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Association of dietary diversity and quality with cognitive performance and odds of Alzheimer's disease: A cross-sectional study.

Asociación de diversidad y calidad dietética con rendimiento cognitivo y probabilidades de enfermedad de Alzheimer: Estudio transversal.

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ABSTRACT

Introduction: Scientific evidence proposes that a healthy and diverse diet may have a role in preserving brain and cognitive performance. We sought to investigate the association of dietary diversity and quality with cognitive performance and odds of Alzheimer's disease (AD).

Methods: This cross-sectional study was undertaken on 89 participants (60 Alzheimer's patients and 29 healthy individuals) over 60 years old (38 men and 51 women). A three-day food record was used to assess the dietary intake of participants. The dietary diversity (DD) score was examined using guidelines by the FAO (Food and Agriculture Organization), and diet quality was assessed using the healthy eating index (HEI) and dietary quality index (DQI). Cognitive performance was appraised via the Mini-Mental State Test (MMSE).

Results: The DD score was significantly lower in the AD group than in the healthy group ($p < 0.001$). However, there was no significant difference in HEI and DQI scores between AD and healthy groups ($p > 0.05$). There was a significant association between DD score with total MMSE score ($\beta = 0.33$, $p = 0.02$), memory ($\beta = 0.35$, $p = 0.02$), and language ($\beta = 0.32$, $p = 0.03$). HEI was positively correlated with calculation ($\beta = 0.32$, $p = 0.02$). A high DD reduced the odds of AD by 79% (OR: 0.21; 95% CI: 0.10, 0.42; $p < 0.001$) in a multivariate model.

Conclusions: A high DD may be associated with improved cognitive status and may reduce the odds of AD.

Funding: Tabriz University of Medical Sciences.

Keywords: Dietary quality index, Dietary diversity, Healthy eating index, Alzheimer's disease, Cognitive performance.

RESUMEN

Introducción. La evidencia científica propone que una dieta sana y diversa puede tener un papel fundamental en la preservación del rendimiento cerebral y cognitivo. Intentamos investigar la asociación entre la diversidad y la calidad de la dieta con el rendimiento cognitivo y las probabilidades de padecer la enfermedad de Alzheimer (EA).

Metodología. Estudio transversal con 89 participantes (60 pacientes con Alzheimer y 29 individuos sanos) mayores de 60 años (38 hombres y 51 mujeres). Se utilizó un registro alimentario de tres días para evaluar la ingesta dietética de los participantes. La puntuación

de diversidad dietética (DD) se examinó utilizando las directrices de la FAO (Organización para la Alimentación y la Agricultura) y la calidad de la dieta se evaluó mediante el índice de alimentación saludable (HEI) y el índice de calidad dietética (DQI). El rendimiento cognitivo se evaluó mediante el Mini-Mental State Test (MMSE).

Resultados. La puntuación DD fue significativamente menor en el grupo AD que en el grupo sano ($p < 0,001$). Sin embargo, no hubo diferencias significativas en las puntuaciones de HEI y DQI entre los grupos con EA y sanos ($p > 0,05$). Hubo una asociación significativa entre la puntuación DD con la puntuación total del MMSE ($\beta = 0,33$, $p = 0,02$), la memoria ($\beta = 0,35$, $p = 0,02$) y el lenguaje ($\beta = 0,32$, $p = 0,03$). El IES se correlacionó positivamente con el cálculo ($\beta = 0,32$, $p = 0,02$). Un DD alto redujo las probabilidades de EA en un 79% (OR: 0,21; IC del 95%: 0,10, 0,42; $p < 0,001$) en un modelo multivariado.

Conclusión. Un DD alto puede estar asociado con un mejor estado cognitivo y una reducción de las probabilidades de padecer EA.

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Palabras clave. Índice de calidad dietética, Diversidad dietética, Índice de alimentación saludable, Enfermedad de Alzheimer.

KEY MESSAGES

- A highly diverse food may be associated with improved cognitive performance.
- A highly diverse food may be associated with a reduced risk of AD.

INTRODUCTION

Alzheimer's disease is a chronic neurodegenerative disorder that impairs the brain's normal functioning. It is the most common cause of dementia in people aged 65 and over globally. The global prevalence and incidence of AD have been a growing public health concern, especially with the growth of the older population globally. The number of new and existing cases of AD and other dementia rose by 147.95% and 160.84%, respectively, from 1990 to 2019¹. The age-adjusted measures of occurrence, prevalence, mortality, and health burden of AD and other dementias increased steadily in both sexes over the period¹. The precise etiology of AD remains elusive, but it is supposed to be related to a combination of genetics

(such as mutations in the amyloid precursor protein), environmental (such as exposure to toxins), and lifestyle factors (such as poor diet)².

Epidemiological investigations propose that modifiable lifestyle factors, such as diet, may have a role in preserving brain and cognitive performance. It has been documented that the intake of certain foods, such as plant foods, and receiving a sufficient value of vitamins and minerals could be beneficial to reinforce cognitive function^{3,4}. In recent years, dietary behaviors have received attention from intensive research as a potential approach to improving brain function. Population-based evidence suggests that compliance with specific food patterns, for example, the Mediterranean diet, possibly has neuroprotection properties^{5,6}.

Dietary diversity (DD) is a qualitative indicator of food intake that represents household access to a range of foods and is also a surrogate for the nutrient sufficiency of an individual diet⁷. Diet quality is an index based on the alignment of the food pattern with the national dietary guidelines. This index helps to understand how close a food pattern is to the recommended guidelines, and a higher score indicates a higher quality⁸. Dietary diversity and quality have been linked to a range of favorable health outcomes, such as dropping the level of total cholesterol, triglycerides, blood pressure, and the risk of metabolic syndrome⁹⁻¹³. A recent study involving 6,737 participants aged between 30 and 60 years with over 11 years of follow-up found that the group with the highest and most stable dietary diversity had a significantly declined risk of all-cause death of 71.0%¹⁴. Robust adherence to a diverse and high-quality diet may confer protective effects against several diseases, including dementia, osteoarthritis, and cardiovascular disease¹⁵⁻¹⁷. In addition, recent evidence suggests a direct relationship between high diversity and quality diet and brain health¹⁸. Therefore, this investigation was performed to appraise the link between DD and dietary quality with cognitive performance and the risk of AD.

METHODS

Study population and procedure

This cross-sectional study includes 60 AD patients (the case group) selected from referrals to the neurology outpatient clinic and 29 healthy individuals (the control group) selected from referrals to public health centers for periodic health examinations. The inclusion criteria were

a positive diagnosis of AD by a neurologist in the case group, no medication use at the time of sampling in the control group, and an age range of 65 to 75 years. Exclusion criteria were adherence to a special diet and the presence of additional mental and neurological disorders. The ethical committee of Tabriz University of Medical Sciences, Tabriz, Iran, approved the study protocol (IR.TBZMED.REC.1400.299). All participating individuals provided informed written consent.

Anthropometric measurement

The participant's weight and height were measured by a digital scale and tape measure with 100 g and 1cm precision, respectively. The individuals' body mass index (BMI) was estimated based on weight (kg)/height (m²) formula. Waist circumference was calculated from the midpoint between the lower rib edge and the iliac crest, and the maximum buttock circumference was measured to obtain hip circumference.

Dietary assessment

Dietary data was collected with a three-day food record by a member of the participants' family who had received the necessary training.

Dietary quality and dietary diversity assessment

DD was calculated based on the standards set by the Food and Agriculture Organization (FAO). DD consists of 17 questions, each of which can be answered with either "yes" or "no". One point is given to each question with an answer of "yes" and no point is given to a question with an answer of "no". The total score can range from 0 to 17; a higher score represents a higher DD⁷.

The Healthy Eating Index 2015 (HEI-2105) and International Diet Quality Index (DQI-I) questionnaires were used to check dietary quality. The HEI-2015 includes 13 components, nine of which (whole grains; total fruit; whole fruit; dairy products; total vegetables; total protein foods; greens and beans; seafood and plant proteins; and fatty acids) evaluate the sufficiency of the food, and the other four (Sodium, refined grains, and saturated fats) need to be taken sparingly. Elements and overall HEI-2015 values were estimated for each food record, and then the mean value of the three records was acquired¹⁹.

DQI-I comprises four main components. The first is DD, with two indicators and a score ranging from 0 to 20 points. The overall diversity of the various food groups (fish and shellfish, meats and meat products, pulses and pulse products, eggs, milk and milk products, fruits, vegetables, and grains) and the diversity of protein sources within each group (fish and

shellfish, meats and meat products, pulses and pulse products, eggs, milk, and milk products). The adequacy component, with a score ranging from 0 to 40 points, assesses the amounts of grains, vegetables, fruits, fiber, protein, ferrous, calcium, and vitamin C. The third factor, with a score of 0 to 30, is moderation (total fat, saturated fat, cholesterol, sodium, and empty-calorie foods). The fourth factor is the overall balance (macronutrient and fatty acid ratio), with a score ranging from 0 to 10. The four elements listed above contribute to the final DQI-I score. The overall DQI-I score varies from 0 to 100. The DQI-I total score was used to group participants into tertiles. The final DQI score was categorized by Bowman et al. using the standards for a healthy population. In terms of quality, a score below 50 denotes a "poor" diet; a score between 50 and 80, a diet that "needs improvement"; and a score over 80, a "good diet," according to this study²⁰.

Cognitive performance measurement

The Mini-Mental State Examination (MMSE) tool was applied to examine the cognitive performance of patients. The test score range was 0–30. Patients with MMSE scores ranging from 21-30, 10-20, and <10 were known as mild, moderate, and severe cognitive decline, respectively²¹. Orientation, registration to time and place, visuospatial status, concentration/attention, language (naming, sentence writing, and comprehension), and recall were cognitive elements that were examined²¹.

Statistical analysis

General characteristics were compared between the two groups using Mann-Whitney and Chi-square tests as appropriate. Anthropometric indicators were compared using the independent sample t-test and dietary scores by the Mann-Whitney test or independent sample t-test between the two groups. A linear regression test was used to analyze the relationship between diet quality score and dietary diversity with the MMSE total score and its components. The odds ratio of AD was calculated according to dietary diversity and quality by binary logistic regression test. The SPSS 20 software (IBM SPSS statistics, IL, Chicago, USA) was used for data analysis. A p-value less than 0.05 (two-tailed) was considered statistically significant.

RESULTS

The study included 89 participants, comprising 60 patients (31 women and 29 men) with an average age of 73 years and 29 healthy adults (20 women and nine men) with an average age of 67 years, which was significantly lower than the AD group ($p= 0.03$). Disease duration of 65% ($n=30$) of AD patients was less than one year, 23% ($n=14$) between one to three years, and 11.7% ($n=7$) were over three years. According to the MMSE score, the cognitive impairment level of patients with AD was moderate in 65% ($n=39$), mild in 25% ($n=15$), and severe in 10% ($n=6$) of people. The two groups had no significant difference regarding sex, education level, and physical activity level ($p> 0.05$) (**Table 1**).

Table 1. General characteristics of the participants

Variables	Healthy (n=29)	AD (n=60)	p-value
Age (years)^a	67.00 (64.00, 75.00)	70.82 (62.00, 78.00)	0.03
Gender^b			0.12
Male	9 (31)	29 (48.3)	
Female	20 (69)	31 (51.7)	
Education^b			0.74
Low	27 (93.1)	56 (93.3)	
Medium	2 (6.9)	3 (5)	
High	-	1 (1.7)	
Physical activity^b			0.64
Low	16 (55.2)	35 (58.3)	
Medium	10 (34.5)	22 (36.7)	
High	3 (10.3)	3 (5.0)	
Disease duration ^b (year)	-		-
<1		39 (65.0)	
1-3		14 (23.3)	
>3		7 (11.7)	
Cognitive impairment level (MMSE score)^b	-		
Mild (20-24)		15 (25.0)	
Moderate (10-19)		39 (65.0)	
Sevier (<10)		6 (10.0)	

^a Data were reported as median (min, max), ^b Data were reported as frequency(percent)

AD: Alzheimer's Disease; MMSE: Mini-Mental State Examination, AD: Alzheimer's Disease

As presented in **Table 2**, a significantly lower BMI was observed in people with AD compared with healthy individuals ($p= 0.04$). Other anthropometric parameters were comparable between the two groups ($p> 0.05$).

Table 2. Findings related to anthropometric indicators

Variables	Healthy (n=29)	AD (n=60)	p-value
Weight (kg)	71.92 ± 10.44	67.25 ± 11.56	0.07
Height (cm)	158.65 ± 4.11	158.73 ± 9.39	0.96
BMI (kg/m²)	28.58 ± 4.08	26.67 ± 3.90	0.04
WC (cm)	100.72 ± 9.74	99.78 ± 12.24	0.72
HC (cm)	106.59 ± 10.09	105.73 ± 11.92	0.74

Data are reported as mean ± standard deviation. P-value is reported based on an independent sample t-test. AD: Alzheimer's Disease, WC: Waist Circumference, HC: Hip Circumstance.

As shown in **Table 3**, the DD score was significantly lower in the AD group than in the healthy group ($p < 0.001$). However, there was no significant difference concerning the HEI and DQI scores between AD and healthy groups ($p > 0.05$).

Table 3. Comparison of dietary diversity and quality (HEI and DQI) scores between AD patients and healthy individuals

	Healthy (n=29)	AD (n=60)	p
Dietary diversity^a	12.00 (2)	10.00 (2)	<0.001
HEI^b	49.86 ± 7.39	50.07 ± 6.52	0.89
DQI^a	66.00 (8)	67.00 (8)	0.66

^aData was presented as median (interquartile range). ^bData was reported as mean ± standard deviation. AD: Alzheimer's disease; HEI: Healthy Eating Index; DQI: Dietary Quality Index

As shown in **Table 4**, there was a significant relationship between DD score with total MMSE score ($\beta = 0.33$, $p = 0.02$), memory ($\beta = 0.35$, $p = 0.02$), and language ($\beta = 0.32$, $p = 0.03$). There was a significant correlation between HEI and the calculation domain of cognitive status ($\beta = 0.32$, $p = 0.02$). DQI score was not correlated with MMSE total score and cognitive functioning domains ($p > 0.05$) (Table 4).

As shown in **Table 5**, adherence to high DD reduced the odds of AD by 77% (OR: 0.23; 95% CI: 0.12, 0.44; $p < 0.001$) in the crude model and 79% (OR: 0.21; 95% CI: 0.10, 0.42; $p < 0.001$) in the multivariate model.

Table 4. Correlation between dietary diversity and quality (DQI, HEI) with cognitive status in patients with AD (n=60)

	HEI		DQI		Dietary diversity	
	β	p	β	p	β	p
Orientation	0.15	0.31	0.09	0.56	0.28	0.06
Registration	-0.06	0.68	0.03	0.81	0.05	0.74
Calculation	0.32	0.02	-0.03	0.84	0.16	0.26
Memory	-0.05	0.72	-0.01	0.97	0.35	0.02
Language	0.11	0.45	0.14	0.33	0.32	0.03
Visuospatial	0.25	0.08	0.14	0.30	0.16	0.26
Total MMSE	0.16	0.28	0.09	0.54	0.33	0.02

AD: Alzheimer's disease; HEI: Healthy Eating Index, DQI: Dietary Quality Index; MMSE: Mini-Mental State Examination. Covariates considered: age, gender, BMI, and disease duration.

Table 5. Correlation between dietary diversity and quality (DQI, HEI) with Odds of Alzheimer's disease

	Univariate		Multivariate	
	Odds ratio (CI)	p	Odds ratio (CI)	p
Dietary diversity	0.23 (0.12, 0.44)	<0.001	0.21 (0.10, 0.42)	<0.001
DQI	0.97 (0.90, 1.05)	0.51	0.98 (0.89, 1.07)	0.61
HEI	1.00 (0.94, 1.07)	0.89	1.01 (0.94, 1.09)	0.71

Covariates considered: age, gender, and BMI. HEI: Healthy Eating Index; DQI: Dietary Quality Index

DISCUSSION

The present investigation provides evidence that higher DD improves cognitive functioning and reduces the odds of AD in the clinically diagnosed AD population. This association remained after controlling for potential confounding variables. In line with our findings, Zhang et al., in a study of adults over 50 years old in China, found a link between high DD and better cognitive status²². Also, Zheng et al., in a long-lasting prospective study on 11,970 individuals over the age of 80 years, concluded that high DD might be beneficial in reducing age-related cognitive decline even in the oldest-old²³. A diet with high DD includes a wide variety of food types²⁴, and consumption of various nutrients in the form of a complex combination in a diet, as opposed to single nutrient consumption, can improve cognitive health. Previous research has shown that bioactive components such as vitamin D, B vitamins, antioxidant vitamins, selenium, long-chain omega-3 fatty acids, and medium-chain triglycerides are useful for

maintaining cognitive health^{24,25}. The positive impact of high DD on cognitive status may also be attributed to the synergistic effect of these nutrients.

According to our findings, the dietary quality of patients was not correlated with cognitive performance and the risk of AD. In agreement with our results, Haring et al., in a study of 6425 women aged 65 to 79 in Germany, found no relationship between dietary quality and cognitive improvement²⁶. Furthermore, a study in the United States on individuals with an average age of 73 years found no correlation between dietary quality and cognitive status²⁷. However, several studies reported that a high-quality diet was connected to improved cognitive status^{28,29}. There could be several causes for inconsistent results across the studies. Differences in sample size, measurement instrument for the cognitive status, age of the participants, and method of dietary intake and quality assessment may explain the disparity among the studies.

The neuroprotective effect of a high-quality and healthy diet has already been confirmed through multiple investigations. A recent Meta-analysis of observational cohort studies concluded that adherence to a diet with high quality may reduce or retard the risk of neurodegenerative diseases³⁰. Vega-Cabello et al., in a prospective cohort study, showed that following a high-quality and healthy diet may reduce the rate of total chronic conditions and neuropsychiatric and neurodegenerative conditions³¹. In addition, Hossain et al. found that a high-quality diet was longitudinally related to a slower decline in verbal memory among women with a greater risk of AD³². Kheirouri et al., in a systematic review study, reported that compliance with the MIND [Mediterranean-DASH (Dietary Approaches to Stop Hypertension) Intervention for Neurodegenerative Delay] diet as a healthy dietary pattern may improve cognitive performance in older adults⁶.

The exact neuroprotective mechanism of a high-quality and healthy diet against neurodegenerative diseases remains unclear. However, aggregation of β -amyloid in the brain, neuroinflammation, and oxidative stress are several mechanisms that are thought to be involved in neurodegeneration^{33,34}. The high-quality and healthy diets emphasize the consumption of diverse food items, including vegetables and fruits, which are rich in phytochemical compounds. Emerging evidence has proposed a high intake of phytochemicals holds promise in preventing neurodegenerative diseases³⁵. Phytochemicals can diminish oxidative stress by raising antioxidant enzymes and decreasing nitric oxide, inducible nitric

oxide synthase, and cyclooxygenase 2³⁵. Furthermore, phytochemicals play a role in reducing inflammation by modulating microglial activation and NF- κ B (nuclear factor kappa B) signaling³⁵. Additionally, they contribute to lowering amyloid plaque formation and reducing tau hyperphosphorylation³⁵. All the pathways in the subsequent lead to the prevention of AD.

Strengths and limitations of the study

Recruiting the clinically diagnosed AD population, the adjustment of many potential confounding factors; the use of more than one tool to evaluate the quality of the diet; and the use of a 3-day food record to examine the participants' diet, which provides sufficient details about the consumption of some key nutrients due to its high accuracy, were strengths of the present study. The small sample size of participants restricted the generalizability of findings. Using just an MMSE qualitative tool to examine patients' cognitive condition may not provide a comprehensive understanding. Moreover, a cross-sectional design of the study may not reveal a cause-effect relationship between the studied variables.

Suggestions for future research

Future investigations are required to explore the association of a highly diverse diet-phytochemicals-cognition or -risk of neurodegenerative diseases. The influence of dietary diversity on neurotransmitters contributed to cognition, brain structure, biomarkers of AD such as β -amyloid, inflammation, and oxidative stress remains unknown and needs to be investigated.

CONCLUSIONS

The findings demonstrate that a higher DD may improve cognitive functioning and reduce the odds of AD.

COMPETING INTERESTS

No potential conflict of interest relevant to this article was reported.

AUTHORS' CONTRIBUTION

S.K. was involved in the conception and design of the study, in the analysis and interpretation of the results, and writing and revising the manuscript. A.Z. participated in analyzing the data. F.V. was involved in sampling. A.T. participated in the diagnosis of AD patients. All authors reviewed the results and approved the final version of the manuscript.

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