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Adherence to Mediterranean-Dash Intervention for Neurodegenerative Delay (MIND) Dietary Pattern in Elderly with Type 2 Diabetes and the Correlation with Cognitive Functions and Metabolic Profile

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ABSTRACT

Background: Dietary patterns are receiving more attention as a potential method for preventing cognitive deterioration. In this line, Mediterranean-dash intervention for neurodegenerative delay (MIND) diet is a pattern exclusively designed to protect the brain and delay brain damage. This study determined the score of adherence to the MIND dietary pattern in the elderly with type 2 diabetes mellitus (T2DM) and its relationship with cognitive functions and metabolic factors.

Methods: In a cross-sectional study performed in Sina Clinic of Arsanjan, Iran, 60 people with T2DM were randomly enrolled. Adherence to the MIND diet pattern (scored as 0 to 15) was computed and the participants took cognitive tests by Persian paper and pencil cognitive assessment package (PCAP), and their scores were recorded. Blood sampling and biochemical tests and blood pressure were measured for participants.

Results: The correlation between score of adherence to the MIND dietary pattern with blood pressure was inversely significant (p<0.0001). The correlation between MIND dietary pattern and cognitive functions were not significant. The correlation between the score of adherence to the MIND diet pattern and biochemical factors was negative and not significant.

Conclusion: Our findings suggest a significant inverse correlation between MIND diet score and blood pressure. However, no significant correlation was observed between the score of adherence to this dietary pattern with biochemical and cognitive factors in the elderly with T2DM.

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Introduction

The elderly population has increased dramatically over the past few decades. In Iran, 8% of the population is currently elderly, and with the continuation of this trend around 1410, there will be an explosion of aging (1). Aging has several complications, one of the most important of which is changes in cognitive functions. Cognitive functions are a set of processes that allow humans to understand properly, evaluate, store, reconstruct,

and respond to information received from internal and external sources (1). Cognitive impairment is one of the biggest threats to the health of the elderly in this century. The biggest consequences for this cognitive impairment and the related diseases, including Alzheimer's, have been the phenomenon of aging itself (2).

Cognitive decline is associated with decreased quality of life, increased risk of hospitalization, inability to live independently, and increased health care costs (3). Therefore, identifying modifiable risk factors to prevent and delay cognitive impairment in the elderly is very important and plays an essential role in the amelioration of their general health. One of these risk factors is type 2 diabetes. Type 2 diabetes (T2DM) is a global epidemic estimated to affect 592 million people worldwide by 2035 (4). The cause of cognitive impairment in type 2 diabetes is unknown, but it is most likely multifactorial. Hyperglycemia, cerebral microvascular diseases, severe hypoglycemia, and increased prevalence of macro-vascular diseases may be associated with increased risk of cognitive impairment (5).

Since to date, no drug has been prescribed and approved by the Food and Drug Administration to treat cognitive disorders. Therefore, most behavioral or preventive interventions are the basis of the present study. Among the behavioral aspects, diet is modifiable, can affect cognitive function, and plays an important role in the causation and prevention of cognitive disorders. In this scenario, the Mediterranean-Dash Intervention for Neurodegenerative Delay (MIND) dietary pattern is intended to preserve the brain and delay the onset of brain damage. This diet combines the Dietary Approaches to Stop Hypertension (DASH) and the Mediterranean dietary (MD) pattern, focuses on consuming natural plant foods and the limited consumption of saturated animal foods (red meat, butter, solid margarine, cheese, pastries and cookies, as well as, fried foods and fast food). Some studies have examined the effects of dietary patterns such as MIND dietary pattern and MD pattern on cognitive function. In some studies, it was shown that higher adherence to the MIND dietary pattern is associated with slower cognitive decline (6). In this line, Jordi Salas-Salvado *et al.* concluded that the MD pattern helps prevent and control T2DM and metabolic syndrome (7).

In general, due to the increasing prevalence of dementia and its consequences, the need to prevent it in the earlier stages, and also due to the greater focus of studies on dietary nutrients rather than dietary patterns, the necessity for further studies examining the relationship of dietary pattern with cognitive functions increased. Therefore, this study aimed to determine the score of adherences to the MIND dietary pattern in the elderly with T2DM and its relationship with cognitive functions and metabolic factors.

Materials and Methods

This cross-sectional study began in December 21, 2020 to April 21, 2021 on the 60 elderly with T2DM aged 60 years and older. Sampling was random, and interested elderlies were invited to participate in the project by telephone calls. The sample size of the present study was 60, according to the article of Shakersain *et al.* (8), and using the formula for determining the sample size below (including 30% drop out).

$$n = \left(\frac{z_{\frac{\alpha}{2}} + z_{1-\beta}}{\frac{1}{2} \cdot ln\left(\frac{1+r}{1-r}\right)} \right)^2 + 3$$

Inclusion criteria were being at least 60 years old, literate, T2DM controlled diabetes (treated with oral medications), mini mental state examination (MMSE) score (9) greater than 24, MIND dietary score questionnaire greater than 4, not having medical history of myocardial infarction, history of schizophrenia, Parkinson's and bipolar disorders, visual and hearing impairments that made assessment difficult, history of cancer in the last two years, excessive alcohol consumption and dietary supplements or following a special diet in the last three months. The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.REC.1399.644). After informing subjects in detail about the study aims, written informed consent was obtained from all of them.

To evaluate cognitive functions, a Persian paper and package of Pencil Cognitive Assessment Package (PCAP) were used in Persian language (10). This cognitive test was performed by a trained researcher. The PCAP test included (i) Forward Digit Span Task to evaluate working memory, (ii) Letter Digit Modality Task to assess executive function, and (iii) Trail Making Task (TMT) and Stroop Task (ST) to assess attention. The status of individuals' adherence to the MIND dietary pattern was investigated using the MIND dietary scoring questionnaire (11). The translated version of these questionnaires was provided by the Department of Geriatrics, University of Social Welfare and Rehabilitation Sciences (12). It is a cognitive test battery to assess working memory, attention, and executive functions. It includes Letter/Symbol Digit Modalities Test (LDMT), Forward Digit Span Task (FDST), TMT and ST. Rezapour

et al. confirmed the validity and reliability of PCAP in an Iranian population (10).

All blood samples were collected from 8:00 to 10:00 AM after having an 8-12 h fasting state at the laboratory of Sina Clinic of Arsanjan, Iran. On the same day of blood collection, fasting blood sugar (FBS), Hemoglobin A1c (HbA1c), triglycerides (TG), total cholesterol level, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and C-Reactive-Protein (CRP) were measured according to standard protocols. Total cholesterol, HDL, LDL, TG and FBS were measured by biosystem kit and enzymatic method. Also, serum CRP was evaluated by Biorex kit and agglutination method. Hemoglobin A1c was also assessed by an enzymatic method.

Trained personnel measured blood pressure (BP) with a validated digital sphygmomanometer, while the participant was in a seated position after 5 min rest. Arm circumference determined the cuff size, and BP was measured in the forearm at heart level. The mean of the three systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements with a 5-min interval between each reading was recorded.

A MIND dietary score questionnaire was used as described by Morris *et al.*, focusing on 15 components. There was a maximum of 15 points (which were classified to brain-healthy and unhealthy food groups. The first food group contained 10 items such as green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine. However, wine consumption was excluded. This beverage is generally consumed less in Muslim countries and is prohibited in Islam, so the information on its consumption among Iranian is limited. Red meat, butter and stick margarine, cheese, pastries and sweets, and fast/fried food, were also considered as an unhealthy food group. Higher intake of brain-healthy food groups were scored 0, 0.5, or 1 point depending on the level of consumption, while for unhealthy food groups, the scoring was reversed (Table 1). Finally, the total MIND dietary score was obtained by summing up the scores of these food items that ranged from 4 to 10. Based on the total scores of the diet rating questionnaire, individuals were divided into 3 groups of (i) high adherence (total score of 15), (ii) mid adherence (total score of 7-14) and (iii) low adherence (total score of 0 to 7).

To describe qualitative data, frequency and frequency percentage were reported and to describe quantitative data, mean and standard deviation were

Table 1: MIND dietary components served and scored.

Diet component	Score		
	0	0.5	1
Green leafy vegetables*	≤2 servings/wk	>2 to <6/wk	≥6 servings/wk
Other vegetables¦	<5 serving/wk	5 to <7 wk	≥1 serving/d
Berriesº	<1 serving/wk	1/wk	≥2 servings/wk
Nuts	<1/mo	1/mo to <5/wk	≥5 servings/wk
Olive oil	Not primary oil	_	Primary oil used
Butter, margarine	>2 T/d	1-2/d	<1 T/d
Cheese	7+servings/wk	1-6/wk	<1 serving/wk
Whole grains	<1 serving/d	1-2/d	≥3 servings/d
Fish (not fried)¥	Rarely	1-3/mo	≥1 meals/wk
Beans§	<1 meal/wk	1-3/wk	>3 meals/wk
Poultry (not fried)	<1 meal/wk	1/wk	≥2 meals/wk
Red meat and products#	7+meals/wk	4-6/wk	<4 meals/wk
Fast fried foods**	4+times/wk	1-3/wk	<1 time/wk
Pastries and sweets∂	7+servings/wk	5-6/wk	<5 servings/wk
Wine	>1 glass/d or never	1/mo-6/wk	1 glass/d
Total score			15

MIND: Mediterranean-DASH diet intervention for neurodegenerative delay. *Kale, collards, greens; spinach; lettuce/ tossed salad. ¦Green/red peppers, squash, cooked carrots, raw carrots, broccoli, celery, potatoes, peas or lima beans, tomatoes, tomato sauce, string beans, beets, corn, zucchini/summer squash/eggplant, coleslaw, potato salad. ºStrawberries. §Beans, lentils, soybeans. ¥ Tuna sandwich, fresh fish as main dish; not fried fish cakes, sticks, or sandwiches. ¶Chicken or turkey sandwich, chicken or turkey as main dish, and never eat fried at home or away from home. #Cheeseburger, hamburger, beef tacos/burritos, hot dogs/sausages, roast. beef or ham sandwich, salami, bologna, or other deli meat sandwich, beef (steak, roast) or lamb as main dish, pork or ham as main dish, meatballs or meatloaf. **How often do you eat fried food away from home (like French fries, chicken nuggets)? ∂Biscuit/roll, poptarts, cake, snack cakes/ twinkies, Danish/sweet rolls/ pastry, donuts, cookies, brownies, pie, candy bars, other candy, ice cream, pudding, and milkshakes/frappes. d: Day. wk: Week. Mo: Month

reported. Spearman non-parametric test was used to investigate the correlation between quantitative variables. Normality distribution was surveyed by applying Shapiro-Willk test and p value<0.05 was considered significant. Data were analyzed by IBM SPSS software (Version 21.0, Chicago, IL, USA).

Results

In total, 60 eligible participants entered our study. The mean participants' age was 62±2 years, and 28 (46.6%) of them were female, and 32 (53.3%) were male. Totally, 83.3% (50 people) of the participants had primary and diploma educational levels, about 15% (9 people) of them had post-diploma and bachelor educational levels and 1.6% (1 person) had postgraduate educational level. About 60% (19 people) of men reported smoking. According to the adherence to this diet, approximately 98% of the participants were in group 2 (mid adherence, total score of 7-14) and one person was in group 3 (low adherence, total score of 0 to 7) (Table 2).

The score of adherence to the MIND dietary pattern had an inversely significant correlation with systolic and diastolic blood pressure (r=-0.449, r=-0.414; p<0.001); so that higher adherence to the MIND dietary patterns lowered the blood

Table 2: General characteristics of the participants in the study.

Variables*	N (%)	Mean	SD
Sex, n (%)			
Male	32 (53.3)	_	_
Female	28 (46.6)	_	_
Education, n (%)			
Under diploma and diploma	50 (83.3)	_	_
Post-diploma and bachelor	9 (15)	_	_
Postgraduate	1 (1.6)	_	_
Smoking, n (%)			
Male	19 (59.4)	_	_
Female	Not smoking	_	_
The degree of adherence of people to the MIND dietary pattern, n (%)			
High (14 points)	0	_	_
Mid (7-14 points)	59 (98.3)	_	_
Low (0-7 points)	1 (1.6)	_	_
Age (year)	_	62	2
MIND dietary score	_	8	0.7
Attention			
Stroop task (first time)	_	2.1	0.8
Stroop task (first time, number of errors)	_	0.5	1.2
Stroop task (second time)	_	4.4	1.3
Stroop task (second time, number of errors)	_	5.4	4.4
Trail Making Task	_	71	31
Working memory			
Forward Digit Span Task	_	8.5	1.9
Executive function			
Letter digit modality task (total)	_	25	10.3
Letter digit modality task (true responses)	_	24	10
Biochemical factors			
FBS (mg/dL)	_	152	51
HbA1c (mg/L)	_	7.5	2
TG (mg/dL)	_	144	73
Chol (mg/dL)	_	152	42
LDL (mg/dL)	_	79	28
HDL (mg/dL)	_	39	10
CRP (mg/dL)	_	1	1
Blood pressure (mmHg)			
Systolic	_	12	1
Diastolic	_	7.9	0.8

*Values are based on mean±standard deviation or reported percentage. MIND diet: Mediterranean-DASH Intervention for Neurodegenerative Delay; FBS: Fasting blood sugar; HbA1c: Hemoglobin A1c; TG: Triglyceride; Chol: Cholesterol; HDL: High density lipoprotein; LDL: Low density lipoprotein; CRP: C-reactive protein

Table 3: The correlation between the score of adherence to the MIND dietary pattern and metabolic factors.

Variables[a]	r	P value[b]
FBS (mg/dL)	-0.174	N_S
HbA1C (mg/L)	-0.114	N_S
TG (mg/dL)	-0.046	N_S
Chol (mg/dL)	-0.114	N_S
LDL (mg/dL)	-0.082	N_S
HDL (mg/dL)	-0.057	N_S
CRP (mg/dL)	0.059	N_S
SBP (mmHg)	-0.414	0.001
DBP (mmHg)	-0.449	0.0001

[a]Shapiro-willek test and Spearman correlation coefficient have been used. [b]P value less than 0.05 was considered significant. MIND diet: Mediterranean-DASH Intervention for Neurodegenerative Delay; TG: Triglyceride; HDL: High density lipoprotein; LDL: Low density lipoprotein; Chol: Cholesterol; FBS: Fasting blood sugar; HbA1c: Hemoglobin A1c; CRP: C-Reactive-Protein; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Table 4: The correlation between the score of adherence to the MIND dietary pattern and cognitive factors.

Variables[a]	r	P value[b]
Stroop task (first time)[c]	-0.217	N_S
Stroop task (first time, number of errors)[d]	-0.164	N_S
Stroop task (second time)[c]	0.025	N_S
Stroop task (second time, number of errors)[d]	-0.092	N_S
Trail Making Task	-0.165	N_S
Forward Digit Span Task	0.194	N_S
Letter digit modality task (total)[e]	0.247	0.057
Letter digit modality task (true responses)[f]	0.245	0.060

[a]Shapiro-willek test and Spearman correlation coefficient have been used. [b]P value less than 0.05 was considered significant. [c]Stroop test time, steps 1 and 2. [d]Number of stroop test errors, steps 1 and 2. [e]The total number of correct answers obtained from the numbers and letters substitution test. [f]Number of correct answers from the numbers and letters substitution test. MIND diet: Mediterranean-DASH Intervention for Neurodegenerative Delay. The Stroop and Trail Making Task was used to assess a person's attention. The Forward Digit Span Task was used to evaluate working memory. Ns: Not significant

pressure. However, the correlation between score of adherence to the MIND dietary pattern and biochemical factors such as lipid profile (TG, Chol, LDL, HDL), blood sugar index (FBS, HbA1c) and inflammatory factor (CRP) were not significant (p>0.05) (Tables 3). As shown in Tables 4, the score of adherence to the MIND dietary pattern had no significant correlation with cognitive functions (p>0.05).

Discussion

In Iran, limited studies have been conducted to evaluate the correlation between dietary patterns with the risk of chronic diseases. From what we know, the present study was the first study to determine the score of adherence to the MIND dietary pattern in the elderly with T2DM and its correlation with cognitive performances and metabolic factors in Iran. In the present study, the score of adherence to MIND dietary pattern was inversely associated with high blood pressure. Thus, higher adherence to the MIND dietary pattern had been related to lower hypertension. In this line, Romina di Giuseppe *et al.* concluded that the Mediterranean dietary pattern lowers blood pressure, with the difference that in this study, the Mediterranean dietary pattern only affected systolic blood pressure (13). The high share of nuts (due to magnesium) and vegetables (due to potassium) as well as the restriction of red meat and processed foods (low in sodium) may be the reasons for the positive effect of this diet on blood pressure.

Also, in the present study, the score of adherence to the MIND dietary pattern was not significantly associated with biochemical factors (FBS, HBA1c, TG, Chol, LDL, HDL, and CRP). Although no observational studies directly assessed the association between adherence to the MIND dietary pattern and metabolic factors, several documents have linked the DASH and Mediterranean dietary pattern to the Metabolic Syndrome (MetS). According to our findings, Azadbakht *et al.* in an 8-week randomized trial of

31 patients with T2DM, showed that adherence to the DASH dietary pattern could increase HDL-C. In contrast, in the study by Obarzanek *et al.*, the DASH dietary pattern led to a decrease in HDL-C, attributed to a reduction in total dietary fat (14). The differences between these studies and the results of our research can be explained by the different amounts of fiber, potassium, and calcium in the Mediterranean diet, DASH or MIND dietary pattern. In the MIND dietary pattern, dairy is limited to just cheese and fruits are limited to berries. Studies have shown that dairy products are inversely related to metabolic syndrome, body weight, and insulin resistance, so they may positively affect all features of the metabolic disorder (14).

On the other hand, the results of a cross-sectional study by Armando Platania *et al.* to determine the relationship between the Mediterranean dietary pattern and dyslipidemia were not in line with our study and the findings showed that high adherence to the Mediterranean dietary pattern was associated with lower prevalence of dyslipidemia. Men were more evident than women. These gender differences can result from complex interactions between sex hormones and food components. Also, some factors such as physical activity, smoking, etc., may affect the health status and prevalence of dyslipidemia. Also, according to Armando Platania's study, job status and lower literacy rate were associated with a higher chance of developing dyslipidemia. In our study, 50 participants (about 83.3%) had a primary educational level, which is no exception to this rule (15). Also in our study, following of MIND dietary pattern could possibly improve executive function of individuals. However, significant effects on other cognitive functions were not demonstrated, additionally interventional studies are needed to clarify this correlation.

These findings were in line with a prospective study by Yian Gu and colleagues that aimed to investigate the relationship between adherence to the Mediterranean dietary pattern and the risk of Alzheimer's disease. No reduction in the risk of Alzheimer's disease was observed (16). In Morris *et al.*'s study of the elderly, in contrast to our study, the MIND dietary pattern significantly improved cognitive function (11). The previous study consisted of 960 individuals, compared to 60 participants in our study, which could be responsible for the difference.

A study was also conducted by Pak-Nahad *et al.* as a clinical trial to investigate the effect of the Mediterranean dietary pattern on the cognitive function of 40 patients with Parkinson's. In this study, the beneficial effects of this dietary pattern directly by reducing oxidative stress, anti-inflammatory effects, and indirectly by reducing the risk of diabetes or cardiac metabolic syndrome through a favorable effect on intestinal microbiota and thus improving intestinal signaling to the brain, were observed. This may dependent on the type of study, as in our study, the dietary pattern was not provided to the patient unlike interventional studies. On the other hand, in the MIND dietary pattern questionnaire, there were few questions to measure some diet components and limited information about the frequency of consumption (especially in the case of olive oil, berries, etc.). However, this imprecision in measuring the MIND score would tend to underestimate the diet effect on cognitive decline. Also, this study's self-reporting of dietary pattern was another weakness, as some studies showed that it led to biased self-reporting in overweight and cognitive disorders, thus may be responsible for differences in the outcomes (17).

Our study had some strength too. To the best of our knowledge, this is the first study to investigate the association between the MIND dietary score and metabolic and cognitive factors in the elderly with T2DM. Other strength of this study was the hard sampling of vulnerable groups in the Corona crisis. However, it should be mentioned that this study had some limitations because of the cross-sectional design, and no causal associations could be identified, and further well-designed and long term studies or intervention studies are needed to confirm these findings. Low sample size, long cognitive tests and low cooperation of this age group as well as lack of measurement of other complementary biochemical indicators due to limited financial budget can be other weaknesses of the study.

Conclusion

The results of this study showed that moderate adherence to the MIND dietary pattern could have a positive effect on lowering blood pressure. However, significant effects on cognitive and biochemical factors were not shown.

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Conflict of Interest

None declared.

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