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Mild Cognitive Impairment among Type II Diabetes Mellitus Patients Attending University Teaching Hospital

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Abstract

BACKGROUND: Type II diabetes mellitus (TIIDM) has been associated with structural and functional changes in the brain. TIIDM is commonly associated with obesity, insulin resistance, hypertension, and dyslipidemia, all of which can have negative impact on brain.

AIM: The aim of the study was to study the risk of mild cognitive impairment (MCI) among both diabetics and non-diabetics and to identify risk factors to MCI among both groups.

METHODS: Two comparative cross-sectional studies were carried out enrolling 100 diabetics and 100 age, sex, and education matching non-diabetics. Cognitive function was assessed using Montreal Cognitive Assessment (MoCA) test and risk factors for MCI were assessed.

RESULTS: The subjective complaint of memory impairment among diabetics was significantly higher (34%) compared to non-diabetics (13.0%), $p < 0.05$. The mean of objective MoCA score was significantly lower among diabetics (25.9 ± 2.5) compared to non-diabetics (27.4 ± 2.4), $p < 0.001$. The rate of MCI was significantly higher among TIIDM patients (22%) compared to non-diabetics (9%), $p < 0.01$ and odds ratio (OR) 2.8 (95% confidence interval 1.2–6.5). Among the two studied groups, the rate of MCI was significantly higher among those aged over 50 years compared to younger age as well as among hypertensive compared to non-hypertensive persons, ($p < 0.05$). Among diabetics, the MCI was significantly higher among those with secondary education, having heart diseases, longer duration of DM, or repeated hypoglycemia attack, $p < 0.05$. A healthy diet, brain training, and social activities were found to be significantly associated with normal cognition. Logistic analysis revealed that diabetics aged above 50 was the only significant predicting factor for MCI with an OR 2.9 (95% CI: 3.8–123.3), $p < 0.001$.

CONCLUSION: TIIDM is significantly associated with 3-times increasing risk of having MCI compared to non-diabetics. The age, hypertension, cardiovascular diseases, duration of diabetes, and frequency of hypoglycemic episodes are risk factors for cognitive impairment. A healthy diet, brain training, and social activities were associated with better cognitive function.

Introduction

Cognition is a collective word for a range of higher brain functions containing language, memory, reasoning, and perception. Mild cognitive impairment (MCI) is an intermediate state between normal ageing and dementia including Alzheimer's disease (AD). MCI is a syndrome characteristic of early stages of many neurodegenerative diseases [1], [2]. Cognitive decline and dementia are among the most feared and most common illnesses of old age, making the identification of changeable risk factors for them, a crucial public health importance [3]. Diabetic patients may be susceptible to develop mental health problems because diabetes is counted as one of the most behaviorally and psychologically serious chronic medical illnesses [4].

The worldwide number of diabetic patients is expected to increase from 171 million in 2000 to 366 million by 2030. The prevalence was highest in the Eastern Mediterranean Region increasing from 5.9% (6 million) in 1980 to 13.7% (43 million) in 2014. The prevalence of diabetes in adults in Middle East and North Africa in 2019, 2030, and 2045 is 12.2%, 13.3%, and 13.9%, respectively. Regarding diabetes-related deaths, 43% occurred before the age of 70, with the highest proportion occurring in low- and middle-income countries [5], [6]. The International Diabetes Federation listed Egypt among the world top ten countries in the number of diabetic patients. It is alarming that the DM prevalence in Egypt has increased quickly within a short period from approximately 4.4 million in 2007 to 8.9 million in 2019 and it is expected to jump to 11.9 million by 2030 and 16.9 million by 2045 [6], [7].

The risk of cognitive dysfunction in Type II diabetes mellitus (TIIDM) may be affected by glycemic control, inflammation, hypoglycemia, macro/microvascular pathology, and depression. The increasing effect of these conditions on the vascular etiology may decrease the threshold of cognition affection by other neurological conditions in the aging brain [8].

For diabetic patients, managerial functions are particularly important as when patients are asked to do complex tasks such as matching treatment dose with carbohydrate content, expecting the effect of physical activity on blood glucose, or identifying, and treating hypoglycemia correctly [9].

The aim of the study is to detect MCI among both diabetics and non-diabetics and to identify risk factors related to MCI among both groups.

Subjects and Methods

The study is a comparative cross-sectional study. It was done at Zagazig University outpatient clinics, Sharkya Governorate. These clinics serve the city and most of the nearby villages. Method for sampling of TIIDM patients was a convenient non probability sampling, where all TIIDM patients attended to the clinic during the period of study were selected from the medical records. It included 100 TIIDM patients with an age which ranges from 40 to 60 years old. The second group composed of 100 non-diabetic subjects with age, sex, and education matched to the diabetic group. They were patients attending the outpatient clinics with mild symptoms (not serious health problem such as abdominal cramps, cough, viral infections, and mild fever) and their fasting blood sugar was below 100 mg/dL. Written consent was obtained from all participants after ensuring their full understanding of the research. The approval of head of diabetes unit at Zagazig University Hospitals before starting the research was taken.

A questionnaire was designed and pilot study was done before implementation. A face to face interview was carried out with studied participants to fulfill the questionnaire. It was used to collect data on general demographics (age, sex, and education), smoking habit (smoking or not), and medical history (memory complaints and its effect on his job and social life, cardiovascular problems, hypertension, and family history of dementia). Diabetic history of TIIDM patients (duration of diabetes, regular treatment or not, and hypoglycemic episodes) was also assessed. Dietary habits were also assessed in the questionnaire regarding (fast food, balanced main meal, canned tuna, eggs, beans, vegetables, fruits, unroasted nuts, dark chocolate, and dairy products). Social activities (going to clubs and mosques), intellectual activities (reading, listening to the radio, using the internet, and playing mental games), and physical activities were also assessed in the questionnaire. Anthropometric measurements (weight and length) and waist/hip ratio, and systolic and diastolic blood pressure were assessed.

The case definition of MCI was based on the recommendations of the National Institute on Aging–Alzheimer's Association [10], depending on subjective complaint, objective detection using cognitive test, and normal daily activities using 36 short form quality of life. Subjective Concern regarding a change in cognition: There should be evidence of concern about a change in cognition, in comparison with the person's previous level. We measured subjective cognitive concerns through two questions according to Lara *et al*. (2016): "How would you best describe your memory at present?," with answer options being very good, good, moderate, bad or very bad, and "Compared to 12 months ago, would you say your memory is now better, the same or worse than it was then?" Participants were considered to have memory complaints if they answered "bad" or "very bad" to the former question and/or "worse" to the latter [11].

Objective impairment in one or more cognitive domains: The current study is planned to detect MCI among both diabetics and non-diabetics, using the Arabic version of the Montreal Cognitive Assessment (MoCA) test after having permission for use. It assesses visuospatial abilities using a clock-drawing task and a three-dimensional cube copy. Short-term memory recall that contains two learning trials of five nouns and delayed recall after approximately 5 min is assessed. Attention, concentration, and working memory are evaluated using a sustained attention task, a serial subtraction task, and digits forward and backwards. Orientation to time and place is evaluated. Multiple aspects of executive functions are assessed using an alternation task adapted from the trail making B task, a phonemic fluency task, and a two-item verbal abstraction task. Finally, language is assessed using a three-item confrontation naming task with low-familiarity animals, repetition of two syntactically complex sentences, and the aforementioned fluency task [12], [13]. The maximum score is 30 points, any score greater than or equal to 26 points indicates a normal cognition. It has high sensitivity (90%) and specificity (87%) for detecting individuals with MCI [13], [14].

Data management and analysis

The collected data were revised, coded, entered, and verified with proofreading data, where one researcher checked the data entered against the original document. Data analysis was done using Statistical Package for the Social Sciences 18 for windows. Qualitative data were presented in frequencies and percentages. Chi-squared test was used for measuring differences meanwhile odds ratio (OR) and 95% confidence interval (CI) were computed to assess the degree of association. Mean, standard deviation, and t-test were used for quantitative data, when comparing between two means. When data are not normally distributed, non-parametric Mann–Whitney test was used. Multivariate logistic analysis was done to predict risk factors significantly associated with MCI.

p < 0.05 was considered significant and p < 0.01 was considered highly significant.

Results

The mean age among diabetic group was 50.7 ± 6.6 years and 56% of them were females and 85% were married. While the mean age among non-diabetics was 50.4 ± 6.4 years and 59% of them were females and 90% were married. The education level in the two groups was more or less comparable and around half of both groups had university education level. About 40% of the both groups had professional jobs.

Table 1 presents subjective complaint of memory impairment among all participants. The percentages of diabetics complained of frequent forgetfulness, bad/good memory, those who family and friends complained from their memory or complained that their memory affected their daily work were significantly higher compared to non-diabetic group (p < 0.05).

Table 1: Subjective complaint of memory impairment among all participants

Variables	Diabetics n=100 n (%)	Non-diabetics n=100 n (%)	p-value
Complaint of frequent forgetfulness			
Yes	34 (34.0)	13 (13.0)	<0.001**
No	66 (66.0)	87 (87.0)	
Describe your memory			
Excellent/very good	38 (38.0)	65 (65.0)	<0.001**
Good	53 (53.0)	32 (32.0)	
Bad	9 (9.00)	3 (3.00)	
Memory compared to previous year			
Same	82 (82.0)	82 (82.0)	1.00
Worse	18 (18.0)	18 (18.0)	
Family and friends complain from your memory			
Yes	21 (21.0)	1 (1.00)	<0.001**
No	79 (79.0)	99 (99.0)	
Does your memory affect your ability to do your daily work			
Yes	8 (8.00)	0 (0.00)	0.04*
No	92 (92.0)	100 (100.0)	

*p<0.05, **p<0.001.

Table 2 shows that the mean of total MoCA score was significantly lower among diabetics than non-diabetics (p < 0.001). The means of certain domains as verbal fluency, abstraction, and delayed recall also showed significant difference between both groups, (p < 0.05).

Table 2: MoCA test cognitive domains and total score among studied participants

Variables	Diabetics n=100 Mean±SD	Non-diabetics n=100 Mean±SD	p-value
Visuospatial	4.0±0.9	4.1±0.9	0.650
Naming (animal)	2.8±0.4	2.9±0.3	0.149
Attention	5.4±0.7	5.4±0.8	0.163
Language	2.0±0.2	2.0±0.3	0.762
Verbal fluency	0.5±0.5	0.9±0.2	<0.0005**
Abstraction	1.7±0.8	2.0±0.1	<0.0005**
Delayed recall	3.8±1.0	5.8±0.5	0.041*
Orientation	5.7±0.5	5.8±0.5	0.406
Total MoCA score	25.9±2.5	27.4±2.4	<0.0005**

*p<0.05, **p<0.001. SD: Standard deviation, MoCA: Montreal cognitive assessment.

Depending on subjective complaint, objective cognitive impairment and normal daily activities, 22 diabetics were suffered from MCI (22%) compared to nine non-diabetics individuals (9%), p = 0.01 and OR 2.8 (95 % CI 1.2–6.5). The mean MoCA score test was significantly lower among diabetics or non-diabetics with MCI (23.2 ± 1.3 and 23.6 ± 1.3, respectively) compared to those with normal cognition in both groups (26.8 ± 2.2 and 27.7 ± 2.1, respectively), p<0.001.

Table 3 presents the socio-demographic, medical, and physical history among diabetics and non-diabetics in relation to MCI. Among diabetics, the prevalence of MCI was significantly higher among those aged >50, those with secondary education, hypertensive patients, those with heart diseases, having longer duration of DM, or repeated hypoglycemia, p<0.05. Among non-diabetics, the prevalence of MCI was significantly higher among those aged >50 and hypertensive patients, p<0.05.

The mean monthly intake of fast food, dairy products, eggs, and nuts was significantly lower among diabetics with MCI than among those with normal cognition, p < 0.05. The mean monthly intake of fast food, balanced main meal, eggs, canned tuna, and unroasted nuts was significantly lower among non-diabetics with MCI compared to those with normal cognition (p < 0.05). Diabetics with normal cognition had higher monthly social activities than those with MCI, p < 0.05. While, non-diabetics with normal cognition spent more hours in praying at mosques and playing mental games compared to those with MCI, (p < 0.001) (Table 4).

Logistic regression analysis for predicting the risk of MCI among diabetics was carried out using age, sex, education, smoking, body mass index (BMI), hypertension, heart disease, regular treatment, and history of hypoglycemia in the model. It revealed that diabetics aged above 50 and those with hypertension were the only significant predicting factors for MCI, p < 0.01 (Table 5).

Discussion

With the growing interest in MCI, our study discussed two major observations: The first, the prevalence of MCI among both diabetics and non-diabetics, and second, risk factors for MCI among both groups.

The prevalence of diabetes and MCI is increasing worldwide partially due to the increase in the aging population and lifestyle choices [15]. In this study, the prevalence of MCI was 22% among the diabetic group and 9% among the non-diabetic group with almost 3 times increased risk of having

Table 3: Relation between socio-demographic, medical, and physical history among diabetics and non-diabetics in relation to MCI

Variables	Total n=100	MCI among diabetics		Total n=100	MCI among non-diabetics	
		MCI n=22	Odds ratio (CI 95%)		MCI n=9	Odds ratio (CI 95%)
Age in years						
≤50	47	1 (2.1)	®	52	0 (0.0)	Undefined OR
>50	53	21 (39.6)	30.2 (3.9–235.9)**	48	9 (100.0)	p<0.01
Gender						
Males	44	12 (27.3)	1.7 (0.6–4.47)	42	1 (2.4)	6.5 (0.8–54.6)
Females	56	10 (17.9)	®	58	8 (13.8)	®
Education						
Secondary	18	10 (55.6)	7.3 (2.4–22.2)**	23	4 (17.4)	3.0 (0.7–12.4)
University and postgraduation	82	12 (14.6)	®	77	5 (6.5)	®
Smoking						
Current or previous smoker	28	9 (32.1)	2.1 (0.8–5.8)	21	4 (19.0)	3.4 (0.8–14.4)
Non-smoker	72	13 (18.1)	®	79	5 (6.3)	®
Obesity						
Non-obese (BMI <30)	70	16 (21.3)	®	64	7 (10.9)	®
obese (BMI ≥30)	30	6 (24.0)	1.2 (0.4–3.4)	36	2 (5.6)	2.1 (0.4–10.6)
Light physical activity						
Yes	39	5 (12.8)	®	29	1 (3.4)	®
No	61	17 (27.0)	2.6 (0.9–7.8)	71	8 (11.3)	3.5 (0.4–29.8)
History of family dementia						
Yes	32	7 (21.9)	0.9 (0.4–2.7)	57	4 (7.0)	1.7 (0.4–6.9)
No	68	15 (22.1)	®	43	5 (11.6)	®
Hypertension						
Yes	69	19 (27.5)	3.5 (0.9–13.1)*	29	6 (20.6)	8.3 (1.6–42.5)*
No	31	3 (9.7)	®	71	3 (4.2)	®
Heart diseases						
Yes	16	7 (43.8)	3.5 (1.2–11.1)*	16	2 (12.5)	1.6 (0.3–8.4)
No	84	15 (17.9)	®	84	7 (8.3)	®
Duration of diabetes				-	-	-
More than 10 years	61	19 (31.1)	5.4 (1.4–19.8)*			
<10 years	39	3 (7.7)	®			
Regular treatment				-	-	-
Irregular	10	3 (30.0)	1.6 (0.4–6.7)			
Regular	90	19 (21.1)	®			
History of Hypoglycemia				-	-	-
Yes	14	8 (57.1)	4.6 (1.4–15.1)*			
No	86	16 (18.6)	®			

*p<0.05, **p<0.001. MCI: Mild cognitive impairment, CI: Confidence interval, ®: Reference group, OR: Odds ratio, BMI: Body mass index.

Table 4: Dietary and social risk factors among diabetics and non-diabetics in relation to MCI

Variables	Cognitive function among diabetics			Cognitive function among non-diabetics		
	MCI n=22 Mean±SD	Normal n=78 Mean±SD	p-value	MCI n=9 Mean±SD	Normal n=78 Mean±SD	p-value
Dietary risk factors						
Fast food	5.09±6.89	8.9±5.6	0.022*	2.2±2.1	7.8±5.7	<0.0005**
Balanced main meal	17.6±4.39	15.8±4.7	0.113	15.3±4.3	18.6±3.4	0.023*
Canned tuna	1.27±2.27	1.07±2.0	0.695	1.3±2.2	3.5±1.3	0.005*
Eggs	3.45±5.2	9.4±5.5	<0.001**	3.1±3.8	8.8±4.7	0.01*
Beans	5.4±7.2	6.6±6.4	0.514	5.7±4.05	7.3±7.1	0.308
Vegetables	16±4.27	15.1±3.9	0.404	16±2.8	14.7±3.6	0.308
Fruits	19.1±6.4	18.5±6.3	0.706	18.6±3.4	18.1±5.17	0.657
Unroasted nuts	0.7±2.0	3.4±4.2	<0.001**	0.4±1.3	3.5±4.2	0.032*
Dark chocolate	0.36±1.7	0.4±1.5	0.902	0.0±0.0	0.3±1.07	0.074
Dairy products	15.2±5.6	18.5±5.6	0.022*	19.5±3.7	19.2±4.6	0.849
Social risk factors						
Going to clubs	0.5±1.87	2.5±4.2	0.031*	0.4±1.3	1.4±3.1	0.343
Mosques	2±2.04	1.7±2.38	0.982	0.0±0.0	2.02±2.8	<0.001**
Reading	17.7±19.4	15.9±23.3	0.747	23.3±20.0	20.27±29.6	0.763
Listening to radio	30±33.3	51.1±41.05	0.01*	53.3±29.1	65.2±38.3	0.154
Using internet	10.9±19.7	6.6±18.3	0.342	6.6±13.2	7.08±24.1	0.959
Playing mental games	3.4±6.4	5.7±13.5	0.430	0.0±0.0	9.3±17.6	<0.001**

*p<0.05, **p<0.001. MCI: Mild cognitive impairment.

Table 5: Logistic regression analysis for predicting the risk of MCI among diabetics

Variables	B	p	OR	95%CI of OR	
				Lower	Upper
Age	0.400	<0.001	1.492	1.229	1.811
Hypertension	1.805	<0.01	6.078	1.054	35.040

B: Regression coefficient, OR: Odds ratio, CI: Confidence interval. Variables entered in the model: age, sex, education, smoking, BMI, hypertension, heart disease, regular treatment and history of hypoglycemia.

MCI, $p < 0.01$ and the mean of total MoCA score was significantly lower among diabetics than non-diabetics ($p < 0.001$) and this was also reported by Li *et al.* (2019) using the MoCA, ($p < 0.05$) [16]. Several studies showed that the prevalence of MCI among studied Type II diabetic patients was higher than among non-diabetics [16], [17], [18]. Other studies as Salama *et al*. (2018) in Cairo and Ding *et al*. (2015) in China found that the prevalence of MCI was 14.2% and 20.1%, respectively, among healthy individuals [19], [20]. The variation in the prevalence of MCI has been due to the demographic characteristics of the source populations, implementation of MCI diagnostic criteria, differences in sampling procedures, the education level, and the age range of participants (especially the studies done in Cairo and Mansoura had age range ≥ 60 years and the dementia of normal aging may have played a role in this prevalence).

The present study aimed to find the risk factors for MCI among both diabetics and non-diabetics. In accordance to other studies [21], [22], and [23], the prevalence of MCI among both groups increased significantly with age with $p < 0.01$ and by making a logistic regression analysis, old age (above 50) was a significant predicting factor for MCI among diabetics, $p < 0.001$. In the current study, the prevalence of MCI among diabetic males was higher compared to diabetic females, $p > 0.05$, while 2.4% of non-diabetic males and 13.8% of non-diabetic females had MCI with $p > 0.05$. More or less similar results were reported by other study [20]. Mindy *et al*. (2017) also found that regarding diabetics 15.7% of diabetic males and 18.5% of diabetic females had MCI with $p > 0.05$. This difference may be due to that females live longer than males and a wider range of age of the mentioned studies [24]. The present study and Li *et al.* (2019) found that education was a protective factor ($p < 0.01$) [16].

TIIDM for more than 10 years' duration was found to be significantly associated with MCI (31.1% of patients) compared to 7.7% among TIIDM patients with duration <10 years with 5 times risk of having MCI, $p < 0.01$. Several studies proved that a longer duration of DM has been implicated in accelerated cognitive decline [18], [25], [26]. History of hypoglycemic episodes was associated with a higher rate of MCI (50.0%) compared to 17.4% among those who had not history (OR = 4.7, 95% CI 1.4–15.5), $p < 0.05$. Similarly, other studies demonstrated that history of hypoglycemia was significantly associated with cognitive impairment [27], [28].

In addition, the present study discussed other risk factors for MCI among both diabetics and non-diabetics. The rate of MCI among hypertensive diabetics (27.5%) and non-diabetics (20.6%) was significantly higher compared to non-hypertensive diabetics (9.7%) and non-diabetics (4.2%), $p < 0.01$. By making a logistic regression analysis, hypertension was a significant predicting factor for MCI among diabetics, $p < 0.01$. Among diabetics hypertensive Chen *et al.* (2012) denoted as well that the percent of hypertension among diabetics with MCI was 58.1% compared to 40.6% among non-hypertensive diabetics ($p < 0.05$)[29]. Amer *et al.* (2012) stated that the presence of hypertension significantly associated with MCI (39.1%) compared to 19.4% among non-hypertensive with MCI patients with $p < 0.05$ [22]. The current study showed that the rate of MCI among diabetics and non-diabetics with history of heart diseases was 43.7% and 12.5%, respectively, compared to 17.9% and 8.3% among those with no heart problems, respectively, ($p > 0.05$). Weinstein *et al*. (2018) reported that 19.3% of diabetics with ischemic heart diseases had MCI compared to 11.5% among those without heart diseases ($p < 0.001$) [30]. Other studies denoted as well that several cardiac problems were associated with subsequent cognitive decline [31], [32].

Several studies evaluated the contributions of specific foods and nutrients to cognitive function. The present study showed that the mean consumption of the certain food items such as eggs, balanced meal, canned tuna, unroasted nuts, and dairy products was significantly higher among both diabetics and non-diabetics with normal cognition compared to those with MCI. The present results were in line with Devore *et al.* (2010) and Ylilauri *et al.* (2017) who suggested that regular consumption of food such as eggs and nuts, could be related to more favorable cognitive outcomes [33], [34]. Moreover, Park and Fulgoni (2013) demonstrated associations between milk products and cheese with cognitive function [35]. Qin *et al*. (2014) supported a better role of canned tuna in slowing rate of cognitive decline among Chinese older adults [36].

Concerning social and mental activities among diabetics and non-diabetics, this study found that both groups with normal cognition were having more social activities (going to clubs, listening to the radio, and praying at mosques) and mental activities than those with MCI with $p < 0.05$. These were in agreement with other studies among TIIDM patients [37] and non-diabetic participants [38] who denoted that among both groups, loneliness and social isolation significantly associated with a decrease in all cognitive function measures ($p < 0.001$). Choi *et al*. (2016) and Fu *et al*. (2018) mentioned that participation in social activities was significantly associated with better cognitive performance [39], [40]. A study in China found that there were statistical differences ($p < 0.05$) in reading, listening to music, and suffering the internet among the TIIDM-MCI group and non-diabetics-MCI group [18]. Similar to the current study, other studies reported that increased participation in mental activities was associated with better performance on grammatical reasoning, spatial working memory, and episodic memory tasks [41], [42].

This study was done without funding, so it was carried out only on 100 diabetics and 100 non-diabetic participants. In the future, larger sample size studies are needed to confirm the results in the current study.

Conclusion

The study concluded that TIIDM is significantly associated with MCI and almost 3-time increasing risk of having MCI. Aging, hypertension, cardiovascular diseases, duration of disease, and frequency of hypoglycemic episodes are risk factors for cognitive impairment. A healthy diet, brain training, and social activities were associated with better cognitive function.

Declarations

Ethics approval and consent to participate

Written consent was obtained from all participants after ensuring their full understanding of the research. Approval of Head of diabetes unit at Zagazig University Hospitals before starting the research was taken.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions

All authors contributed to the design and implementation of the research. NHE conducted the field visits and data collection, while IIS, GAA, NHE, MSG, and AMH performed data entry, analysis, and interpretation. IIS and GAA took the lead in writing the manuscript. All authors discussed the results and commented on the manuscript. All authors reviewed and approved the manuscript.

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