker for evaluating glycemic index in diabetic patients. We performed this study in type 2 diabetic patients referring to the Tehran city (Capital of Iran) hospitals.

Material and Methods

Study design

In a retrospective study, the data were from 632 patients referring to Tehran city hospitals with diagnosed Type 2 diabetes mellitus already. Diagnosed type 2 diabetes was the only inclusion criteria. Patients were recruited between July 2017 to March 2018. Five hundred and twelve adults, 219 males and 293 females with diagnosed type 2 diabetes by their primary care physicians. Exclusion criteria were: dementia, CNS diseases, unstable medical diseases, another psychiatric disease (including bipolar disorder), dependency on drug or alcohol, or history of head trauma. Subjects were not admitted if they were taking anti-depressant or psychotropic drugs. All diabetic patients were taking combinations of insulin and oral hypoglycemic agents for blood sugar control.

Data collection tools

All subjects were administered a structured clinical interview. Patient Health Questionnaire-9 (PHQ-9) which is a 9-question instrument given to patients in a primary care setting to screen for the presence and severity of depression. Cognitive functioning was assessed through the MMSE (Mini-Mental Status Exam). The MMSE's purpose has been not, on its own, to provide a diagnosis for any particular neurological entity [8]. It takes 5 to 10 minutes to administrate the test, and the test examines attention, registration (repeating named prompts), and calculation, language, recall, ability to follow simple commands and orientation [9]. Originally it was designed to differentiate organic from functional psychiatric patients [10], [11].

Procedures

The study was performed following the policies of the Human Subject Protection Committees and approved by the University Institutional Review Board. Written informed consent was obtained from all participants after the procedures had been successfully explained. All subjects received an in-person or telephone introductory interview, followed by an in-person psychiatric evaluation. This evaluation included psychiatric and medical history, health and functioning status. All patients were referred to laboratories, and after taking a blood sample, HbA1c was analysed. This subject was investigated by University Ethics group, and the Ethics Code is IR.AJAUMS.REC.1396.79.

Statistics

All data obtained were recorded in tests checklists, and the SPSS version 24 (Chicago, Illinois, USA) for Windows was used to perform a chi-square test for relationships between variables.

Results

Of 512 patients with type 2 diabetic disease, 219 (42.77%) were male, and 293 (57.23%) were female. The age range of patients was 33 to 90 years old with an average of 61.84. HbA1c mean in all patients was 7.58%. The mean of HbA1c in male was 7.54% and in female was 7.61%. MMSE score mean in total was 27.28 of 30 (scores from 14 Min and Max to 30). PHQ-9 scores mean in all participants was 9.58 of 27. The rate of different factors, according to gender, is shown in Table 1.

Table 1: The rate of different factors in 512 patients with diabetic disease

Patients	Age (mean)	HbA1c (%)	MMSE (of 30 scores)	PHQ-9 (of 27 score)
Male 219 (42.77%)	61.93	7.54	27.52	9.14
Female 293 (57.23%)	61.77	7.61	27.11	9.92
Total 512	61.84	7.58	27.28	9.58

MMSE: Mini Mental Status Exam; PHQ-9: Patient Health Questionnaire-9; HbA1c: Hemoglobin A1c.

This study showed that the depression rate was 83.3% among all patients. It was 84.6% and 81.7% among female and male respectively. There was a significant relationship between age and depression (P = 0.022). There was no significant statistical association between sex and depression (P > 0.05). According to PHQ-9 scores, 184 patients have a score between 5-10 which suggesting a mild depression. Due to PHQ-9 scores, 160 patients have a score between 10-14 which suggesting a moderate depressive disorder. Sixty-three patients have a PHQ-9 score 15-19 reminding of moderately severe depression. Twenty patients have a score higher or equal to 20 which suggesting a severe depression. Other factors related to patients participating in the study are presented in Table 2.

Table 2: Overview of PHQ-9 test results of 512 patients with diabetic disease

PHQ-9 score range (Type of depression)	Male (%)	Female (%)	Age (mean)	HbA1c (%)	MMSE mean (Of 30 scores)	PHQ-9 mean (Of 27 scores)
≤ 4 (normal)	40 (47.1%)	45 (52.9%)	61.18	7.56	27.74	2.62
5-10 (mild)	82 (44.6%)	102 (55.4%)	61.13	7.60	27.41	7.06
10-14 (moderate)	66 (41.3%)	94 (58.7%)	61.94	7.75	27.16	11.8
15-19 (moderately severe)	22 (34.9%)	41 (65.1%)	63.14	7.60	26.95	16.87
≥ 20 (severe)	9 (45%)	11 (55%)	66.3	7.52	26.25	21.6
Total	219	293	61.94	7.57	27.16	11.8

MMSE: Mini Mental Status Exam; PHQ-9: Patient Health Questionnaire-9; HbA1c: Hemoglobin A1c.

Chi-square test showed no significance between HbA1c level and PHQ-9 (P = 0.276). An overview of the MMSE test in patients is shown in Table 3.

Table 3: Overview of MMSE test results of 512 patients with diabetic disease

Single cutoff method of MMSE	Male	Female	Age (mean)	HbA1c (%)	MMSE mean (Of 30 scores)	PHQ-9 mean (Of 27 scores)
MMSE < 24	14 (31.8%)	30 (68.2%)	69.27	7.74	21.43	10.27

MMSE: Mini Mental Status Exam; PHQ-9: Patient Health Questionnaire-9; HbA1c: Hemoglobin A1c.

In this research, 44 subjects have a score of less than 24 on the MMSE test which means a possible cognitive problem (Table3). Of this, 14 were men (31.8%) and 30 (68.2%) were women. The mean of age, HbA1c, MMSE score, PHQ-9 score was 69.27, 7.74, 21.41 and 10.27 respectively. Statistic test showed that there was no significant relationship between MMSE score and HbA1c level (P > 0.05). Chi-square test showed that there was no significant association between sex and age with MMSE score less than 24 (P > 0.05) (Table 3). Also, there were no significant differences between sex, age and MMSE score less than 24 (P > 0.05). Chi-square test showed that there was no significant association between MMSE score and HbA1c level in the 33+ (33-49, 50-69, 70-90) age groups (p > 0.05). Also, the significant correlation was not observed between PHQ-9 score and HbA1c level in all age groups (p > 0.05). Also, the mean level of HbA1c is higher in clinically depressed patients in contrast with not-depressed participants (7.60 and 7.56 respectively), but there was no significant relationship between depression severity and HbA1c level. But there was a significant relationship between MMSE score and PHQ-9 score with each other in the analysis of the entire subjects (P = 0.013).

In a partial correlation analysis of age groups, there was no significant relation between MMSE score and PHQ-9 score in the first (33-49) and last (70-90) age groups (p > 0.05). But there was a significant correlation between those two with 50-69 years old group (P < 0.05). After controlling ageing and sex, there was no significant relationship between an HbA1c level and MMSE score or PHQ-9 score and MMSE score and PHQ-9 score in all three age groups of male and female except a significant relationship between MMSE score and PHQ-9 score in 50-69 years old group (P < 0.05). We considered Question 4 (spelling backward) of MMSE for checking attention and question 5 (recall 3 words in 5 minutes) for checking recent memory. Mean of scores of question 4 was 4.03 of 5, in male it was 4.35 and there was no significant relation with an HbA1c level (P = 0.997), In females the score mean was 3.78 but there was no significant relationship with an HbA1c level (P = 0.921) Also there was no significant relation between attention deficit and sex (P = 0.130) and age (P = 0.235). Mean scores of questions 5 were 1.66 0f 3. In male score mean was 1.41 and there was a significant relation between HbA1c level and recent memory impairment (P = 0.03). In females, the mean score was 2.10, and there was a significant relationship between HbA1c levels and memory impairment (P = 0.01). Also, there was a significant relation between recent memory impairment and sex (P = 0.005). But there was no significant relationship between age and recent memory impairment (P = 0.231).

Discussion

This report aimed to provide the role of HbA1c level in cognition decline and depression in type 2 diabetic patients. The data of 512 patients with Type 2 diabetes mellitus who referred to Tehran city hospitals between July 2017 to March 2018 were collected. This study showed that both sexes were susceptible to the disease, and most of the patients (83.3%) had a depressive disorder in different grades. An investigation in Iran reported similar findings. This study showed a high level of depression (85.3%) among diabetic patients [12]. IN another study, researchers reported that depression is more common among diabetic patients and 77% of the subjects had a severe kind of depressive disorder [13]. The results of a study in Iran showed that type 2 diabetic patients had a more severe level of depression and depression incidence was 72% among them [14]. Our findings were consistent with the results of these studies. Our study showed that there was a significant difference between age and depression, but there was no relation between sex and depression. Mahmoudi et al. reported a significant relationship between age and sex with depression [13]. In some studies, researchers in foreign countries reported similar results. Ronny et al. showed a 75% rate of depression in rural older African Americans, Native Americans, and whites' diabetic patients [15]. This is close to our findings. We found a higher prevalence of type 2 diabetic (84.6%) among female patients. In another study, researchers reported a higher prevalence of depression among type 2 diabetic patients and they also reported that depression has a higher prevalence among female patients [16]. Other investigations in the Netherlands, US, Bangladesh and Iran continually report the raised prevalence of depression in diabetic patients, in a range between 5% to 71.8% [17], [18], [19], [20], [21]. These studies show a higher level of depressive disorders among type 2 diabetic patients,

but the prevalence percentage is lower than ours because of the lower incidence of depression in those countries. Another study in Finland reported no significant relationship between cognitive function and diabetes. There was no significant difference in cognitive scores of the MMSE test; however, the female had better performance [22]. The results of this study have concordance with our results in Tehran. On the other hand, the English physician Thomas Willis suggested that in diabetic patients, the mental function might not be the same as others. Currently, cognition is an important issue in diabetic patient's health, especially for postmenopausal women.

In a large study, researchers used Telephone Interview of Cognitive Status (TICS) and suggested an effect of diabetes on cognition state. In this study, subjects with diabetes scored lower on mental health and energy indices [23]. Also many studies suggest positive relationship between diabetes and one or more cognitive domains declines, including attention/concentration [24], [25], [26], [27], [28], [29] which is opposed to our findings. In another study, the possible relation between HbA1c level and memory decline was evaluated [30]. In this study diabetes was related to a 10% faster rate of memory decline and higher HbA1c was associated with memory decline. A relative biological mechanism that describes the association between type 2 diabetes and cognition is chronic hyperglycemia as well as hyperinsulinemia and deficiency of insulin in the brain. Also, other risk factors of memory decline such as severe hypoglycemic events and depression are more common among type 2 diabetic patients and could explain the possible association [30].

In this study, there was no significant relationship between HbA1c level and cognitive disorders and depression, but diabetic patients' recent memory and depression level had been influenced. We suggest that these patients go through regular memory and depressive state surveys.

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