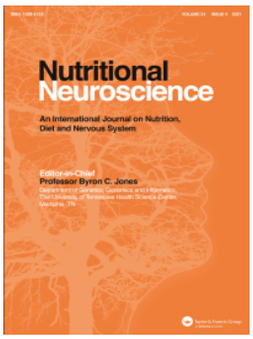

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Association of level of adherence to Mediterranean diet with cognitive and dementia status in subjects with chronic diseases: a cross-sectional study

Abeer Al Hatab [a], Kishore Ganana Sam [a], Semira Abdi Beshir [a], Asim Ahmed Elnour [b,c], Nadia Al Mazrouei [d], Khalid Awad Al-Kubaisi [e], Maisoun Alkaabi [f], Abdulla Al Amoodi [g], Vineetha Menon [h], Abuelnor Mohammed [i,j] and Sami Fatehi Abdalla [k]

[a]Department of Clinical Pharmacy and Pharmacotherapeutics, Dubai Pharmacy College for Girls, Dubai, United Arab Emirates (UAE); [b]Clinical Pharmacy Program, College of Pharmacy, Al Ain University, Abu Dhabi, United Arab Emirates; [c]AAU Health and Biomedical Research Center, Al Ain University, Abu Dhabi, United Arab Emirates; [d]Department of Pharmacy Practice and Pharmacotherapeutics, Faculty of Pharmacy, University of Sharjah, Sharjah, United Arab Emirates; [e]Department of Pharmacy Practice and Pharmacotherapeutics, College of Pharmacy-University of Sharjah, Sharjah, United Arab Emirates; [f]General Manager, New Medical Center (NMC) Royal Women's Hospital, Abu Dhabi, UAE; [g]Ambulatory Healthcare Services, Academic Affairs, Abu Dhabi Health Services (SEHA), Abu Dhabi, UAE; [h]Department of Pharmacy Practice, College of Pharmacy, Gulf Medical University, Ajman, UAE; [i]Department of Basic Medical Sciences, College of Medicine, Dar Al Uloom University, Riyadh, Saudi Arabia; [j]Department of Histology and Embryology, School of Basic Medical Sciences, Tongji Medical College, Huazhong University of Science and Technology Wuhan, People's Republic of China; [k]Clinical Department, College of Medicine, University of Almaarefa, Riyadh, Saudi Arabia

ABSTRACT

Background: The Mediterranean diet has been linked to brain neuroprotection. Evidence from meta-analyses showed reduced risk of dementia with greater intake of vegetables and fruits, fish, and the Mediterranean diet. The current study raises important questions about the association between low risk dementia and Mediterranean diet.

Objective: The objective was to evaluate the association between levels of adherence to the Mediterranean diet and dementia and cognitive status in subjects 50 years of age and older.

Method: The Mediterranean Diet Adherence Screener (MEDAS), the modified 30-item 'Diagnostic and Statistical Manual of Mental Disorders Third Edition (DSM-III) risk of dementia, and the Standard Mini-Mental Status Examination (SMMSE) cognitive status scores were used to assess the levels of adherence to the Mediterranean diet'.

Results: A total of 150 subjects were enrolled in the study. Forty-one (27.3%) had 'suspected or confirmed dementia, while 48 individuals (32%) were categorized as having moderate to severe cognitive decline. Subjects who reported moderate to high adherence to the Mediterranean diet (55, 36.7%) had significantly lower dementia scores (7.0 3.8 versus 17.6 5.1) and higher cognitive (25.4 3.8 versus 8.6 7.2) scores compared to those (38, 25.3%) who reported low adherence to the Mediterranean diet.

Conclusion: Subjects who were highly or moderately adherent to the Mediterranean diet had significantly lower dementia scores and better cognitive status than those with low adherence.

KEYWORDS
Adherence; cerebrovascular disease; cognitive decline; dementia; dementia protection; Mediterranean diet; stroke; Nutrition

Background

With the increasing aging population, the incidence of dementia and other cognitive disorders is also escalating. Cognitive disorders are the main cause of dementia, which has a clinical, social, humanistic, and economic burden. A report by the World Health Organization (WHO) illustrates that the number of confirmed dementia cases worldwide [1] is around 55 million and is expected to rise to 139 million by 2050 [2]. The social burden of dementia is increasing due to the delay in diagnosis and cumbersome procedures to differentiate between the stages of cognitive impairment and the disease's progression [3]. On the contrary, the incidence of dementia is decreasing in some countries [4], and that is probably because of advanced standards of education, the healthcare system, a healthy lifestyle, and healthy nutrition. Risk factors for neurological disorders such as low education, smoking, obesity, depression, diabetes, hypertension, hearing impairment, low social activity, excessive alcohol consumption, traumatic brain injury (TBI), and air pollution can play a significant role in dementia pathogenesis [4]. Reports show that people living in Mediterranean countries have fewer incidences of dementia cases when compared to other Western

CONTACT Kishore Ganana Sam dr.kishore@dpc.edu Department of Clinical Pharmacy and Pharmacotherapeutics, Dubai Pharmacy College for Girls, Dubai, United Arab Emirates

countries, such as the United States of America (USA) [5]. Physical activities and adopting healthy diets are modifiable risk factors that might contribute to reducing the risk of dementia and delaying the progression of cognitive decline in subjects at high risk. Reports have shown an association between adherence to anti-inflammatory diet patterns like the Mediterranean diet (MD) and a reduction in the risk of developing dementia. This is attributed to the antioxidant-rich diet, which decreases the neuroinflammatory process and can delay neurodegenerative progression [6]. MD is reported to benefit subjects with cardiovascular and cerebrovascular diseases (stroke), but its role in neurocognitive dysfunction is rarely reported [7]. Intake of the MD, which is one of the anti-inflammatory diets, can have a positive effect and neuroprotective properties on the brain. Therefore, there is a need to assess the association between levels of adherence to MD and dementia and the cognitive status of subjects at risk of developing cognitive disorders.

Ethics approval

The ethics committee, Dubai Scientific Research Ethics Committee (DSREC) at Dubai Health Authority (DHA) in Dubai-UAE, dated February 9, 2022, approved the research proposal under the number DSREC-SR-02/2022_05.

Method

The current research is a cross-sectional study conducted in two healthcare facilities: a long-term care hospital and a senior happiness center in Dubai, UAE. The study population was subjects aged 50 years and older with a history of cerebrovascular, cardiovascular, endocrine, and/or neurological disorders. The subjects were identified from the daily admission records of the study hospital. The medical records were reviewed to identify the subjects, and a convenient sampling technique was used for the sampling frame. The inclusion and exclusion criteria were subjects 50 years of age or older with a history of chronic diseases who were willing to participate and gave consent (random enrollment). However, healthy adults, subjects with electrolyte imbalance, unconscious subjects with low Glasgow Coma Scale (GCS), respiratory distress, poisoning, renal azotemia on dialysis, any other severe exacerbation of respiratory illness, and substance abuse were excluded from the study. We have used a convenient sample for sample size calculation [8].

Research tools

Modified 30-item 'Diagnostic and Statistical Manual of Mental Disorders Third Edition (DSM-III) questionnaires (Kawas C. 1994)', 'Standard Mini-Mental Status Examination' (SMMSE) tools, and 'Mediterranean Diet Adherence Screener' (MEDAS) questionnaire scales were used to assess the status of dementia, cognition, and adherence to the Mediterranean diet, respectively. Informed consent was obtained before administering the three questionnaires. The original DSM III questionnaire consists of 49 questions, out of which 30 were adopted in the current study (due to repeated questions and duplication between the three instruments) after a discussion to suit the study objectives and the social context of the target population. The maximum possible score for the DSM III questionnaire is 30 points. Subjects were grouped into three categories: 'normal mental status', 'suspected dementia,' or 'confirmed dementia' if the scores attained were less than or equal to 12 points, 13–20 points, or 21–30 points, respectively. The SMMSE tool used to estimate the level of cognition was adopted for routine use by the Independent Hospital Pricing Authority of Australia and worldwide (Hospital Pricing Authority 2014). The questionnaire includes domains of cognitive functions, orientation, registration, short-term memory, language use, comprehension, and basic motor skills. The maximum expected score for this tool is 30. Based on the score, the subjects were grouped into four categories: 'normal cognitive function', 'mild/early cognitive decline' 'moderate cognitive decline' or 'severe cognitive decline', if they scored a sum of 25–30 points, 21–24 points, 10–20 points, or 0–9 points, respectively. The MEDAS questionnaire was officially adopted as a domain in the Food Frequency Questionnaire (FFQ) [9]. The MEDAS tool was previously validated in Spain and recently used in other countries, such as Germany [10]. The MEDAS questionnaire consists of 14 items. The maximum expected score for MEDAS is 14 points. Based on the sum of the scores obtained, the subjects were grouped into three categories: 'strong/high adherence,' 'moderate adherence,' or 'poor adherence' if they scored more than or equal to 10 points, 6–9 points, or equal to or less than 5 points, respectively [9]. All three tools were adopted after email communications were sent to the corresponding authors to obtain permission. Following the permission responses, the questionnaires were reviewed and checked for content validity by three faculty experts from the pharmacy college. Based on the comments obtained from subject experts and subsequent discussions, some of the questions were either modified or removed to suit the social context. Each questionnaire was first translated by the investigator from the English language into the Arabic language (forward and backward technique), and the translation was validated by three clinical experts in the field.

A pilot study was conducted among 40 subjects to evaluate the reliability of the three questionnaire tools. The Cronbach alpha tests were repeated after editing the questionnaire until a final acceptable target value of 0.89 (good), 0.939 (excellent), and 0.615 (acceptable) was obtained for all the DSM, SMMSE, and MEDAS questionnaire tools, respectively.

The tools were administered by the investigators through a direct face-to-face interview in the subjects' preferred language. In addition to the direct interview, the patient's medical records and all lab reports or radiological reports of CT scans, MRIs, and X-ray images of the brain were carefully reviewed to evaluate their mental and cognitive status. MRI or CT scans are the most common type of brain scan used in dementia diagnosis and are useful for ruling out other conditions that cause similar symptoms to dementia and at showing changes to brain structure that occur in Alzheimer's. Both scans type can show stroke related damage, brain shrinkage (atrophy) and blood vessel changes seen in dementia, signs of a brain tumor, and build-up of fluid or blood in the brain. Other modalities used such as Single-photon emission computerized tomography (SPECT) imaging can provide true 3D images (MRI or CT scan tend to produce 2D images of the brain). SPECT study the flow of blood throughout the brain (each type of dementia is associated with different patterns of blood flow and distinguish between types). SPECT permit the diagnose ad which disease is causing dementia and tailor treatment.

Positron emission tomography (PET) scans is used to detect specific molecules in the brain (more commonly used in research than for diagnosis) to produce an image of where the target molecules are by detecting the dyes. PET scans are used to show abnormal build-up of proteins that cause Alzheimer's, how much glucose is present in the brain, and to view brain activity. The investigators received structured training by the expert consultant psychiatrist on how to use the DSM-III questionnaire in a direct patient interview. The three instruments were usually used and adopted in routine psychiatric clinical practice. The main outcome measure was the association between level of adherence to the MD and dementia or cognitive status, defined as low, moderate, and high levels.

Data analysis

Descriptive statistics were used to summarize the demographic characteristics of the subjects. Continuous variables are summarized as the mean standard deviation (SD). The chi-square test was used to describe the association between demographical variables and the incidence of dementia, cognitive status, and MEDAS adherence categories. The Independent Student *t*-test and ANOVA were used to compare the mean DSM, SMMSE scores, and MEDAS scores between two groups and three groups, respectively. A relative risk was estimated. The data were analyzed using SPSS version 26 software.

Results

A total of 150 subjects were randomly enrolled in this study, which included a preponderance of males (82, 54.67%). Most respondents (93, 62%) were aged 66 years or older. There were a total of 45 (or 30%) in the age groups of 56–65 years, while only 12 (or 8.0%) were aged 55 years or less. Slightly less than half (69, 46%) of the respondents were UAE nationals, while the rest were mixed nationalities from Asia, Africa, and Western countries [Table 1]. The incidence of suspected or confirmed dementia was higher among females compared to males. There was no significant association between the demographic characteristics and the dementia categories. The proportion of subjects with moderate to severe cognitive dysfunction was higher among males. Subjects aged 66 years or older had a higher relative risk of dementia (RR = 1.48) and cognitive decline (RR = 1.49) compared to those in the younger age groups. However, the differences were not statistically significant.

The majority (112, or 74.7%) of the respondents reported moderate to high adherence to MD. More than two-thirds of males (58, 70.7%) reported moderate to high adherence compared to females (54, 48.2%). More than half of the respondents ($n = 68$, 60.7%) aged equal to or above 66 years reported moderate to strong adherence to the MD compared to the younger age groups. Subjects from Asia had a higher proportion of subjects with moderate to strong MD adherence ($n =$

Table 1. Demographical characteristics of patients enrolled in the study.

Demographical Variable	Frequency $N = 150$	Percentage %
Gender		
Male	82	54.7
Female	68	45.3
Age		
$\leq$ 55 yrs.	12	8.0
(56–65) yrs.	45	30.0
$\geq$ 66 yrs.	93	62.0
Geographical demography		
UAE	69	46.0
Asia	66	44.0
Europe	4	2.7
Africa	10	6.7
USA and Canada	1	0.7
Total	150	100

Table 2. Association of demographic characteristics with DSM, SMMSE and MEDAS categories.

	DSM score categories			SMMSE score categories				MEDAS categories		
Demographic Variable	No Dementia (<12) *N* = 109 (%)	Suspected Dementia (13–20) *N* = 25 (%)	Confirmed Dementia (21–30) *N* = 16 (%)	Normal (25–30) *N* = 76 (%)	Mild (21–24) *N* = 26 (%)	Moderate (10–20) *N* = 27 (%)	Severe (0–9) *N* = 21 (%)	Poor adherence (≤ 5) *N* = 38 (%)	Moderate adherence (6–9) *N* = 57 (%)	Strong adherence (≥ 10) *N* = 55 (%)
Gender:										
Male *N* = 82	62 (75.6)	11 (13.4)	9 (11)	46 (56.1)	8 (9.8)	15 (18.3)	13 (15.9)	24 (29.3)	30 (36.6)	28 (34.2)
Female *N* = 68	47 (69.1)	14 (20.6)	7 (10.3)	30 (44.1)	18 (26.5)	12 (17.6)	8 (11.8)	14 (20.6)	27 (39.7)	27 (39.7)
Age:										
≤ 55 yrs. (*n* = 12)	10 (83.3)	2 (16.7)	0	8 (66.7)	3 (25)	1 (8.3)	0	1 (8.3)	8 (66.7)	3 (25)
(56- 65) yrs. (*n* = 45)	35 (77.8)	5 (11.1)	5 (11.1)	24 (53.3)	8 (17.8)	7 (15.6)	6 (13.3)	12 (26.7)	21(26.7)	12 (26.7)
≥ 66 yrs. (*n* = 93)	64 (68.8)	18 (19.4)	11 (11.8)	44 (47.3)	15 (16.1)	19 (20.4)	15(16.1)	25 (26.9)	28 (30.1)	40 (43)
Nationality:										
UAE *N* = 69	43 (62.3)	13 (18.8)	13 (18.8)	29 (42.0)	12 (17.4)	15 (21.7)	13 (18.8)	21 (30.4)	21 (30.4)	27 (39.1)
Asia *N* = 66	53 (80.3)	10 (15.2)	3 (4.5)	37 (56.1)	12 (18.2)	12 (18.2)	5 (7.6)	13 (19.7)	32 (48.5)	21(31.8)
Africa *N* = 10	9 (90)	1 (10)	0	7 (70)	2 (50)	0	1 (10)	2 (20)	3 (30)	5 (50)
Europe *N* = 4	3 (75)	1 (25)	0	3 (75)	0	0	1 (25)	1(25)	1 (25)	2 (50)
USA *N* = 1	1 (100)	0	0	0	0	0	1 (100)	1(100)	0	0

Keys: DSM-III: Modified 30 item 'Diagnostic and Statistical Manual of Mental Disorders Third edition; **MEDAS**: Mediterranean Diet Adherence Screener; **SMMSE**: Standard Mini-Mental Status Examination. *All demographic characteristics were not significantly associated with DSM, SMMSE, and MEDAS categories.

53, 47.3%) compared to those from the UAE (*n* = 48, 42.9%) or other countries (*n* = 11, 9.8%). However, among demographic characteristics, only the age group category was associated with the level of adherence to the MD [Table 2]. Subjects who had moderate to high adherence to the MD (112, 74.7%) had significantly lower risk for dementia (7.0 + 3.8) and cognitive decline (25.4 + 3.8) compared to those (38, 25.3%) who had poor adherence (17.6 + 5.1 and 8.6 + 7.2), respectively [Table 3]. The comparison of DSM, SMMSE, and MEDAS scores with comorbid diseases has revealed that subjects with hypertension, diabetes, depression, stroke, Parkinson disease, and seizures with moderate and high adherence had better DSM and SMMSE scores compared to those with similar comorbidities with poor adherence to MD. [Table 4]. The subjects were receiving medications for cerebrovascular, cardiovascular, endocrine, and/or neurological disorders. Indicating that some subjects were receiving regular medications that might have affected their cognition.

Table 3. Comparison of Mediterranean-diet adherence with DSM and SMMSE scores.

MEDAS adherence level (%)	DSM score (Dementia severity) (Mean ± SD)	SMMSE score (Cognitive function) (Mean ± SD)
Poor adherence ≤ 5 38 (25.3)	17.63 ± 5.101*	8.61 ± 7.15*
Moderate adherence (6–9) 57 (38.0)	7.44 ± 4.38*	23.95 ± 4.38*
High adherence ≥10 55 (36.7)	6.64 ± 2.96*	26.96 ± 2.39*
*$P < 0.001$	Mean scores 9.73 ± 6.19	Mean scores 21.17 ± 8.81

Keys: *$P < 0.001$ significant difference of mean scores between the three MEDAS adherence levels.

Discussion

The current cross-sectional study was conducted to assess the association between the level of adherence to MD and dementia and cognitive status in subjects 50 years of age or older. The main finding of the current study indicated that the assessment of gender differences in dementia scores (DSM) illustrated that the incidence of suspected to confirmed dementia was similar between females and males. Further, a higher proportion of males had moderate to severe cognitive dysfunction as compared to females. Our sample subjects of

Table 4. Mean DSM, SMMSE and MEDAS score according to different comorbidities.

Comorbid disease	DSM Mean ± SD	SMMSE Mean ± SD	MEDAS Mean ± SD
Hypertension			
n = 124 (82.7%)	10.1 ± 6.3	20.91 ± 8.8	7.86 ± 2.6
Diabetes mellitus			
n = 90 (60%)	10 ± 5.8	21.2 ± 8.4	8.1± 2.6
Primary Stroke			
n = 79 (52.7%)	10.6 ± 6.7*	19.9 ± 9.2	7.4 ± 2.5
Secondary Stroke (>1stroke)			
n = 23(15.3%)	14.7 ± 6.2	15.4 ± 9.0	7.1 ± 2.6
Parkinsonism			
n = 52 (34.7%)	13.3 ± 6.8*	17.6 ± 10.6*	7.5 ± 2.7
Seizures			
n = 8 (5.3%)	19.5 ± 5.1	12.5 ± 11.9	6.6 ± 2.3
Depression			
n = 47 (31.3%)	14.5 ± 6.0*	16.8 ± 11.0*	7.1 ± 2.8

Keys: *Significance difference in mean scores with moderate to high adherence.

UAE nationality had worse DSM and SMMSE scores compared to the others from different nationalities. In addition, subjects with moderate and strong adherence to MD had significantly lower DSM scores and higher SMMSE scores when compared to those with poor adherence to MD.

A narrative review reported by Rocca et al. [11], however, reported that European females in the Mayo Clinic, USA, were more likely to have dementia or Alzheimer's disease (AD) than the males. This demographic difference is attributed to the neuroprotection of estrogen, which may be declining during menopause [11]. A study by Chene and colleagues [12], on the other hand, reported a significant association between gender and dementia incidence in the mid-age group. They explained that anatomical differences such as thinner gray matter and cortical thickness, as well as the smaller brain size and volume in women compared to men, contribute to the differences [12]. A study by Bhalla et al. [13] suggested that vitamin D deficiency is another possible reason why females have a higher risk of developing dementia at advanced ages. Other studies also report that moderate to severe vitamin D deficiency is strongly associated with the risk of dementia and AD [14]. A similar study has reported that women are more affected by dementia (61%) than men (39%), likely attributed to women living longer than men, which could increase their risk of developing dementia and Alzheimer's disease [15].

On the contrary, a higher proportion of males had moderate to severe cognitive dysfunction as compared to females. The supportive argument for our present study was proposed by one study [12]. The author of the later study reported a higher prevalence and incidence of mild cognitive impairment (MCI) among men than in women, which was inconsistent with the higher incidence of dementia reported elsewhere among women [12]. The age distribution of dementia showed that suspected or severe dementia was more frequent in the age group equal to or above 66 years compared to the subjects of the younger age groups, though the difference was not statistically significant. A previous study reported a good correlation between age and the incidence of dementia, which was very common among those in advanced ages above 65 years, and the incidence increased above 90 years [16].

Our sample subjects with UAE nationality had worse DSM and SMMSE scores compared to the other subjects of other nationalities. Previous studies evaluating the incidence of dementia in the Middle East and North Africa (MENA) region showed that the prevalence of dementia in Qatar was 30.5% and the incidence was lower compared to those in the same age group (>65) in the UAE. A higher proportion of male, elderly, and Asian subjects reported moderate to strong adherence than females, younger people, and other nationalities, respectively. Where in the present study or else, if else, need reference.

People with good adherence had a lower risk for dementia and a better cognitive status compared to those with poor adherence. A previous study reported that using MD can reduce the risk of cognitive decline in the elderly, especially those with chronic diseases or neurological disorders. MD is rich in vitamins, natural antioxidant components, and non-hydrated unsaturated fats like olive oil [17]. The antioxidant properties of MD are responsible for providing a significant anti-inflammatory effect and thus protecting the brain from neurological diseases and dementia progression. It was observed that subjects with comorbid diseases who were strongly adherent to the MD had a lower incidence of dementia and lower cognitive decline scores when compared to those who were poorly adherent. Hypertensive subjects with moderate and strong adherence had significantly lower DSM and higher SMMSE scores compared to those with poor adherence. A previous study conducted in Spain by Razquin and coworkers reported that hypertension has a negative impact on cognitive functions and could be alleviated by moderate to high adherence to the MD [18].

A similar trend of significantly lower DSM scores and higher SMMSE scores was observed among diabetic subjects with better levels of adherence to MD. Georgoulis and associates reported that adherence to MD has health benefits in decreasing cardiovascular diseases, cancer, and type 2 diabetes mellitus [19]. Another study conducted in Boston and Puerto Rico revealed that diabetic adult subjects with high adherence to MD had better improvement in cognitive functions, especially in those under adequate glycemic control [20].

Subjects with depression and moderate to strong adherence had significantly lower DSM scores and higher SMMSE scores as compared to those with poor MD adherence. A study by Canton-Habas and colleagues illustrated that elderly subjects with a history of depression had a more than 50% risk of developing neurodegenerative diseases like dementia or AD in advanced ages, which may be due to the progressive accumulation of amyloid and tau proteins [3]. A study conducted in Sweden also showed that women with strong adherence to the MD during their middle years had a reduced risk of depression in their later lives [21]. A meta-analysis by Shafiei et al. [22] reported that there is no significant association between adherence to MD and the risk of depression. A study by

Ihle-Hansen and associates in Norway showed that 57% of subjects in the geriatric department who had the first incidence of stroke suffered from cognitive impairment after one year of having the stroke [23].

In the present study, subjects with secondary stroke revealed a higher risk of dementia than those without stroke (increases the odds). This has been supported by an earlier review of nine studies [24]. In addition, subjects with moderate and strong adherence to MD had significantly lower DSM scores and higher SMMSE scores when compared to subjects with poor adherence to MD. A study in the USA reported that strong adherence to the MD and DASH diets was associated with slower cognitive deterioration after a history of stroke incidence [25]. Similar results were observed among subjects with Parkinson's symptoms. These results correspond with a previous study conducted in Italy that reported a higher prevalence of dementia among subjects with Parkinson's disease compared with general people [26]. Similarly, a study in Iran showed subjects with Parkinson's disease who were adherent to MD had a better cognitive score compared to the control group [27].

Subjects who had a history of seizures had a higher DSM mean score and significantly lower SMMSE scores compared to those without a history of seizures, while those with moderate to strong adherence had significantly lower DSM scores and significantly higher SMMSE scores, indicating that subjects with strong MD adherence had a lower cognitive decline compared to those with poor adherence. A study by Turkey Kaner and associates that included 85 children with a history of epilepsy reported that most of the children were moderately adherent to MD. However, the study reports that there was no significant association between adherence to MD and the incidence of seizures [28].

Future prospects

Recently, there are epidemiological and clinical researches that explored the protective effects of dairy product intake against dementia and cognitive decline which may pave the development of new approaches for the prevention of dementia. Oleamide and dehydroergosterol were agents for these protective effects of dairy products [6,29,30].

Limitations

Though the current study is the first to give insight on MD diet adherence, cognitive status, and dementia status of subjects at risk of developing cognitive disorders in the UAE and their interrelationship, it has a few limitations. Firstly, due to our limited sample size, our results might not be generalized to all elderly populations. Secondly, the influence of the severity and duration of comorbid diseases, medications taken, and their impact on cognitive status or dementia score were not evaluated. Thirdly, the modified versions of instruments used to assess dementia, cognitive status, or MD adherence considering the local scenario.

Conclusion

Nearly one-third of the subjects had moderate to severe cognitive decline and suspected or confirmed dementia, and almost two-thirds were moderate to strong adherents to MD. The adherents to MD had significantly better dementia and cognitive status compared to those subjects with poor adherence. Prospective case–control studies, cohort studies, or randomized clinical trials with a larger sample size or with a longer duration are recommended to prove the causal relationship.

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Author contribution

All of the authors were responsible for the study concept, design, acquisition and analysis of observed data, have contributed equally to the preparation whole manuscript, literature review, developing and proof reading. All authors have approved the manuscript and its submission to the journal. The authors have not published or submitted any related papers from the same study. This article is not under consideration or submission for any other journals.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Data availability statement

The data from this study was not made public.

Submission statement

The paper not been submitted elsewhere in similar form.

Notes on contributors

Abeer Al Hatab (M. Pharm), is a known Pharmacist, Department of Clinical Pharmacy and Pharmacotherapeutics; Dubai Pharmacy College; Dubai-United Arab Emirates (UAE).

Kishore Ganana Sam (Ph.D), is a professor at the Department of Clinical Pharmacy and Pharmacotherapeutics; Dubai Pharmacy College; Dubai- United Arab Emirates (UAE).

Semira Abdi Beshir (Ph.D), is a known Professor at the Department of Clinical Pharmacy and Pharmacotherapeutics; Dubai Pharmacy College for Girls; Dubai- United Arab Emirates (UAE).

Asim Ahmed Elnour (PhD, MSc), is a known Professor at the Clinical Pharmacy Program, College of Pharmacy, Al Ain University, Abu Dhabi campus, Abu Dhabi-United Arab Emirates. AAU Health and Biomedical Research Center, Al Ain University, Abu Dhabi, United Arab Emirates.

Nadia Al Mazrouei is a known Professor at the Department of Pharmacy Practice and Pharmacotherapeutics, Faculty of Pharmacy, University of Sharjah, United Arab Emirates.

Khalid Awad Al-Kubaisi, is a known Professor at the Department of Pharmacy Practice and Pharmacotherapeutics, College of Pharmacy-University of Sharjah, United Arab Emirates.

Maisoun Alkaabi is a known Chief Executive Officer at the New Medical Center (NMC) Royal Women's Hospital, Abu Dhabi, UAE.

Abdulla Al Amoodi, is a known Specialist of family Medicine, Ambulatory Healthcare Services, Academic Affairs, Abu Dhabi Health Services (SEHA), UAE.

Vineetha Menon, B.Pharm, Pharm.D, PGDPv, Ph.D. is a known Assistant Professor at the Department of Pharmacy Practice, College of Pharmacy, Gulf Medical University-UAE.

Abuelnor Mohammed, Ph.D., Peng Ting Ph.D. is a known Professor at the Department of Basic Medical Sciences, College of Medicine, Dar Al Uloom University, Riyadh, KSA.

Sami Fatehi Abdalla, is a known Professor at the Clinical Department, College of Medicine, University of Almaarefa-Dirriyah, Riyadh, Saudi Arabia.

ORCID

Abeer Al Hatab http://orcid.org/0000-0003-2720-6239
Kishore Ganana Sam http://orcid.org/0000-0001-6537-2786
Semira Abdi Beshir http://orcid.org/0000-0003-4990-4783
Asim Ahmed Elnour http://orcid.org/0000-0002-4143-7810
Nadia Al Mazrouei http://orcid.org/0000-0002-1339-9730
Khalid Awad Al-Kubaisi http://orcid.org/0000-0002-4260-1117
Maisoun Alkaabi http://orcid.org/0009-0009-0013-4221
Abdulla Al Amoodi http://orcid.org/0000-0001-5248-9598
Vineetha Menon http://orcid.org/0000-0002-2030-0962
Abuelnor Mohammed http://orcid.org/0000-0003-4435-3791
Sami Fatehi Abdalla http://orcid.org/0000-0002-7396-8376

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