International Journal of Research in Medical Sciences
Cakir E et al. Int J Res Med Sci. 2020 Jun;8(6):2039-2043
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20202240

Original Research Article

Evaluation of cognitive functions in diabetic patients

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Received: 31 March 2020
Accepted: 29 April 2020

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ABSTRACT

Background: Diabetes Mellitus is an independent risk factor for cognitive impairment and dementia. In this study, authors investigated cognitive functions in the diabetes and control group with Mini Mental State Examination (MMSE). Authors analyzed the association of cognitive status with age, sex, duration of diabetes, insulin use and HbA1c in diabetic patients.
Methods: Fifty patients with diabetes diagnosed between the ages of 50 and 70 who applied to this Diabetes and General Internal Medicine Clinics between January 2017 and September 2017 were included. Fifty patients with nondiabetes diagnosed with similar age and demographic characteristics were included in the control group. MMSE was applied to both groups. In the diabetic group, cognitive functions were investigated in relation with age, gender, duration of diabetes, insulin usage and HbA1c.
Results: The MMSE score in diabetic patients was lower than the control group ($p<0.05$). In addition, cognitive impairment in diabetic patients was associated with duration of diabetes and HbA1c level. There wasn't significant difference was found between cognitive impairment and age, sex, insulin use.
Conclusions: Diabetes Mellitus is a risk factor for cognitive impairment and dementia with many possible mechanisms. In the routine, there is no screening for cognitive impairment and dementia in diabetic patients; but if authors detect early cognitive impairment, authors can prevent cognitive impairment progression to dementia with medical treatment and cognitive exercises.

Keywords: Diabetes Mellitus, Cognitive functions, Hemoglobin A1c

INTRODUCTION

Diabetes mellitus is the most common endocrinological disease and a major health problem all around the World. The number of diabetic patients increased from 108 million in 1980 to 422 million in 2014.[1]

Though the harmful effects of diabetes on the peripheral nervous system have been clearly determined currently; it's effects on central nervous system has not been fully explained.[2] Type 2 diabetes mellitus is associated with increased risk of accelerated cognitive impairment and mild cognitive impairment, Alzheimer's and vascular dementia in elderly patients.[3] Even if there is moderate effect of diabetes on cognitive function, it has important consequences of public healthcare.[4]

Although diabetes is a major risk factor of cognitive impairment; cognitive functions are not controlled in routine outpatient examination. If early dementia is properly detected and treated, progression can be prevented by regulating blood glucose and planning cognitive exercises.

MMSE (Mini Mental State Examination) was developed by Folstein et al. It's widely used to detect cognitive

impairment around the World. It does not require any medical equipment for testing and can be easily implemented by any healthcare worker with a short training.

The effects of controlling and duration of diabetes and micro vascular complications on cognitive impairment has not been fully determined on current studies.[5]

In this study authors investigated the impairment of cognitive functions and the relationship of this cognitive impairment between age, gender, duration of diabetes, HbA1c levels and insulin using status in diabetic patients.

METHODS

In this current study authors recruited 50 type 2 diabetes mellitus patients and 50 control group who were admitted to this Diabetes Mellitus and Internal Medicine Outpatient Clinic between January-September 2017. Control group was similar in terms of age and demographic features with the patient group. The study group's age are between 50 and 70. Control group was consisted of fifty people who don't have any chronic diseases. Both patients and control groups were at primary and secondary school level according to the education status.

Inclusion criteria

- >18 years age, Diagnosis Type 2 DM according to European Association for the Study of Diabetes 2013 and minimum primary school education.

Exclusion criteria

- Patients with mental retardation, acute and chronic psychotic disorders, mood disorders, vascular dementia, Alzheimer's dementia, delirium and other amnestic disorders; acute cerebrovascular and neurological diseases; with severe visual impairment and unable to use the upper limb

MMSE was applied the patient and control groups. It takes average 5-10 minutes for each patients. MMSE is shown in Table 3.

Authors categorised the cognitive impairment with the criterion of MMSE scores; Score more than 27 shows the normal cognitive function; however score between 21-26 mild, score between 11-20 moderate and score under 10 denotes serious cognitive impairment.

Diabetic patients group were divided in to three groups according to age and HbA1c levels as; 50-56, 57-63 and 64-70 years old and under 7% between 7-8% and more than 8% respectively. These groups were also separately evaluated according to using or not to using insulin treatment.

Statistical analysis

Statistical Analyzes were performed by using MedCalc Statistical Software Version 12.7.7 Program (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013). Descriptive analysis were used to define continuous variables (mean±standart deviation, minimum, median, maximum). The relationship between the two independent continuous variables that do not fit the normal distribution was examined by Mann-Witney U test; more than two independent continuous variables that do not fit the normal distribution was examined by Kruskal Wallis Test. Chi-Square (or Fisher Exact test where appropriate) was used to examine the relationship between categorical variables. Sensitivity and Specificity calculations are made to examine the power of applied diagnostic tests. Statistical significance level was $p<0.05$.

RESULTS

The demographic characteristics and laboratory parameters of the diabetes and the control groups are summarized in Table 1 and 2. There was no statistically significant difference between demographic characteristics of diabetes and control groups.

Table 1: Patients with DM and control group.

		Control		Diabet	
		n	%	n	%
Diabetes Duration (years)	1-4	0	0.00	13	26.00
	5-10	0	0.00	12	24.00
	≥10	0	0.00	25	50.00
treatment	OAD	0	0.00	23	46.00
	Insulin	0	0.00	27	54.00
Hba1c Levels (%)	<7	50	100.00	15	30.61
	7-8	0	0.00	11	22.45
	>8	0	0.00	23	46.94
Age (years)	50-56	22	44.00	17	34.00
	57-63	18	36.00	17	34.00
	64-70	10	20.00	16	32.00
Gender	Female	35	70.00	33	66.00
	Male	15	30.00	17	34.00
Education time	Primary school	43	86.00	43	86.00
	Middle school	7	14.00	7	14.00

Table 2: HbA1c and mean age of diabetes and control group.

	Control		Diabetes	
	Mean	SD	Mean	SD
Age (years)	58.06	5.51	59.10	6.35
HbA1c (%)	5.64	0.26	8.21	2.26

A statistically significant difference was found about cognitive function degree between the diabetes and control groups (p<0.001). When MMSE scores of diabetic patients are evaluated; 27 patients (54%) had normal cognitive function (MMSE≥27) and 23 patients (46%) had mild cognitive impairment (MMSE 21-26). The control groups MMSE scores were; 44 (88%) normal cognitive function and 6 (12%). Serious cognitive impairment was not found neither in patients nor in control groups (Table 3).

A significant relationship was found between cognitive dysfunction and presence of diabetes mellitus (Fisher's Exact p<0.001). The majority of mild cognitive impairment group constitutes from diabetic patients (79.3%) and the majority of normal cognitive function group constitutes from nondiabetic people (62%) (Table 3).

Table 3: Comparison of the degree of cognitive function according to diabetes mellitus.

	Cognitive Function Degree		
	Normal cognitive function N (%)	**Cognitive disfunction N (%)**	**p**
Control	44 (62.0)	6 (20.7)	<0.001
Diabet	27 (38.0)	23 (79.3)	

MMSE average scores are significantly higher in non-diabetic group (Mann-Whitney U p<0.05). Also in the diabetic group MMSE scores are significant high in noninsulin subgroup (Mann-Whitney U p<0.05) (Table 4).

Table 4: Comparison of all patients by MMSE.

		Ort.±SS	p
Diabetes	+	27.8±1.8	0.006*
	-	26.4±3.9	
Diabet Duration (years)	1-4	27.7±2.02	0.058**
	5-10	27.1±2.02	
	≥10	25.4±5.1	
İnsulin Dependent	+	27.4±1.7	0.039*
	-	25.6±5.1	
Age (years)	50-56	27.8±1.7	0.010**
	57-63	27.4±2.1	
	64-70	25.7±5.1	
Gender	Female	27.01±1.9	0.913*
	Male	27.3±1.9	
Education Degree	Primary school	27.2±1.9	0.232*
	Middle school	26.4±7.1	

There is a statistically significant difference in terms of MMSE distribution by age (Kruskal Wallis p <0.05). According to the Post-Hoc binary comparison results; there is a statistically significant difference between 50-56 and 64-70 ages in terms of MMSE distribution (Mann-Whitney U p <0.016 Bonferroni correction). When MMSE scores analysed according to age, scores of between 50-56 aged group is higher than the other groups, and also between 57-63 aged group's score is higher than between 64-70 age group. So that MMSE scores decreases with aging. No statistically significant difference was found between education level, gender and MMSE distribution (Table 5).

Table 5: Binary comparisons for MMSE level among age groups.

Age	p
50-56 vs. 57-63	0.439
50-56 vs. 64-70	0.003
57-63 vs. 64-70	0.027

Diabetic patients were divided into 3 groups according to their duration of diabetes: 1-4 years (n: 13), 5-9 years (n: 12), 10 years and above (n: 25). Cognitive functions were found to be impaired as the duration of diabetes prolonged (p=0,043). Sixty-nine percent of cognitive impairment group have more than of 10 years or more, 17.4% have a 5-9 years and 13% have a 1-4 years diabetes duration. This percent is 33.3%, 29.6% and 37% respectively in cognitive normal group (Table 6).

In the evaluation according to HbA1c level, authors found that cognitive functions deteriorated as the HbA1c level increased (p=0.042). In the cognitive normal group percent of HbA1c levels were <7%, 7-8% and >8% is 46.2%, 15.4% and 35.5% respectively. In the cognitive impairment group this percent were 13%, 30.4% and 56.5% respectively (Table 6).

Table 6: Comparison of cognitive functions in diabetic patients.

		Cognitive function degree				
		Normal cognitif function N (%)		**Mild cognitif disfunction N (%)**		**p**
Diabetes duration	1-4	10	37.0	3	13.0	0.043
	5-10	8	29.6	4	17.4	
	≥10	9	33.3	16	69.6	
Insulin dependent	+	16	59.3	7	30.4	0.052
	-	11	40.7	16	69.6	
Hba1c Levels (%)	<7	12	46.2	3	13.0	0.042
	7-8	4	15.4	7	30.4	
	>8	10	38.5	13	56.5	
Age (years)	50-56	11	40.7	6	26.1	0.100
	57-63	11	40.7	6	26.1	
	64-70	5	18.5	11	47.8	
Gender	Female	18	66.7	15	65.2	1.00
	Male	9	33.3	8	34.8	
Hba1c Levels (%)		7.7±2.3		8.8±2.05		0.031

DISCUSSION

Dementia is a common problem in the geriatric population. Four and e half million new cases are diagnosed in each year, and the number of patients with dementia is doubled every 20 years. Diabetes mellitus can increase the risk of cognitive impairment and conversion it to dementia with many potential mechanisms. These are known as; insulin homeostasis disorder in the brain, hyperinsulinemia, and insulin resistance syndrome, advanced glycosylation end products, and hyperglycemia. With any of these mechanism, diabetes increases the risk of dementia in all age groups, especially in the geriatric group. Cognitive impairment related to diabetes is not only caused by vasculopathy, but also deleterious effect of diabetes to astrocytic cells contribute to dementia.[6] Diabetes is not only a risk factor for mild cognitive impairment, but also for progress from mild impairment to severe dementia. Patients with mild cognitive impairment with advanced age may progress to advanced cognitive impairment and dementia. It is important to predict this progression in terms of preventing and treating this major health problem. For this reason, authors examined the relatively young population of 50-70 years old and also investigated mild cognitive impairment in the diabetic population.

In this study, authors used the MMSE test while examining the effect of diabetes on cognitive functions. The cut-off value for the diagnosis of dementia has been determined as 23 in many studies. However, authors aimed to detect mild cognitive impairment by determining the cut-off value as 27. Authors found a significant relationship between diabetes and cognitive dysfunction.

In a big metaanalysis by Biessels GJ et al, it was found that the frequency of Alzheimer's and vascular dementia increased in 7 of 10 studies in the diabetic population.[5] In another study by Gregg EW et al; it was found that MMSE score was lower in the diabetic population in women over 65 years old as similar to this study.[7]

Gao Y et al, retrospectively screened patients with dementia and mild cognitive impairment. In this study the frequency of mild cognitive impairment was found to be increased in the diabetic patient population compared to general population.[8] Also in this study, the prevalence of mild cognitive deficiency was found more frequently in the diabetic population. Crum RM et al studied the relationship between education level and cognitive dysfunction and found that cognitive dysfunction, evaluated with mini mental scoring was inversely proportional between education levels. Those with higher education had significantly higher MMSE scores[9]. In this study, all this patients were at primary school education level and there was no significant difference in terms of MMSE scores.

The study conducted by Alencar RC et al, which compared the MMSE scores with the duration of diabetes and HbA1c levels; they found a significant relationship between duration of diabetes and the MMSE scores. However, they did not find a significant difference between hba1c levels and cognitive dysfunction.[10] Similarly to this study, authors found a significant relationship between duration of diabetes and cognitive dysfunction in this study, but unlike this study authors also found a significant correlation with Hba1c levels. In edition similar to this study Maggi S et al, and Okereke O. et al, had found a relationship between Hba1c level and cognitive dysfunction like this study.[11-12]

This study's limitations are; this is a single-center study, the number of patients and control group was low, mild visual impairment has not been evaluated in the patient group, and cognitive function evaluation is done only with MMSE. More comprehensive enlightening studies are needed in order to reach definite opinion.

CONCLUSION

Diabetes Mellitus is an independent risk factor for cognitive dysfunction. Permanently high blood glucose levels and long duration of diabetes can accelerate cognitive impairment. Unfortunately in routine clinical practice, diabetic patients are not evaluated in order to cognitive functions. If mild cognitive impairment in diabetic patients can be detected and treated properly at an early stage, the progress of mild cognitive impairment in to severe dementia can be prevented.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Cakir E, Harmankaya NO, Cengiz H, Varim C. Evaluation of cognitive functions in diabetic patients. Int J Res Med Sci 2020;8:2039-43.